Biochemical Engineering

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Module No. 01

Lecture No. 11

Regulation of Enzyme Activity: Inhibition (Contd.)

Lecture on Regulation of Enzyme Activity through Inhibition. In the previous lectures, we talked about different kinds of inhibition competitive, uncompetitive, non competitive, substrate and so on. And we also discussed why we need inhibition, which is to regulate the amount of enzyme that is produced, so that other biochemical pathways are non disturbed, so that the energy required for the product formation is minimised and all these concepts. So, we went into great detail and try to understand a competitive inhibition and then, we started working on uncompetitive inhibition and which is what we will do today. We have started on it in the last class, but did not get the time to finish.

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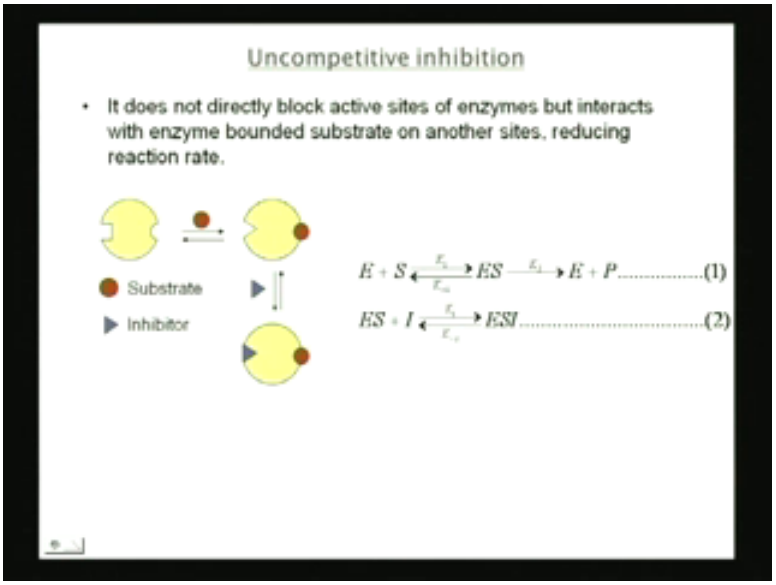

So, we will get back and and find remember the concept of uncompetitive inhibition. So, if you look at on your screen, what we had in competitive inhibition was that, the substrate and the substrate and the inhibitor they were competing for the active sites of the enzyme, where as an uncompetitive inhibition that is not like that; the reason is that, in the uncompetitive inhibition, the inhibitor does not go and set in the active site of the enzyme, but in some other site right. So, that is what happens.

If you seen the picture here, the active site is given by this no this semicircle where as the slot for the inhibitor the other side is a square. So, the inhibitor goes and fits into this slot and the substrate goes and fits in the other slot. So, as a result at one point each one point of time you can have two options; one is the substrate combining with the enzyme to form the complex which is needed for the product formation P and the other possibility is both the substrate and the inhibitor combining with the enzyme to form this complex ESI, which is not required for us, as a result this will not lead to product formation right.

So, if you go back to your notes you will see that, we started working on it. So, what what are my assumptions for the process for the system, what what are they going to be? One is that, if you look at the two reactions; one is that, reaction two attains the equilibrium. The second one is that, this species S over here attains quasi steady state and the third one would be the constraint equation; so, at any point of time when I give you this system so and if I give you lot more complicated system right, it does not have to be just competitive or uncompetitive inhibition, it could be a combination of different kinds of inhibition.

So, if I at any point of time in an assignment and test give you problems, where these different kinds of inhibitions as sort of combine. So, what would be the thumb rule? One you have to figure out, three things you have to figure out quickly. One is which are the reactions that attain equilibrium right so figure that out a first. Second is, which are the species that have that are in quasi steady state? And third, what would be the third step? Apart from the constraint the constraint is there, but that apart from that what else do you need to figure out?

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Right, which is the rate limiting step or the slowest step because, the rate of product formation is going to be dictated or governed by that particular state.

So, any combination I give you, these are some examples we are doing, which are prototypes, but if we go beyond these prototypes and come up with more complicated things, what you have to figure out is, what are the what are the reactions that attains equilibrium a, what are the species that attain quasi steady state? And c, which is the reaction that is the quasi that is rate limiting step, which will govern the rate of product formation? And finally d, you have to figure out that, what are the what is the product constraint equation? So, what are the what are the elements that are present in the constraint equation, which is to figure out that, in what forms the enzyme is present? So, what are the different complex forms? In this case as you look at the screen, you will see the enzyme is present as ES, as ESI and also as E, which is the free enzyme, so your constraint equation is going to be that.

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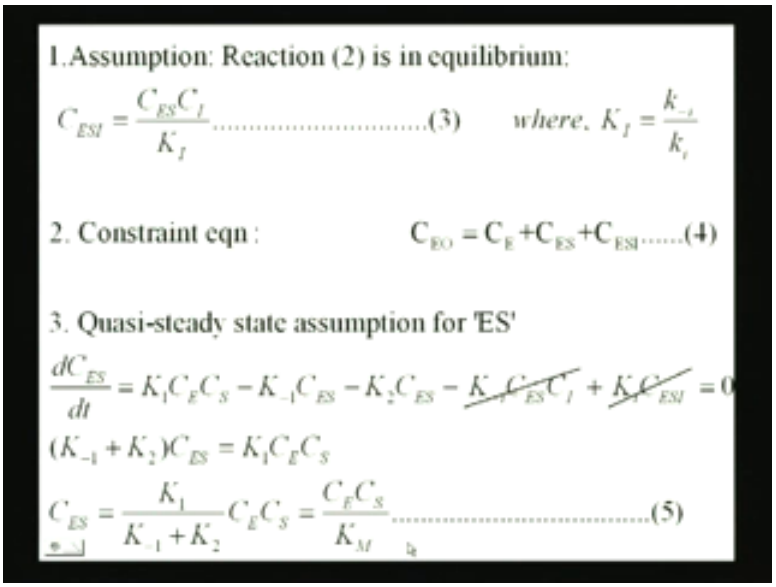

So, if we go over here, so this is the reaction equilibrium equilibrium for reaction 2 right you see on the on the screen, so which is ESI gives ES C ES times C I over, K I, K I being the equilibrium constant the backward over the forward rate constant. Say next, next right next is the constraint equation which I have already discussed, the C E plus C ES plus C s C ESI that is the enzyme in two complex forms plus one free form together equals the total amount of enzyme that, you put into the system at the start.

And the last one is the quasi steady state, one of the things, I pointed out in the last class if you remember, what is the major difference between this quasi steady state and the

quasi steady state, we wrote for competitive; it is that, we have two extra terms it is so, that it turns out that those two extra terms cancel each other, because you make a equilibrium assumption for reaction 2, but you should be careful enough to write those terms, because there could be cases where those terms do not necessarily cancel out, the way it does over here.

So, that is another thing I am trying to point out because, see what we are trying to figure out through these examples, that we are doing, what would be a strategy or a mechanism to solve a problem of enzyme you know inhibition in in in cases, where there are different kinds of inhibitions that are involved; the reason is the biochemical pathway's that there that are there in the body are much more complicated than the simple prototypes of simple competitive, non competitive, uncompetitive that we are doing.

