**Material and Energy Balances**
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**Module No # 06**
**Lecture No # 30**
**The Unreasonable Effectiveness of Material Balance**

Hello everybody, welcome back to the course on material and energy balances, so until now we have covered all the fundamentals related material balances when we talk about process industries. So we looked at many chemical and biochemical processes been able to apply material balances and perform calculations based on law of conservation of mass. And this has helped us in designing processes understanding what would be required the input required output and desired output and so on.

Today we are going to have a guest lecture so he is faculty in IIT Madras this is Mr.Karthik Raman he is actually working as a faculty in a department of Biotechnology IIT Madras. He is going to talk about an application of material balances to biological systems instead of looking a process level systems he will be talking about how to apply material balances for metabolism and metabolic pathways.

So he will be talking about how these principles are discussed till now can actually be applied for simple metabolic pathways and obtained effective balances and perform calculations which are similar to once which we have been performing. So for the first few lectures of this week it will be Dr.Karthik Raman who will be teaching these aspects. So welcome to this video so today I am guest lecturer my name is Dr.Karthik Raman I am also from the department of biotechnology IIT Madras.

And I work in the area of computational system biology I am guest lecturer in this course on material and energy balances that Dr. Vignesh has been teaching and today my lecture you may see is title the unreasonable effectiveness of material balances this is actually a play on a very popular essay in the sixties which was the unreasonable effectiveness of mathematics in the natural sciences.

So basically they found that math was able to answer several interesting question in biology and natural sciences. And similarly I will show you how you know you think that material balances very simple very you know it is just a systematic thinking and so on and as applications to say chemical reactors or small chemical process so on. But today I will show you how we can apply the large cellular system like say a growing equal cell to predict its growth rate and so on. So really speaking my talk as title constraint base analysis of cellular metabolism.

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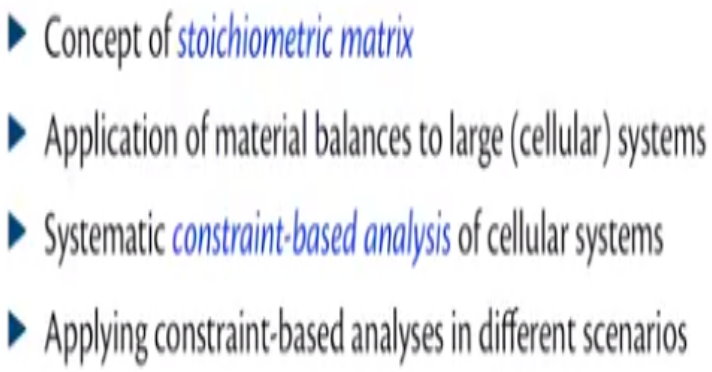


So what is it I am going to look at today I am going to teach you the concept of what is known as the stoichiometric matrix and how do you apply material balances to cellular system large cellular systems and how we systematically apply this concept known as constraint base analysis. To predict the growth rate or the pheno type or the behavior essentially of the cellular system.

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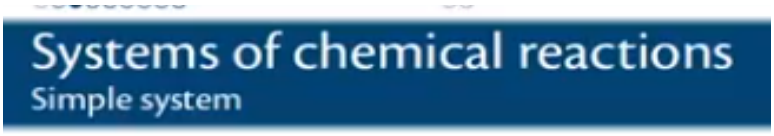


R1: A+B → 2C
R2: B+2C → D
R3: B+3D → E

And how do you for example apply it when you remove a genie from a cell and so on so what is metabolism or what kind of system are we talking about here you must be familiar with these kinds of system where in a simple reaction A + B going to 2C, B + C going to D, B + 3D going to E and so on. What is important to notice it? There is stoichiometric in each of these cases and we have only three reactions here.

