Thermodynamics for Biological Systems:
Classical and Statistical Aspects

Prof. G.K. Suraishkumar
Department of Biotechnology
Indian institute of Technology - Madras

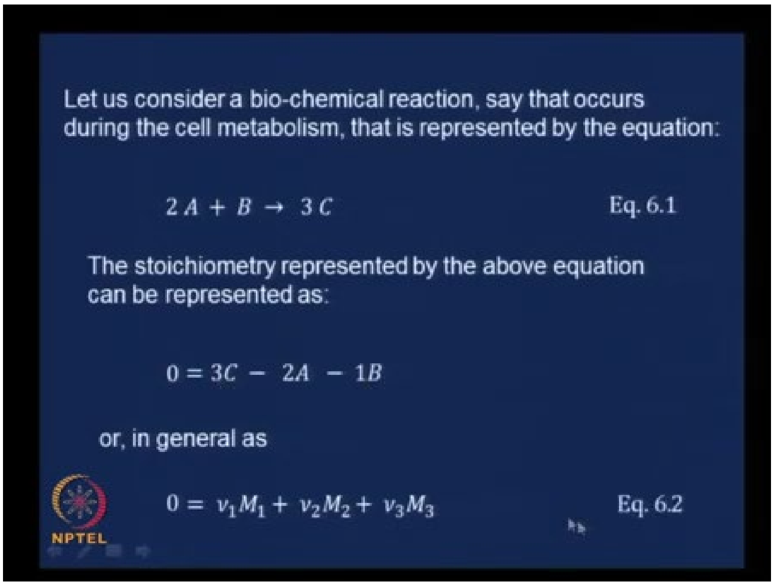
Lecture – 46
Criteria for Bioreaction Equilibria

Welcome back!

In this lecture, we will begin the last module for this course. The last module is module six on reaction equilibria. If you recall in the last module, we had explicitly said that we will not consider any reactions. We had situations like that in biological systems, plenty, and therefore we could use whatever we developed in that module to explain many situations. But as you all know reactions take place all the time. Whether it is macro-biological system, for example, a bio-process – there is reactions taking place. Or even at the cell level - the cell is alive and kicking only because of the thousands of reactions that take place in a cell.

Under … reasonable conditions, we could still consider this cell as a continuum, and therefore apply these principles of analysis to the cell also. Therefore, the reactions that take place in the cell can also be considered to be a valid system for the application of these principles. So, let us start looking at the bases to develop reaction equilibria, the conditions for the same, or the criteria for the same. Earlier, if you recall, in module five, we had criteria for the phase equilibria or when there were no reactions that we are taking place, and so on. We will develop similar criteria, when reactions are present.

(Refer Slide Time: 02:14)



Let us consider a bio-chemical reaction, say that occurs during the cell metabolism, that is represented by the equation:

$$2\,A + B \rightarrow 3\,C \qquad \text{Eq. 6.1}$$

The stoichiometry represented by the above equation can be represented as:

$$0 = 3C - 2A - 1B$$

or, in general as

$$0 = \nu_1 M_1 + \nu_2 M_2 + \nu_3 M_3 \qquad \text{Eq. 6.2}$$

To do that, we will touch up on many things that you may already be somewhat familiar with, because of exposure in eleventh, twelfth standards, or even in courses that you took before … you took this thermodynamics course. … Let us consider a bio-chemical reaction, say that occurs during a cell metabolism, say a reaction in glycolysis. Let us represent that … this is a hypothetical equation … let us represent that by

$$2\,A + B \rightarrow 3\,C$$

I had just picked random numbers here, 2 A plus B giving you 3 C. Let us call that equation 6.1. The stoichiometry represented by the above equation can be written as