So, that is that is the reason what I want you to be able to figure out, so what we are doing is that, given a system if at any point of time in your research you are working on a system which has these multiple enzyme pathways and and multiple inhibitors inhibiting or regulating those enzyme activities how to come up and solve be able to solve we are taking things one step at a time doing the simple cases, but in real life when you do there could be a combination of these these different kinds of inhibition in the network of reaction.

So, typically in the human body biological biochemical pathways is the networks of reactions, which are series and parallel, they cut across, intersect with each other and they are parallel to each other and then, there are complex inhibitors that are there and there could be inhibitors, which inhibit more than one reaction, simultaneously. So, what is needed is to be able to bring those ideas together and we are trying to come up with the strategy of formal theoretical framework for that.

So that, these are the steps in that theoretical framework and so if you do that you know you will find that your C ES; first here C ES C E C E ESI has been broken up into C ES and C E I, now C ES is broken up into C E times C s over K M. So, that you can substitute over here and then, you will get the C ES as the product of the 3 3 components fine.

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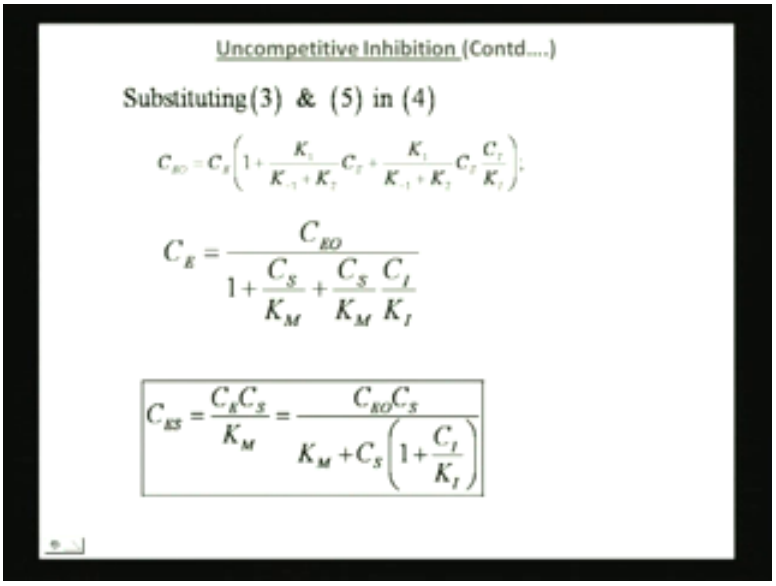

So, I think this is this is probably where we are right in the last class, did we stop here somewhere somewhere around here we stop yeah. So, if we look over here, what is happening is that, the C E C E C E is now expressed in terms of C E naught and as I said before the reason we do that is because, it is not possible to measure the free enzyme right. So, C E E now is given by C E naught over the denominator, which is composed of the substrate as well as the inhibitor right fine, is it clear.

So, in the absence of the inhibitor they would they should go to go back to the simple simple model, no inhibitor model. So, C ES now, C ES which is written as C E times C s over K M, now could be written as C E naught over C s over K M plus C s 1 plus C I over K I, I will give you a few seconds to write this term, if you want to. So, what is the rate going to be? Simply K 2 times C ES, because the rate limiting step is the product formation step (No Audio from 08:32 to 08:46).

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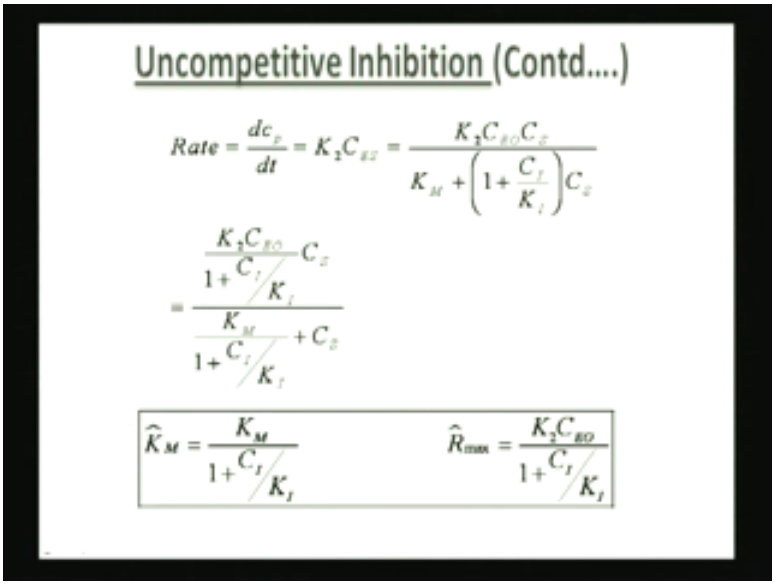

So, what we will do is we simply compute the compute the rate here, which is dc p the product formation rate is dc p dt equals K 2 C ES, K 2 times C ES. Now, that can be expressed as in terms of C E naught and C ES. So, what we find over here, if you look is it again we have been able to revert back to the Michaelis-Menton form that is that is, what we find look at the rate equation up there on the screen.

So, you will see that, we have been able to revert back to the Michaelis-Menton form. So, what is the difference if I ask you you know those who over here for the competitive inhibition? What is the difference between the rate we find over here and the rate we had in competitive inhibition?

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Yeah, maximum rate has increased and what else is increased? The both the slope and other asymptote both of them has have been increased right. So, your K M (( )) also changed sorry your K M hat has change and the maximum rate has has changed right. Now, your K M hat is this number given over here and your R max is the numerator over here. So, you might just want to write down these two, K M hat and the R max for the new system, which are K M hat and R max hat actually (No audio from 10:30 to 10:40).

So, if you look at these two once you have written, I will ask you quick question on this (No Audio from 10:44 to 11:02). So, once you have written this K M K M hat and R max

hat, can you make some comment on this, is there something that you that you think is worth saying both have changed fine, but what else, just look at the them a little carefully (No Audio from 11:23 to 11:33) both K M hat and R max hat have changed, but what what is interesting about them?

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Not so complicated, just look at these two quickly and tell me these two numbers, what if I compared to say without inhibition, I am giving a hint here, in the absence of inhibition and in the presence of inhibition, so both K M hat, K M hat has increased decreased?

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Or in other words, the ratio remains you know the same right. So, that that is one of the things you notice. So, this is one of the differences between this and competitive inhibition. In competitive inhibition, one of them changes, but the ratio also changes, in this case, both of them change with the same factor as a result of which the ratio remains the same, why is that important? We will see in the plot you can (( )) guess also right.

