Material and Energy Balances

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Module No # 07
Lecture No # 32
Flux balance analysis – Part 1

So flux balance analysis is the most important concept when it comes to constraint based modeling it is one of the first technique that was you know used so it involves a steady state mass balance right.

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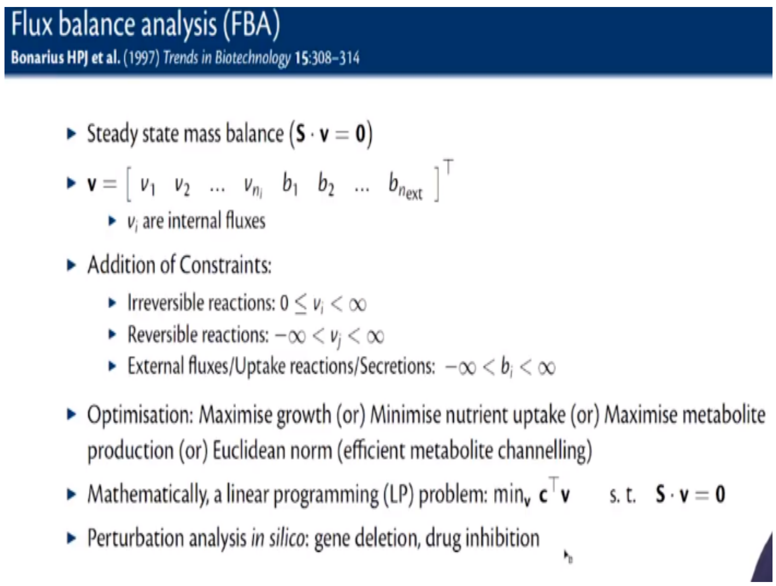

What is steady state? There is no accumulation right so whatever substitute is coming out there are some conversion in a steady state substances are going out right. So what would be DX/DT under steady state.

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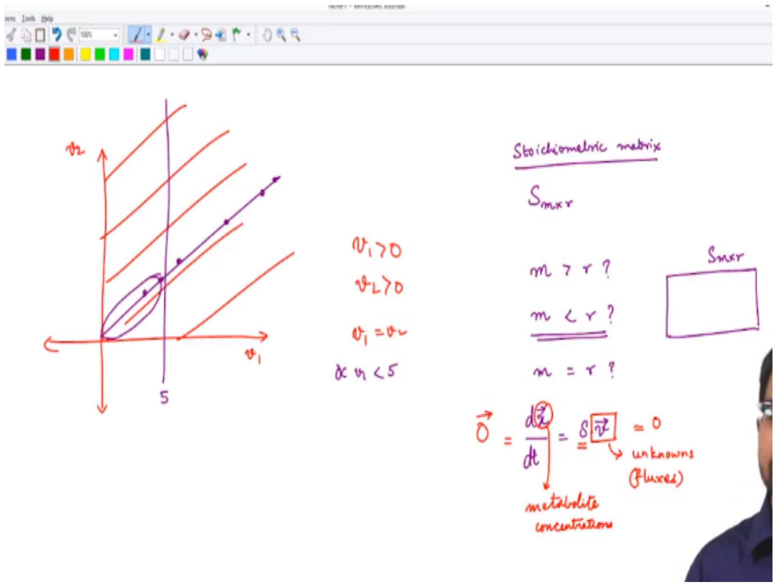

It will be equal to 0 rate of change of every rate of accumulation of every metabolite will be 0. Is that right? So what does that mean? It means that SE = 0.

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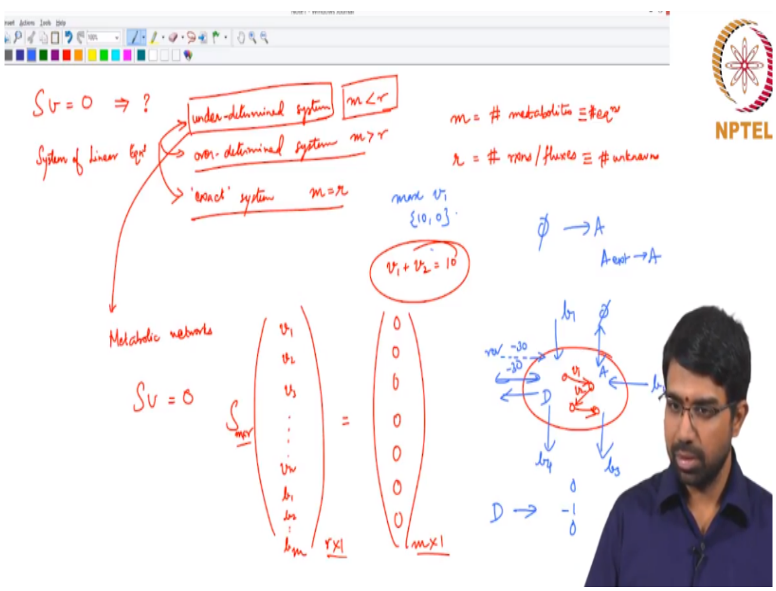

What does this mean? What is this? What is SV = 0 is the system of linear equations. Is it the moment we have a system of linear equations you could have an under determined system and over or it call an exact system right. So this is N = R what does over determine mean M greater than R, M less than R. So once again what is M? Which is the same as the number of equations every metabolite have a equations.

R number of reactions or fluxes which is the same as variables or unknowns so if you gave a equations V1 + V2 = 10 and as you dissolve it how many solutions would you have obviously infinitely many solutions which is the same thing we expect for undermine system. So whenever you have more reactions then metabolites you will have an undetermined system for fact matrix right.