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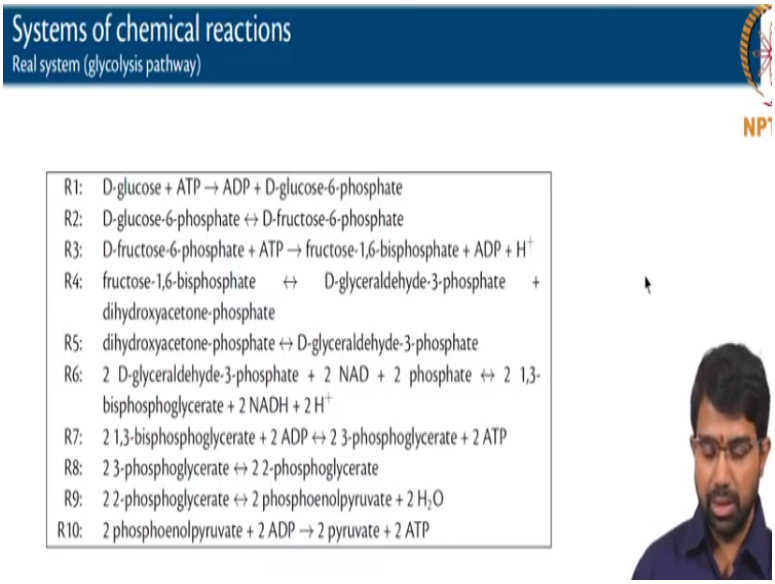


This is the more real system which is like glycolysis so it starts from de-glucose + ATP ADP +glucose 6 phosphate and you have about 10 reactions finally (()) (03:47) in the production two moles of ATP and 2 moles of pyruvate from 1 mole of glucose right. So this is very important so we will see why it is become important aspect when we model the cellular system and so on.

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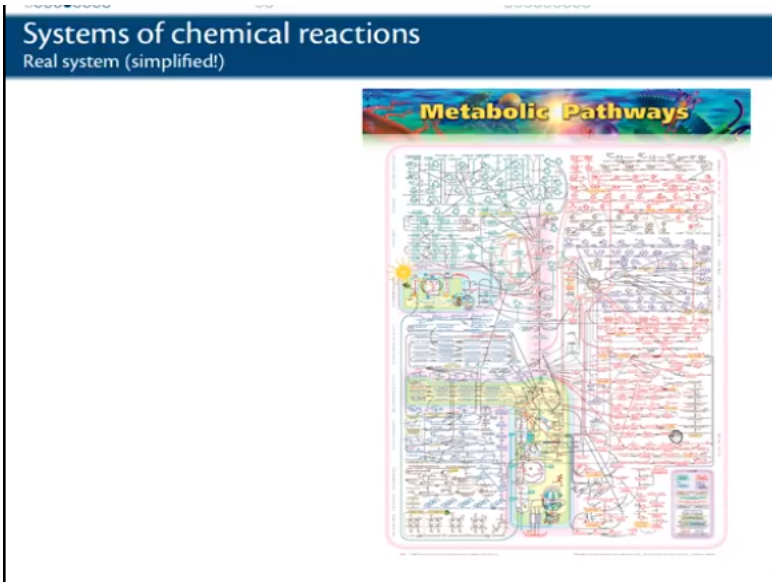


And this is the simplified view I like to say it as simplified because of various reasons so to simplified view of what happens within a living cell right. So what you have here is you have thousands of small molecules are metabolites all undergoing different fades you know there are thousands of reactions happening in the cell causing conversions in several of these molecules to other molecules and so on.

And this changes with time and with the time of the day what you eaten and so on so there is a very complex network that operates with inside living cell depending upon the availability of various nutrients and various metabolize and I call this simplified because each of these molecules actually represent avocado number of molecules like Nano molar concentration so we are talking about 10 to the 15 molecules and so.

So there are 10 to the 15 molecules of each type right that you see here interacting in thousands of or thousands of different ways within a any living cell.