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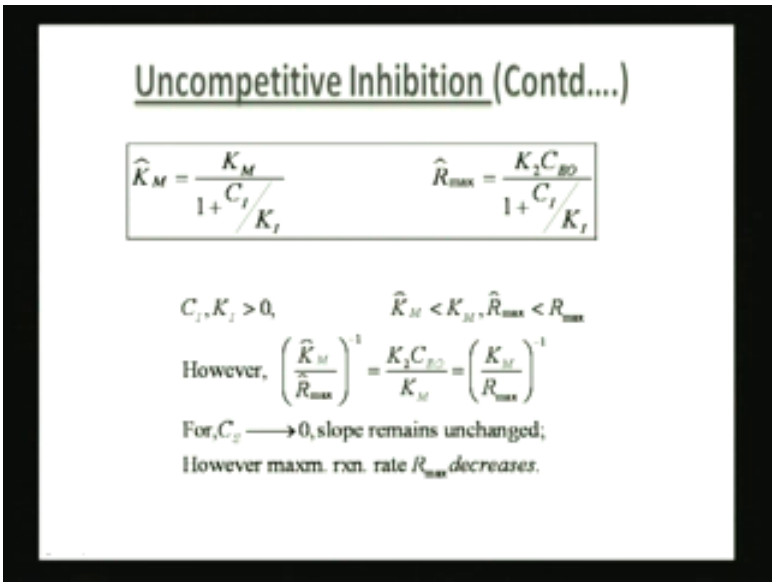

So, this is this is it and so this is your K M hat and R max hat and since your C I and K I bar both equal to 0 greater than 0 which means that your K M hat and R max hat are both lowered now, as compared to in the presence of absence of inhibition, which makes sense because, in you know if you add you add inhibition not to increase it, but to

decrease the maximum rate and; however, this is what I wanted to point out and now it is on the screen is that, the ratio remains the same as a result the slope in the plot remains the same.

So, maximum reaction rate decreases, but the slope in the curve remains the same and we will show you a picture of that in a while. So and this is on an uncompetitive inhibition. We will now go to non competitive inhibition, but if there is any quick question on uncompetitive inhibition you can ask me right now, no questions.

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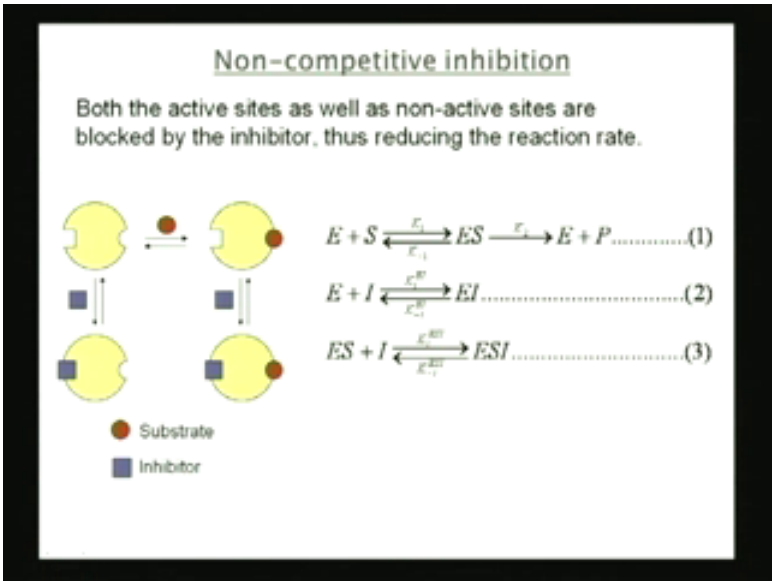

So, uncompetitive inhibition is sorry non-competitive inhibition is essentially this you know what a little bit written will do on the screen. So, what happens is that, the both the active sites and the non-active sites are blocked by the inhibitor both the active sites and the non-active sites have blocked by the inhibitor. So, this is the most potent form of inhibition. So, to say right you are talking of different forms.

So, this is a form where both the active sites and the non-active sites are blocked by the inhibitor. So, if you want to inhibit as much as possible then, probably this is a mechanism that you would go for. Now, I would like to ask you in terms of reaction because, we have done three different kinds before without inhibition, competitive and uncompetitive.

What do you think would be the reaction mechanism not in detail, but just give me a sense what do you think would be the reaction mechanism for this?

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Which two?

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Uncompetitive and competitive very good that is the answer. So, it is a combination of those two. So, as I it is it is now on your screen. So, as you will see that, this is see the see the yellow thing and red dots over here. So, the red is the substrate, the blue is the inhibitor so this is where you can have the inhibitor blocking the non-active site, this is inhibitor blocking, this is the substrate taking up the active site, but there is a possibility that inhibitor might also block the active site.

So, the reaction scheme as you see is a combination is just to be said of the last two. So, in the competitive inhibition you had equations 1 and 2 right. So, which was the equation 1 is the general equation in the absence of inhibitor, which is substrate in the enzyme reacting to form the complex that forming the product.

Equation 2 was for competitive inhibition, where the inhibitor was competing with the substrate for the attention of the enzyme, for the attention of the active sites the enzyme rather and these two form the competitive inhibition. And 1 and 3 formed the uncompetitive inhibition, where the enzyme was not directly binding to the active site of the sorry the inhibitor was not directly binding to the active site of the enzyme, but it was binding to the non-active site to the complex of this say.

So, here they said this is the most potent form of inhibition and here what happens is that, all three together all three reactions together happen, which is the first reaction, the normal reaction, the first kind of inhibition that is the competitive inhibition and the uncompetitive inhibition all three together happen, it is (( )) kind of why this name comes a non-competitive, but it is competitive in a way.

So, I will give you few seconds to write down the reactions if you want (No audio from 16:49 to 17:11). So, there there is a slight error here and I need to point that out these K that you see here the forward and the backward rate constants all through are going to be

little k small k not the big K because, big K are for equilibrium constants and small k are used for reaction rate constant. So, please make that small change you know in all the reactions 1, 2 and 3 the K are going to be small k.

Now, so we talked of a strategy. So, what are strategy is going to be in terms of framework for deriving what we want to what what does the first, what is the first thing we should consider? What are the reactions that attain equilibrium? So, what are the reactions that attain equilibrium here? What we assume, these are assumptions essentially we are not sure, if they attain equilibrium or not?

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No, just E I and ESI, these two we assume that attain equilibrium just E I and ESI. And ES, that reaction does not attain equilibrium; it attains quasi steady state, because we have to figure out, why can it not attain equilibrium answer me, tell me this, why do you think it should not attain equilibrium, because if it attains equilibrium then, what will happen?

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How will product be formed you know? So, it would be just engaged in the backward and the forward reaction, but if for the product to be formed, it is not possible for that to attain equilibrium, what it attains is the quasi steady state.

So, as I said that, what we do first we figure out, what are the reactions that attain equilibrium a, my first (( ))? So that the answer to that is, reactions 2 and 3 attain equilibrium. My second question that I ask myself is what are the species that attain quasi steady state? The answer here is only one species which is ES.

My third question is what is the rate limiting step? The rate limiting step here again is the formation of ES to E and P right and as you know that you know reactions that attain equilibrium are much faster any way and the last one would be that, what is the constraint equation? So, what would be the constraint equation here how many species it should involve?

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For the first time it will involve four species, which are the free enzyme E, then the complex one ES, complex two, E I and complex three, ESI right.