So you have a undetermined system you now need some of the ways of solving it what happens if you have an exact system. What is the solutions? All zeros here right hand side is 0 right so you know that all zeros is her solutions you know that it is that was her solutions right and over determine system it could be inconsistent right or you might be able to fit solutions a solutions that satisfies most constraint within something you can do early squares solutions and so on right.

So let us focus mostly on underdetermine system which is what we already observe in biological systems of metabolic networks right. So now you have a system SV = 0 how do you solve it? So let us just recap so we are looking at a steady state mass balance as SV = 0 right and we want to look at what is V? So V is the set of fluxes write it in horizontal fashion of the transpose the space on the slide.

So V is nothing but and you can also think of external fluxes this is going to be your R cross 1 vector you are going to find out this is what metabolize S. What is the size of the vector right this is going to M cross R this is R cross 1 this is M cross 1 clear. So we basically discriminate between the internal fluxes and the external fluxes involve exchange with outer environment. So you will typically have a cell like this all these are internal fluxes and let us say.

So think of a cell was several internal success internal reaction so these are metabolites and you can think of all these as internal fluxes and then you can also some nutrients coming in things being secreted outside by the cell important products and so on. So these are what we call the exchange fluxes and these are the internal fluxes and so on. These are not necessarily reactions so you could still write them as a reaction I would you would write them as or essentially A coming in this cell.

And this would just be something like D going out so the stoichiometric column corresponding to this it would just be -1 and everything else is 0 this would actually has been we can also have it as A external and giving A and so on. But the easiest way to write it as just you know A coming in right so then you can balance it with the rest of A it will become clearer then we look at it example.

And then you go ahead and add constraints what kind of constraint you add stoichiometric is accounted for right this is your stoichiometry constraints right whereas you can constraint on reversibility. So there are irreversible reactions which you will say can go in only one direction so you can say 0 less than Z less than infinity in practice not infinity but a large number and you have reversible reactions with basically can go in either direction and you can exchange fluxes that take can either be irreversible or reversible.

So you could think of a particular flux being like this you can go in both direction so you get this value as -30 it means it goes in this direction you have to commit to a narrow sign in this directions place but once you do that let us say this is a reversible reaction. If it now have a value -30 it means it is actually 30 moles per liter of (( )) (09:57) going in the opposite direction. So how do you go about solving this problem now.

You have a overhead domain system which means you have to find out a single solutions if you want to find out a single solutions to the problem you need to come up some other constraints or some other strategy. How would you go about it. So if I wanted to solve this this system V1 + V2 = 10 one way of potentially solving it is if I said told you some other conditions if I said this makes it a little better but the problem is that I have no again it almost classify the solution.

Now there is only one possible solutions let us possible so 5 + 5 right is it clear? So you need to give some other constraints or going for some optimization. So usually resolve to maximize something let us say solve this subject Max V1 then the answer is ready simple 10, 0 solve this subject to Max V2 0, 10 right. So it is easy to find potentially a easy solution not necessarily always when you start specifying an optimization criteria.

So typically we found that if you try to maximum growth or minimum nutrient uptake they are useful optimization to carry out to find out what is the possible flux distribution. So it turns out to the maximization growth is a very useful objective function. (()) (12:24) different objective functions like minimizing neutering uptake and maximize metabolize production or a efficient metabolize channeling and so on we look at these little later.

But you basically minimize or maximize some linear combination of fluxes subject to your stoichiometric mass balance constraints right. And you also look what is perturbation analysis and you do in silico, gene deletion, drug inhibition so on and henceforth. We will see what these are you know in later class.

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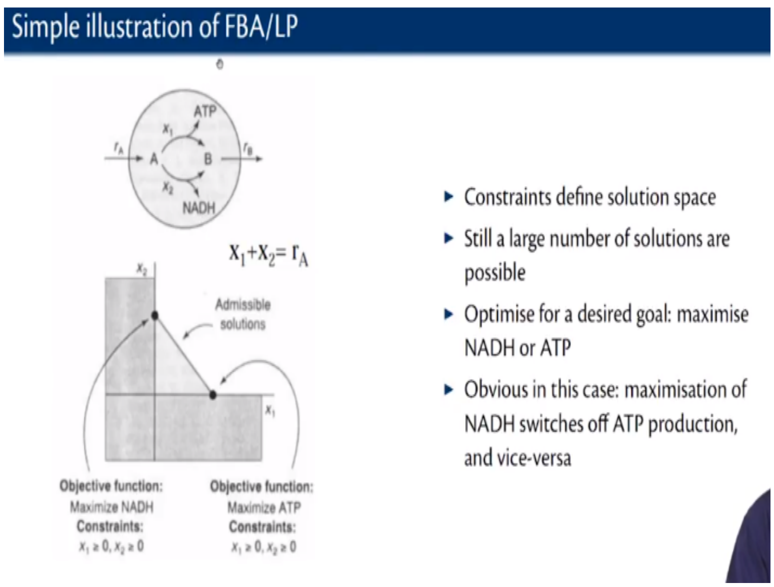

So let us look at very simple example right so here you have reaction coming here like this A giving B + ATP giving you now NADH + B on this deduction so it is not exactly balance in that sense but you can imagine that RA = RB = X1 + X2. This is again very similar to something you studied in school this kind of circuit diagram which splits across (())(13:32) Law. (()) (13:40) is basically charge balance here we have mass balances.

Essentially a very same think so here you have constraints say X1 greater than 0 X2 greater than 0 and X1 + X2 = RA. So because of that all your solutions lie on this line now you can say maximize X1 which means we will get this point X1, you know RA, 0 or you know you maximize you know this point you will get to again RA0 , RA as the other point right.

So here you basically have switching of one production and so on right so in this case the maximization of NADH stiches of AT production and maximization of ATP switches of NAH production right but in you can have whatever appropriate objective function you want.