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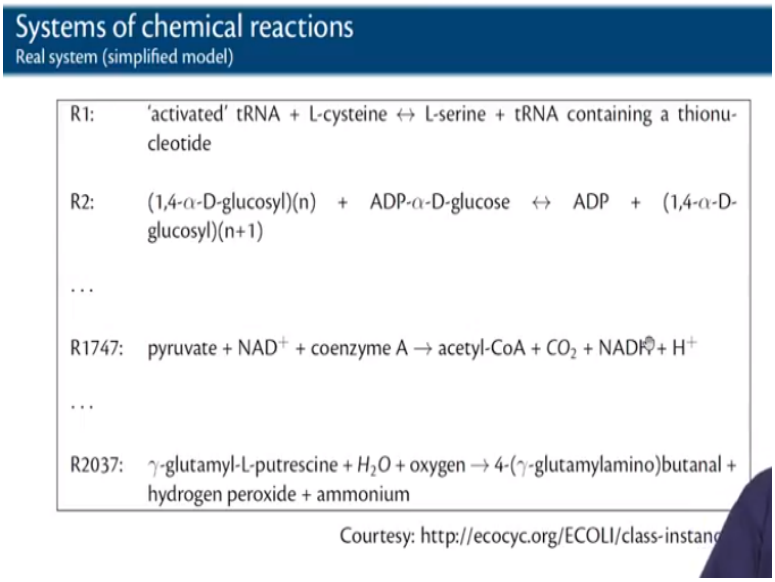


But if you are going to model it I would just write it down long linear set off reactions so this is an alphabetical list which goes from activated TRNA + Cell 16 something all the way up to gamma glut amyl putrescine and somewhere on the middle may be able to recognize that you have this (()) (05:28) acid cycle reaction right so this is what a model essentially works with.

We have a long system of reactions and we want to because we are discussing in this course you want to write a mass balance for it or a material balance for it and then see how we can model it.

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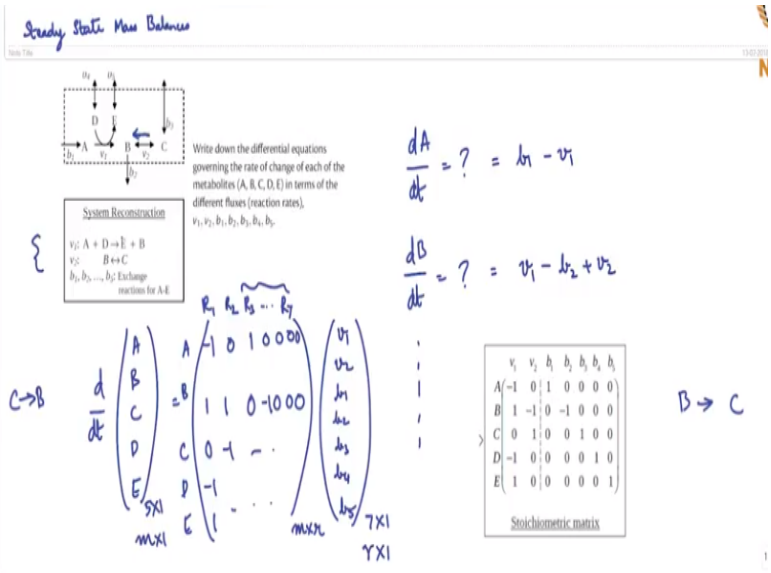


So let us just step back and take a very simple system that you see on the screen here and can you write down the equations governing the rate of change of each of these metabolites. So what

is DS / DT? What is DB / DT an d so on? You may be able to say that DA / DT will be B1 – V1, DB / DT could be V1 which brings in V1 – B2 which takes out B and you may have to commit to a particular angle here.