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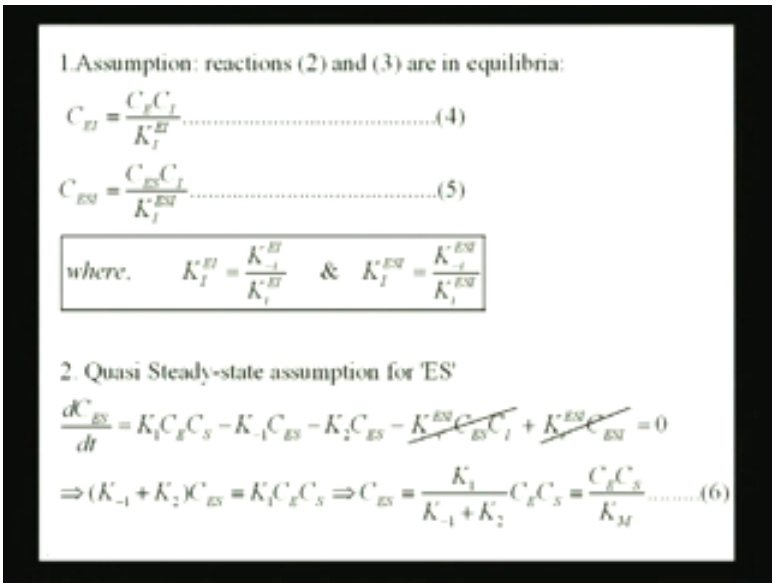

So, what I want you to do is I have the things here, but I want you to quickly go and write some of them. So, first one is that reactions 2 and 3 attain equilibrium. So, this is what you have and if you want you can make a note. So, C E I is given as C E times C I over K E I that first, second is C s C E ES C ES ESI sorry is given as C ES times C I over K E I, but our goal is to be able to express these complexes in terms of the elements right those are the respective element.

So, again you know as I said, there is a slight type of graphical error here, these K are going to be small I mean well even with big K it makes sense as long as you are consistent, but the nomenclature the standard nomenclature is that small k is for reaction rate constant so we will stick to that. So, then so equation 5 that you see in equation 4 we have been able to already accomplish what we wanted which is express C E I in terms of C E and C I. Now, in equation 5 we still want to express C ES in terms of the C E and C S, how do we do with that by using the quasi steady state for C ES right.

So, if we do a quasi steady state for a C ES what will you get? How many terms will you get for quasi steady state for C ES, when you write the quasi steady state equations. So, d dt s C ES how many terms?

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Five terms you had five terms, is it clear to everybody you get five terms two of which will cancel out, because of the equilibrium assumption given by equation 5 right. So, as you see on the screen now. So, you have five terms (( )) has five terms three from the first reaction 1, two from reaction 3 and the two terms from reaction 3 cancel out because, we make this equilibrium assumptions, for reaction 3. So, that is essentially the same as equation 5, is that clear to everyone.

Now, after doing this we have been able to express. So, if you see the bottom thing here the last line out here we have been able to express our C ES as a product of C E and C s divided by the Michaelis constant K M right. So, the Michaelis constant still the same, it still retains the same form clear, then what else, what else is left to do?

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Constraint equation, so these are the steps you should be able to you know by now you should be completely thorough, because we are at end of this chapter. So, this is the way to go. So, you we finished our equilibrium assumptions, we finished our quasi steady state assumption, the last thing left is the constraint, which is not an assumption, but it is a reality, it is a it is something that really happens. So, the constraint is going to have four species as we have discussed.

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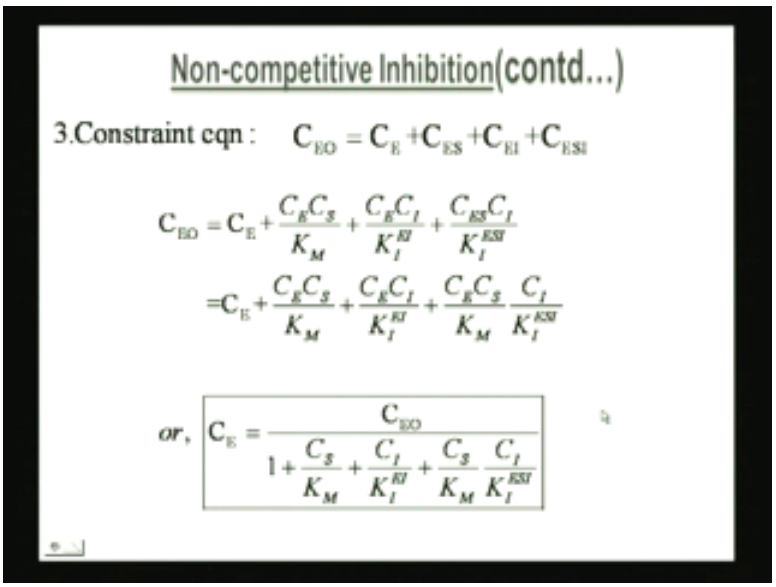

So, all the free enzyme and the enzyme in its three difference forms which is ES, EI and ESI together should be E C E naught, which is the total amount of enzyme, present in the system to start with. So, what do you do is keep this and then you substitute for each of those complexes, so C ES can be substituted as C E times C s over K M, C E I could be substituted as C E times C I over K I K E I and C ESI could be substituted as C E times C s times C I over K M over K E K S K ESI right.

So, now we have been able to express all of these complexes in terms of the basic elements. Now, the next step is as I said C E is also not something we really know and we want to express everything in terms of C E naught. So, we express everything C E in terms of C E naught as C E equals C E naught over this denominator and then, we can put it back into a last equation, which is which equation is that, the last one is the?

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Rate limiting step, the rate of product formation right clear with this point. So, in case you need more time to write things down, let me know.

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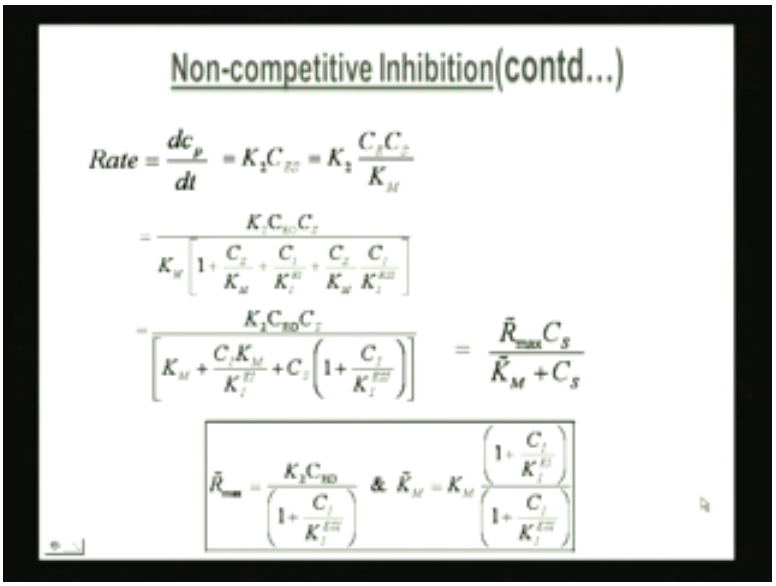

So, the final thing that we are going to do is the rate rate of product formation, which is d dt of c p, which equals K 2 times C ES and K 2 times C ES is C E times C s over K M. Now, this C E we can replace by what we just calculated in terms of C E naught and this is what you get right. So, once you have written that, what I would like you to do is

rearrange it in terms of the M M form, the Michaelis-Menton form if it is possible, it may not be possible always, but may be.

So, this is a little quick thing I want you to do, the rate is given on the screen, what I want you to do is, rearrange it in terms of the so that it los like Michaelis-Menton form (( )) (No Audio from 25:54 to 26:46) done. So, what you essentially you have to do is you have to have a C s in the numerator and the denominator should have a constant plus C s right.

So, you have to evaluate that constant and and the other constant that are pre factors of the C s in the numerator. So, if you are stuck you can just look up in the screen, the answer is there. Now, we can write this as R max C s over K M hat R tilde I used hat for the last one, so on this one I am using tilde. So, R max tilde C s over K M tilde plus C s. So, this is the Michaelis, so the Michaelis-Menton from essentially you has to do it like an R max C s over K M plus C s that is the form to get to right.

So, your R max is now K 2 C E naught over this term right here, because see what is what happens is, this is the pre factor of C s pre factor post factor; however, you want to call it. So, this is comes with the C s, but you want the C s free right you do not want it with any other constant. So, we divide the numerator and denominator by this term 1 plus C I over E ESI right. So, then you get your R max as K 2 C E naught plus 1 plus C I over K ESI and your K M tilde as, whole K M times 1 plus C I over K I that comes from here, divide it by 1 plus C I over K ESI fine. Now, can can you tell me by looking at R max tilde and K M tilde, if these are going to be larger and smaller, then your K M and R max?

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Smaller always right. We cannot conclude about this right answer here. So, R max is if you look up there, R max is smaller than smaller than always smaller, but we cannot make because, why is R max always smaller because, C I is larger than 0 and K ESI is larger than 0, so it is always smaller, but we cannot make such conclusive you know comments on K M tilde, the reason being what is the reason?

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So, it depends on the relationship between K I K E I and K ESI. So, depending on whichever is greater or smaller you will have different kinds of relationships so. So, why is this useful you know, why is this probably this is more useful method, if you want to control regulate the enzyme inhibition of all the three methods that we have learned, this is probably the most useful because, you can control both the slope and the and the maximum rate see why you know think from a realistic point of view. So, in most cases you want to reduce the maximum rate right that is something that we discussed, because we do not want excess product formation, we want product formation up to a certain range.

So, that why if you go back to some of the things that we discussed is that, the products are typically active within a certain range because, they might be triggering of some of the biochemical pathway some desired biochemical pathways within that range and outside that range, they might be triggering of other biochemical pathways a and b is that, you do not want excess product formation, because essentially it is a waste of energy.

So, you want to reduce your maximum reaction rate always, but your slope which gives you the rate of initial product formation how you start of and how you reach that asymptote that is given by the slope, that is something that you want to regulate and by regulate I do not necessarily mean that, you want to decrease it that is something that you want in your hand you should be able to increase it or decrease it.

So, in one kind of inhibition you essentially so first kind of inhibition the competitive one you saw we saw that you can you can change it, but you can change it in only one way. In the second kind of inhibition that we saw the uncompetitive we found that, we you cannot even changed it change it because, what turns out that the K M and the R max differ by the same ratio and the slope is dependent on the ratio of these two as a result of which, there is no dependence on the in of inhibition on the initial rate.

Here you find that, there is dependence of inhibition on the initial rate and you can change it change it by and change by change it well I mean that you can change it positively or negatively, they can decrease it or increase it.

So, this is the this is the most convenient form of inhibition, because of both reasons, it is most potent and most flexible because, you can make the most amount of changes in this.

The next thing I am going to show is the comparisons of the plots because, I have not showed you plot for either competitive or uncompetitive and non-competitive.

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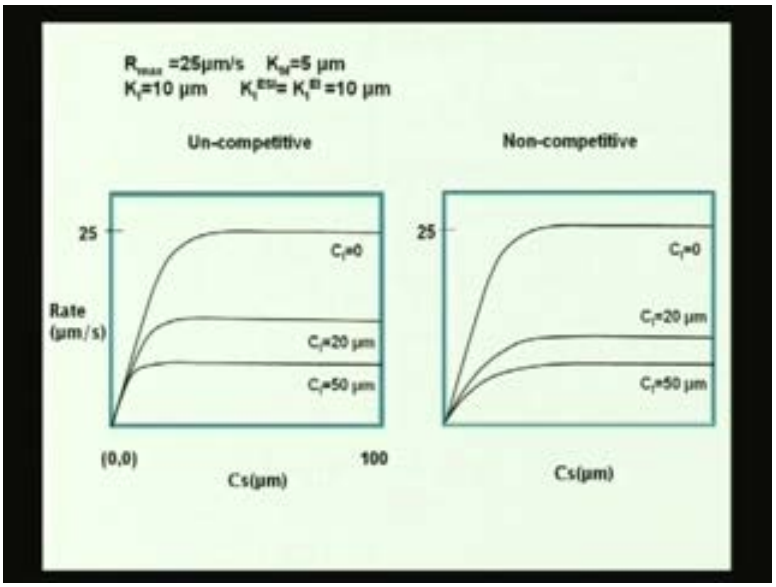

I am going to show you the comparison of the plots, but by now I think I have clarified most of the concepts. So, what the plot is going to catch is essentially that, in uncompetitive the initial rate of product formation is a is independent of the inhibitor concentration right, the initial rate is independent of the inhibitor concentration. The reason being that, the slopes are slope is a constant, it is independent of initial concentration independent of initiator concentration whereas, in non-competitive both the both the you know the slope and the maximum rate could be changed by the inhibitor.

Now, as you see over here the constants for C E ESI and E I have been taken to be the same out here, both of them have been taken to be the same, but if I varied it accordingly I can decrease change the slope the way I want. So, this (( )) taken the same as a result you get some one kind of vision what you might want to do go back home and do a quick calculation as that as you change the (( )) your K ESI is 10 times that of K E I how which way the slope will go and if the other way it is like 1 10^{th} of that. So, you do three different cases equal, one is 10 times again that one is 1 10^{th} of the then, you will see you will have a sense that one particular inhibitor concentration how you can bring it forward and backward, so that something that you might be able to do.

So, this is about you know inhibition or enzyme regulation using inhibitor this is all we wanted to do, the last thing that we are going to do is the another kind of inhibition, but which is not initiated or influenced or dictated by inhibitors, it is a natural process an intrinsic inhibition. So, when we talk about inhibition in the first one of the earlier lectures, we talked about intrinsic and extrinsic inhibitor.

So, in extrinsic inhibitor you can add the inhibitor from outside say and make this kind of inhibitor inhibition happen and in intrinsic inhibition, there are two possibilities one is the inhibitor is there inside the system itself and kind of inhibits, the inhibits the set of reactions, other possibilities is that, it substrate itself inhibits the reaction, there could be possibilities where the product itself inhibits the reaction.

Some of you you know probably might know quite a few reactions, where the product itself is inhibits the reaction. So, if the product itself inhibits the reaction and you do not want inhibition for example, what would you do very straight forward answer? What did you do, if the product is inhibiting the reaction and you do not want the inhibition to happen?

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Constantly take out the product yes that is the that is the right answer. But, see if you have a there is a problem if you have a big reactor anyhow c s t r essentially. So and what happens if you have big c s t r, what what is what is large c s t r, what would be large in large c s t r?

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Volume large means what?

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The residence time right, the residence time is large in a large c s t r right. So, if the residence time is large even if you are taking the product out at a certain rate then, still because what does residence time signifies? Signifies the the the the the amount of time not the exact amount, but a representative amount of time that each of these species get to spend in the reactor right that is the definition of residence time.

So, even if you are taking it out at the constant rate say say in a c s t r, what is the problem, the problem is it gets to spend the product gets to spend a fair amount of time in the reactor right as a result it is still being awaited. So, this taking the product out continuously is theoretically correct answer, but it is not a practically correct answer because, if you are using a c s t r; it has a certain residence time and you cannot do anything beyond it right.

So, what would be the other mechanism one of the ways of course, is to keep the volume same, but increase their input output rate right for a steady state c s t r to increase the input output rate. So, that the residence time is decreased, that is one of the possibility, but what could be other possibility?