So this is shown in both arrows because it is a reversible reaction, but essentially we have to you can say that it is goes in this directions and if the value V2 is greater than 0 then it goes in this directions if it is less than 0 it is B going to C. Let us assume that it goes in this direction so in that case it would be V1 – V2 + V2 and so on. So if you were to write out all these reactions you can potentially show them in a matric form so this is going to be a 5 cross 1 or number of metabolites cross 1.

This is going to be 7 cross 1 or number of fluxes or number of reactions last one and this is therefore going to be N cross air. So you can actually think of writing this as corresponding to reaction V1 or maybe I could say reaction 1, reaction 2, reaction, 3, reaction 7 and the first two are real reactions you see here and the remaining 5 were what are known as exchange reactions. So this is a nice matrix we look at in greater detail in a may be in a few slides but this is basically all you have to how you have to fill up this matrix is.

We can write out the equations carefully fill it up but more easier is you just whatever is on left hand side whatever reactant you get a negative coefficient whatever is on product side we give it up positive coefficient side. So you can think of this as a so A is on the left hand side + B is on the right hand side right and again D is also on the left hand side and E is on the right hand side. So this is basically A + D going to A + B.

So this is the first column of the stoichiometric matrix and if you see DA / DT will be -1 into V1 + 1 into B1 right. So rest of them will all be 0 will have 4 zeros so DB / D will be V1 – V2 + V2. But if you see B is on the so this is second reaction V is on the left hand side because V is on the reaction is C going B right and so on. So and C will have a – 1 right because that DC / DT will be – V2 and so on. Because V2 takes away –D2 + D3 and so on right so you can fill this up so final matrix will look like this.

You may see there is like a minor variation here or not yes because I have assumed this as B going to C as the direction not this way. But essentially you can basically just fill this out directly from the set of reactions that you have.

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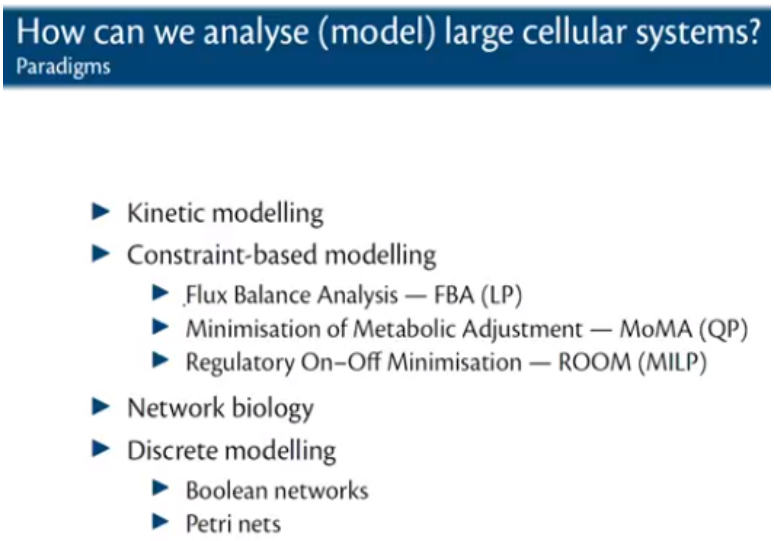


So once you have the stoichiometric matrix you can do a lot of things so let us now take a step back and look at what are the strategies to model large cellular systems? You can write down differential equations and model them that is known as kinetics modeling and I will tell you shortly why that is difficult or then you can do something know as constraint base modeling which is what I will focus on for most of today's lecture.