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Then, how will you use that?

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No, flow rate we already said that is the possibility that you can decrease or increase the flow rate as a result of which you can decrease the residence time that is the one possibility. What are other possibilities?

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No, r p m no, let us not goes get into mass transfer resistance at this point. The answer is this that, you know instead of using one large reactor replace it by several reactors. So, if you have a reactor of say 10 hours residence time, replace it by three reactors or four reactors or 2.5 hours each. So, that the total residence time is still the same and if you keep the total amount of the flow rate as the same, then you essentially divide up (( )) attain to reactor you divide it up divide up into 4 2.5 litre reactor right.

So, as a result of which the say if your flow rate is 1 litre per hour or something and your 10 litre reactor is (( )) is there. So, your residence time is 10 hours right. So, now if you split up into four different reactors, the residence time is 2.5 hours each and your volume, reactor volume is 2.5 hour each. So, what will happen is that, intimatently you can take out the product.

So, without changing the total residence time, you still keep the total residence time and the total reactor volume the same, but what happens is that, as soon as the product comes out as a mixture of product and reactant and other things that come out of the first reactor you take it out you pass it through membrane separator unit take it take out the product and recycle back the rest of the thing into the next reactor and then, you keep doing this all the time right is it clear.

So, as a result you will intermediately take out the product. So, this is one way you can you can stop inhibition from the product, but the problem is life is little more difficult when the substrate traps to inhibit and when the substrate starts to inhibit and there is another kind of reaction you probably know that it is called auto catalytic reaction. So, autocatalytic reaction is autocatalytic, what is autocatalytic reaction it is just?

(( ))

Catalyst yes, so we had essentially what we talked about just now, it is also inhibit reaction, where the product inhibits the reaction and then, you can have auto catalytic reaction, where the product catalyses the reaction. Now, just as a auto inhibitor reactions are bad and you do not want the product to inhibit the reactant, the autocatalytic reactions could be bad as well. Why do you think so?

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Then, what will happen?

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Right that is very good answer.

So, what happens is the is the phenomena called reactor runaway, the phenomenon called reactor runaway and these reactor runaway typically happen in auto catalytic reactions. One of the things that you do not know I will tell you in a few minutes, but you talked about exothermic forget about exothermic and I will come to that in a minute. See, simple known as isothermal reaction for example, A plus B, A plus say let us say A plus B giving 2 B, so that is an that is an auto catalytic reaction.

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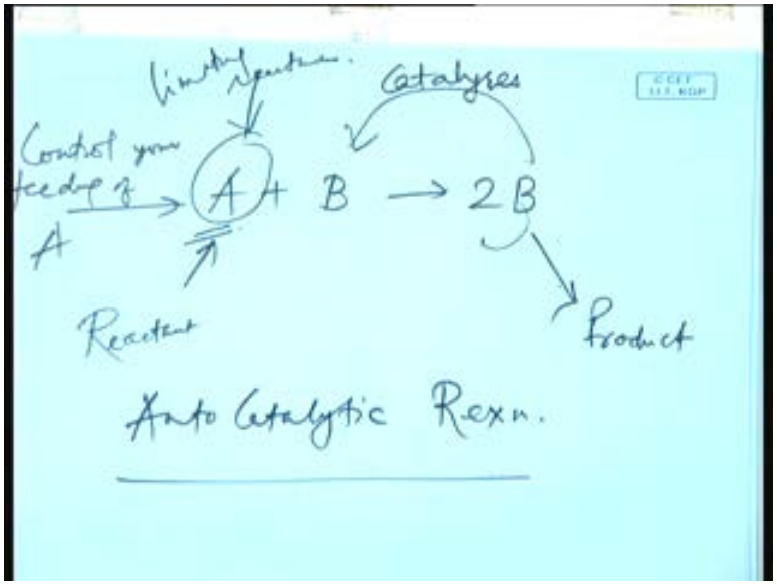

So, here for example, A is here reactant, B is your product and this B itself goes in catalyses. So, this is an autocatalytic reaction. So, the the thing is that this these going and catalysing. So, more B you produce over here, the more the reaction is catalysed. So, what you talking is about exothermic reactions. So, the reactor can go through what is known as you know burst it burst out completely, but even apart from that, the reaction rates goes out of control reaction rate will rate will go out of control because, what will happen with time more and more product is going to be formed and the more and more product is formed, the more and more it reacts, but the way to stop that is to control your feeding of A. So, control your feeding of A.

So, what you do is you do not put in all the A at the start, you put in slowly and the rate at which though your A is now going to be the limiting reactant, A is going to be your limiting reactant and the more you limit the amount of A that is formed that is there in the system, the more the reaction is limited.

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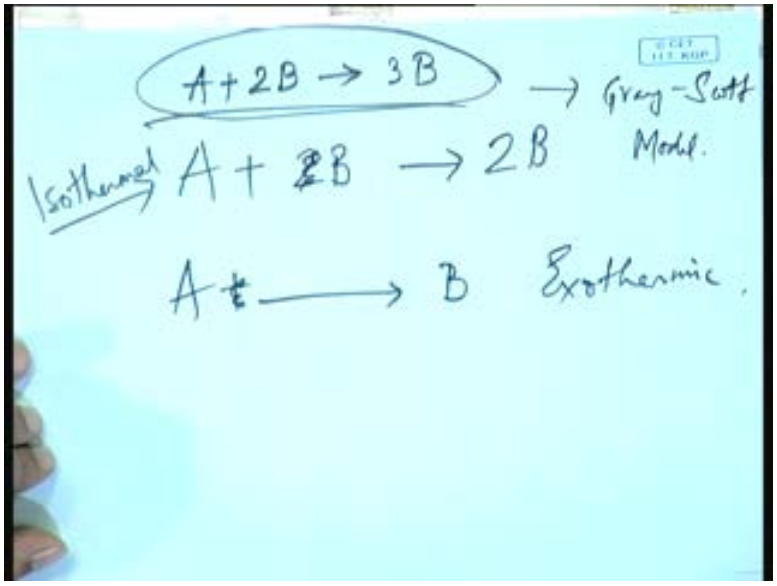

So, this is this is good, but what I am going to talk about now is, what he said and that is a more interesting phenomena let us say 2 B or you can have it differently also you know, this is a more famous form actually this is what I wrote on the top is a more famous form, this is you know this is Gray Scott model this is known as Gray Scott model. So, a huge amount of theoretical and experimental studies have been done on these autocatalytic systems and I will come to minute why these studies actually have been done, these autocatalytic systems. So, you can have a system like this or so let us call this isothermal or you can have a system as A going to B, exothermic.

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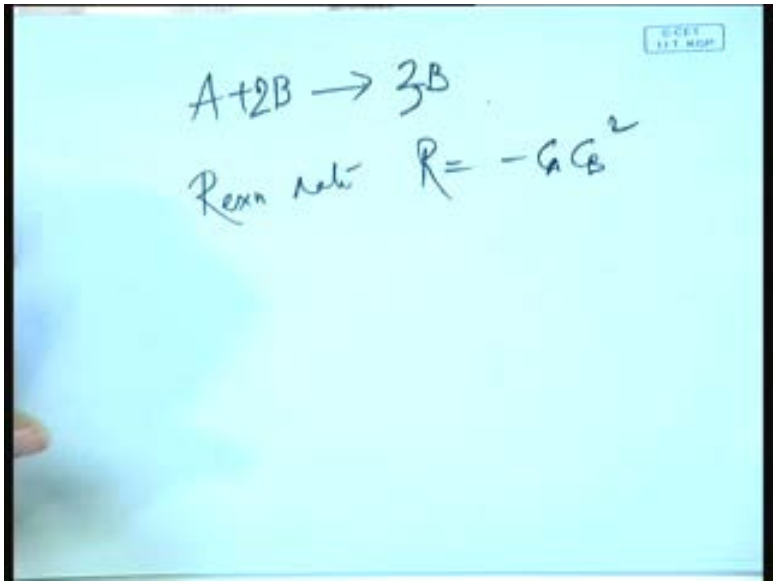

So, if I have A plus B giving 2 B, what would be the reaction rate?

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Or if we have A plus 2 B giving 3 B, then the reaction rate R equals minus C A C B square right fine.

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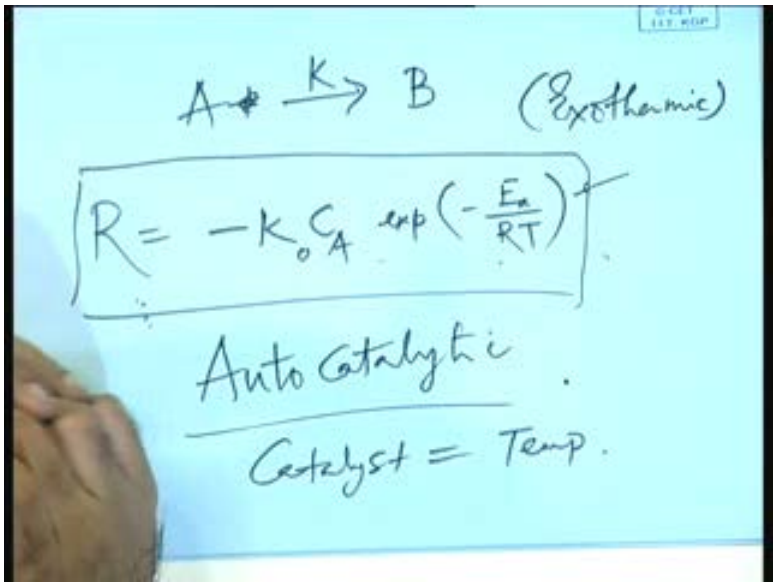

Now, let me ask you this A plus, A just giving B, exothermic. What is my reaction rate R equals?

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Minus K into so let us called this K into C A, that is it?

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First order, but exothermic what is the reaction rate?

(( ))

K naught into exponential minus (( )) and this is problem sure this is something that this is something you know, but there is something I am going to tell you that you do not know, this reaction is auto catalytic do you know this you have learn this before, this is autocatalytic, this is autocatalytic right think about it for half a minute.

You see what I am trying to say you see why it is autocatalytic?

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Temperature is a catalyst here, catalyst equals temperature. So, here catalyst equal to temperature do you see why I am saying, because this is exothermic. So, heat is going to be generated, more heat is more the heat is generated more the temperature is raised, more the temperature is raised, more this term goes up, why? Because, its temperature in the denominator and there is a negative sign. So, essentially it is a positive effect, temperature goes up, this term goes up right. So, the more this term goes up, the more the reaction rate goes up clear and more reaction would happen and that would raise the temperature even more right and this would go on.

Now, this is you know all of you are chemical engineers most of you are going to go into industries to work and what you see is most of the reactions that happen in the industries are of this type, not many reactions are endothermic, most reactions are actually exothermic. So, exothermic reactions this is the simplest case we assumed first order, if you take second order and so on you know third order is hard to come across, but second order if you say, it gets more complicated.

So, the simplest case we are looking at simplest exothermic reaction and that is auto catalytic. So, that is the huge huge trouble that is the huge huge trouble in industry I think you are telling me that you know in your company you use to have accidents very often. So, no wonder you would have you know accidents is the possibility and that is why it is very important to able to control these reactions either by inhibiting them or by coming up with other means for example, feeding it in a different way or you know for what happens is that, now now let us now come to the concept of reactor runaway.

So, one of the things continue to do is cool it, cool it either by jacketed cooling or by kind of cooling where in couple of exothermic and endothermic reactions. So, that the heat produced by exothermic reaction is quickly taken off by the endothermic reaction. So, these are different strategies that you that you come up with.

Now, what is what is the reactor runaway, reactor runaway is not necessarily the fact that, this would get very hot this you know, because of the reaction the heat generated this is this is the reaction rate and because of the heat generated, the reactor becomes

very hot and burst, no that is not possible because, as engineers we design these reactors properly enough so that, they would not burst so easily, so that there is no reactor runaway.

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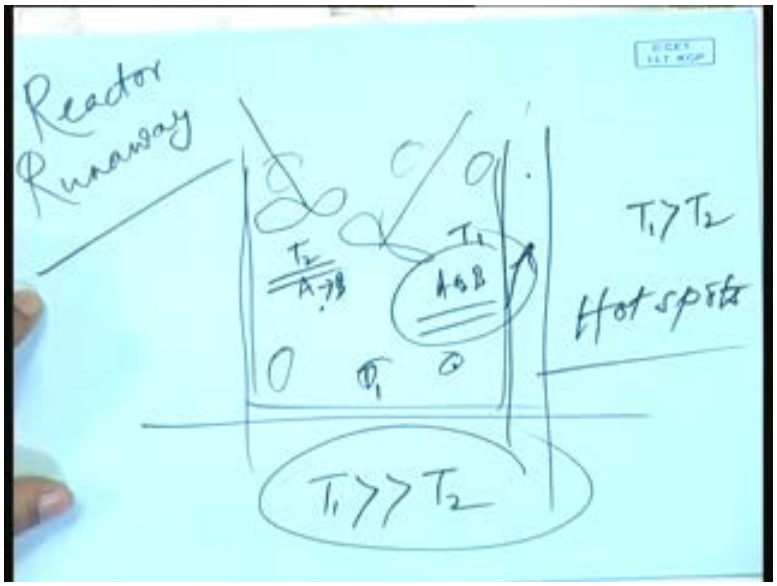

Reactor runaway is essentially that, if you have a reactor like this, these are large reactors and you are mixing them at several points let us say and here is your reaction happening A, everywhere it is happening. Now, what happens is? These reactors are real reactors and there are different kinds of perturbations, disturbances. So, you know so there could be disturbances of the floor, there could be disturbances in the jacket, on the side; there are different disturbances in different different places.

So, for example, if you are having a jacketed cooling, the cooling in one side may be different from the cooling on the other side, this is normal thing that happen in in in a chemical reaction and this is these are things that you cannot control, you can control the amount of coolant that flows in, you can control the amount of reactant that comes in, but you cannot control these things, which are out of your control essentially you knows for example, influences or perturbations are are changes the fluctuations in the coolant rate and so on.

So, as a result what happens is that, the temperature is not uniform a lot of effort is put in to make these temperatures uniform you know put in as many (( )) as you want, but the

temperatures are not uniform in the reactor that that is the that is the reality one has to live with. So, what happens, when the temperature is not uniform in the reactor?