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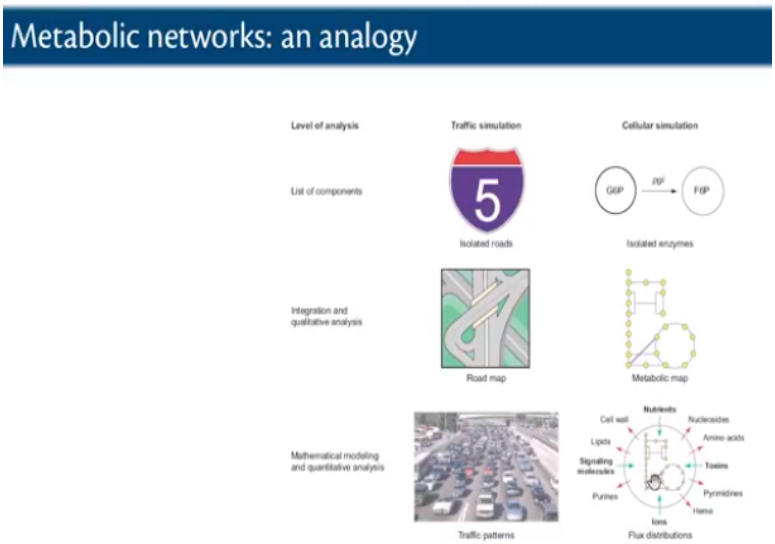

So this is to be a another analogy of another metabolic network really is so we can think of it is essentially a set of long set of reactions as whereas model is concerned but give you a picture is going to think of isolated reactions like being road if you were to analogy with traffic networks when a metabolic map is similar to a road map and the most interesting part comes when you look at the flux distribution or the metabolize or traffic distributions.

You know how much traffic is being carried in each road so you know what are all the important roads what are the block roads and so on and you can make similar analysis when you are looking metabolic networks.

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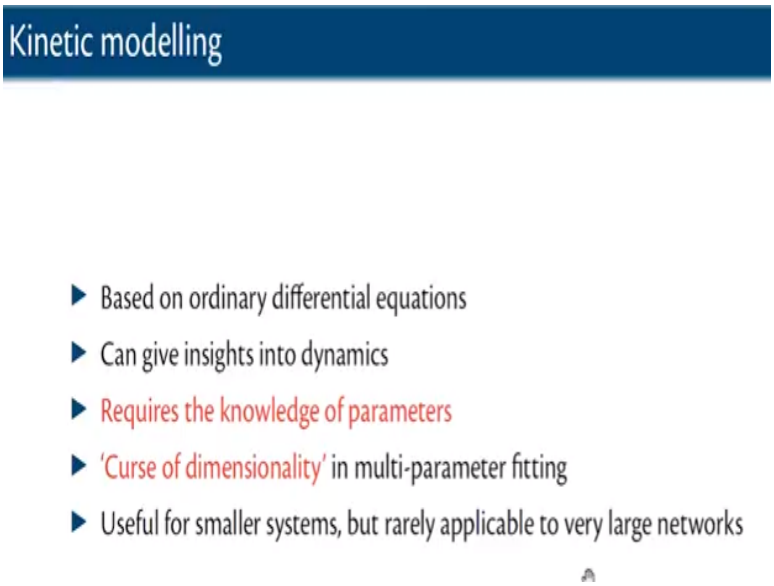


So what is kinetic modeling you basically write DA / DT is some you know V max into S / K + M if you know my (()) (11:34) and so or the mass action as the case may be and so on and important thing is it can obviously give you insides into dynamics. So how does A change with time how does it B change with time and so on but it requires a knowledge of parameters you need to know all the case in your system like K1, K2, K3 and so on.

And this becomes and nightmare if you want to estimate them from data I will not get in the details in this course but this is basically very tricky especially when you have a large number of parameters of it right you may have fit simple equations or you deduct simple (()) (12:07) and so on experiment and just to find out two parameters like the KM and V max correspond to the

enzyme where it becomes much harder when you are trying to solve let say a system of 2000 reactions right.

So you can think if there are two parameters to reach reaction we are looking at a sematic 4000 parameters from data which is very difficult wide difficult it is impossible. So it is useful for smaller systems but rarely applicable to larger networks of the start with we want to work with right. So you want to take equal I which has 2000 reactions and make predictions this is not going to work. So what do we do we going to something known as constraint based modeling