(( ))

Hot spots will generates, but essentially in terms of the reaction what would happen if I look at this reaction, A plus B what happen? You think about in these in these terms of reaction rate. So, if temperature is more at a certain place and this reaction these reactions are autocatalytic, where the catalyst is temperature. So, if temperature is higher in one particular end of the reactor then, the other end then, what would happen is that? That the reaction would be higher in that particular end as compared to the other end.

So, what will happen is that, so what will happen is this A going to B over here and A going to B over here as well, but if the temperature T here is T 1 and T this is T 2 and T 1 is greater than T 2 then, this will the reaction rate will here go up and so more heat would be generated over here and that heat heat will catalyse even more reaction. So, what will happen is the hot will get hotter. So, this is like the rich getting richer. So, a very capitalistic model works inside the inside a chemical reactor. So and this is a very normal case I am taking a very simple case of an exothermic first order reaction number, this is not very complicated reaction, no network nothing. The very simple case of first order exothermic reaction which you come across all the time and this is what happens.

So, those things that so these hot areas that are generated are called hot spots. So, these are called hot spots. So, hot spots are essentially when one part of the one part of the reactor starts to get hotter and hotter and hotter and what will happen? What will coincide with hot spot, what if there is a hot spot in one part of the reactor, what will happen?

(( ))

But in other parts of the reaction, reactor, the reactor reaction rate will might go down you know the cold spots the reason is that, the total amount of energy that is typically typically given to the reactor is more or less a constant. So, there is a possibility that the other other regions might cool down, there is a possibility I am not saying that, it will necessarily happen, but there is a possibility.

So, when these hot spots blow up that is you have hot spots in different parts and the temperature. So, few hot spots in different parts of the reactor and the temperatures in these hot spots become much greater. So, if the average temperature elsewhere is T 2 and T 1 is the temperature in the hot spot then, if T 1 is much much greater than T 2 when this happens, the reactor blows up. So, when a reactor blows up? It is not that the entire reactor blows up, it is not that the temperature in the whole reactor is very high exact certain parts of the reactor become extremely hot and cannot be handled and it blows up and that is called reactor runaway that is the this phenomenon is called reactor runaway. So, why you know, if I talk about let me go go little bit more into the detail at this point of time.

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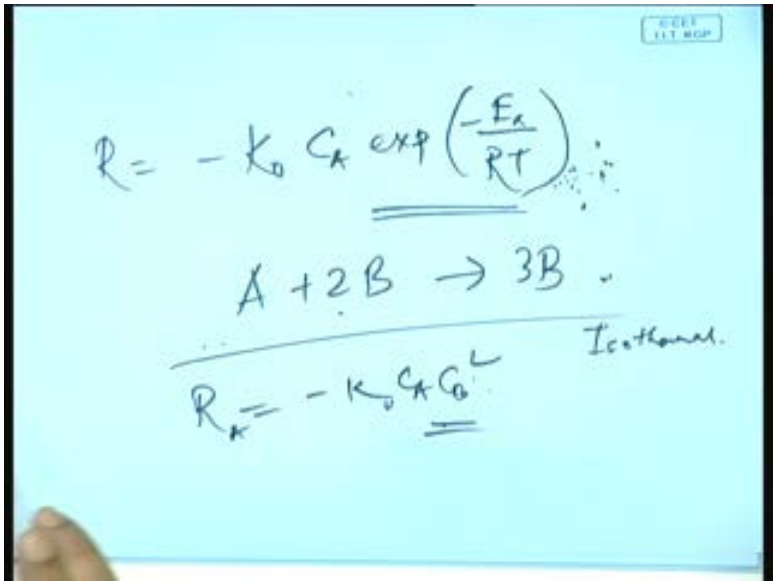

So, if I take a reaction like this, minus K say R is equal to minus K naught C A exponential minus E over R T. So, I take a reaction rate like this, now we thought about it practically and we load at practical part of it, but you know one of the things we want to do bring down a theory and practical things together. If you look at this equation mathematically now, what is there in this equation you know I am I want you to think from completely different angle now, if you look at this equation mathematically, what is there in this equation that can make such a thing happen?

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No, not right, what is there about the exponential of course, the fact that it goes up and so on, but mathematically I want you to think think more mathematically now.

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Fine, but if I had given you know, if I had just given you any other increase form of increase what what is so in curious about this particular form (No Audio from 53:29 to 53:45), what what is so interesting about yes?

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I will give you a simpler example.

(( ))

I will give you a simple simpler example this A plus 2 B giving 3 B let us look at this isothermal, so that also gives the similar kind of thing right that that is also why is it, because this is also autocatalytic, this is also autocatalytic. So, this is little more complicated. So, let us lo at the simpler form. So, here R R A equals minus K C A C B square C A is same here let us call this K naught, K naught is same here. So, if you compare this with this part this part with this part. What is interesting, what what is important about that, this and this you have to get this mathematically no let us not think about the (( )).

(( ))

What is the basic thing I want you to utter that word, what is the basic thing this is non-linear dependence you know that is the thing. So, this catalyst whatever the catalyst could be B or the catalyst could be temperature that is the non-linear dependence on this catalyst and that is what is allowing such a thing to happen conceptually let us may be at some other time next class I will talk about little more, but conceptually let us try and understand what is happening that so coming back to this picture.

So, the temperature is T 1 over here and the temperature is T 2 over here, this is supposed to be a completely thoroughly mixed reactor continuous stirred tank reactor you know one thing that in the continuous stirred tank reactor, only one temperature is

allowed, but here what is happening may be two or more than two temperatures that are present in the same reactor does it make sense to you.

So, what is happening, what is this phenomena called do you know this. So, at same point of time in different point and space, two different temperature or two or more different temperatures coexist and that is allowed by this form of these equations, this equation and that equation.

So, at the same at same point in time and two different point in space two different temperatures coexist or if you are talking about A plus 2 B giving 3 B, two different values of B coexist two different amounts coexist and but, these are suppose to be continuously stirred tank completely mix reactive, so despite all the mixing. So, this is the this is allowed because of the form of the equations and this is multiplicity. So, essentially there is multiplicity.

So, these equations, these these forms allow that kind of (( )). So, you know may be next class I will talk a little bit about bifurcation or multiplicity because, there are other things that will show also, which have to deal with multiplicity, but because of the basic thing that multiplicity is allowed by these equations.

So, at same point of time there could be two temperatures in space or two values of a certain constant substrate or certain product in space within a continuously stirred tank reactor that is multiplicity, because multiplicity is allowed that this is allowed to happen right otherwise, unless multiplicity is not allowed, then temperature in one spot cannot go up, while the temperature in other spot remains the same is that clear, but that see see that is the from physical point of view you are thinking that make sense, but it has to be supported and allowed by your theoretical framework your theoretical equations that you have and that is supported and allowed by this particular thing.

So, this is I think something very important I wanted to discuss today, it is not completely directly related to what we are doing, but as chemical engineer you should know that a very simple equation like first order exothermic reaction, which is something that you handle all the time and you will handle all the time for the rest of your life is autocatalytic and these are some of the very complex phenomena that it can lead to and that is why it has been studied in such great detail over the last say 30 year, 30 40 years it has been studied in great detail you know lots of work has been done on it.

So, little bit we will come across in our next lecture, which has to be deal with bifurcation multiplicity and I will give you some sense of it. So, next class we will finish the substrate, inhibition and rest of the chapter. So, this week we will finish that is all thank you for and here. So, we will continue with this with this substrate inhibition and the rest in the next lecture thanks.