$$0 = 3C - 2A - 1B$$

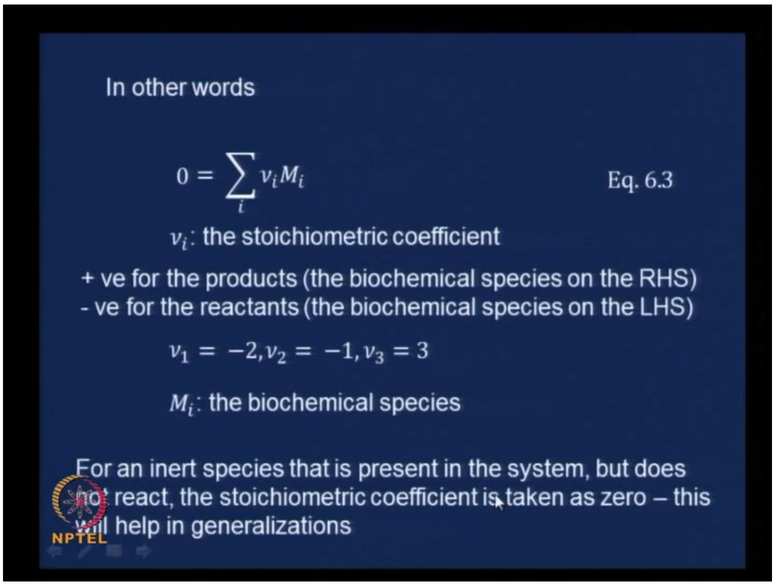
I have deliberately written it like this.

I have taken 3 to be positive, you know the product associated coefficient to be positive, minus 2 A minus 1 B equals 0. Or, in general, I could write this stoichiometry as, or I could represent the reaction as 0 equals

$$0 = \nu_1 M_1 + \nu_2 M_2 + \nu_3 M_3$$

In a minute, I will tell you what nu s and M s are. Let us call this equation 6.2, I wrote it in this form for a reason.

(Refer Slide Time: 05:20)



In other words

$$0 = \sum_i \nu_i M_i \qquad \text{Eq. 6.3}$$

ν_i: the stoichiometric coefficient

+ ve for the products (the biochemical species on the RHS)
- ve for the reactants (the biochemical species on the LHS)

$\nu_1 = -2, \nu_2 = -1, \nu_3 = 3$

M_i: the biochemical species

For an inert species that is present in the system, but does not react, the stoichiometric coefficient is taken as zero – this will help in generalizations

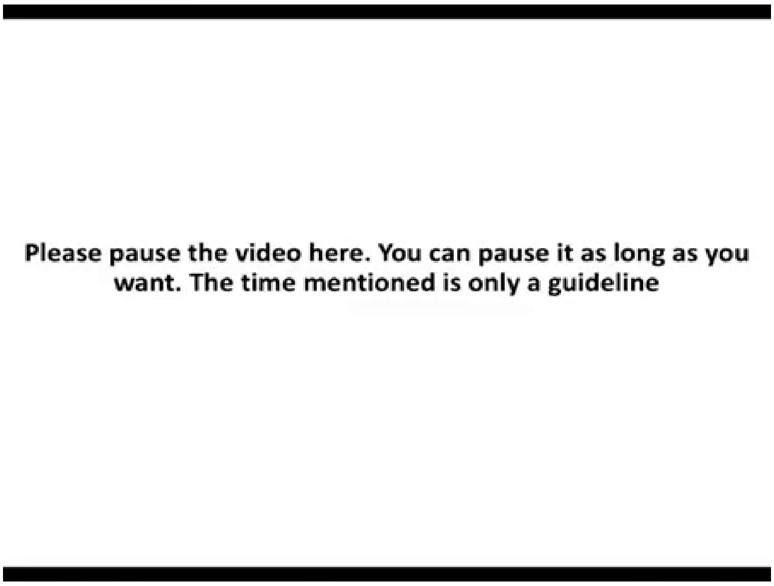
I can now make this into a compact notation,

$$0 = \sum_i \nu_i M_i$$

This is the reason why I had written at that way; equation 6.3, where nu i is this stoichiometric co-efficient which we will take as positive for the products of the reaction or the bio-chemical species on the right hand side of the equation. Like this; you know, if this is the equation, the coefficients on the right hand side, we are going to take as positive. And the coefficients on the left hand side, which is that for the reactance, we are going to take as negative.

So that works well here, 3 C was positive minus 2 A, reactant, negative, minus 1 B, reactant, negative. Therefore, negative for the reactants, which are the bio-chemical species on the left hand side. I have already given you an answer, but why did not you take about five minutes and complete it? Why don't you write down nu 1, nu 2 and nu 3 for the reaction that we just saw? Go ahead, take about five minutes, and write this down. Go ahead please.

(Refer Slide Time: 05:44)



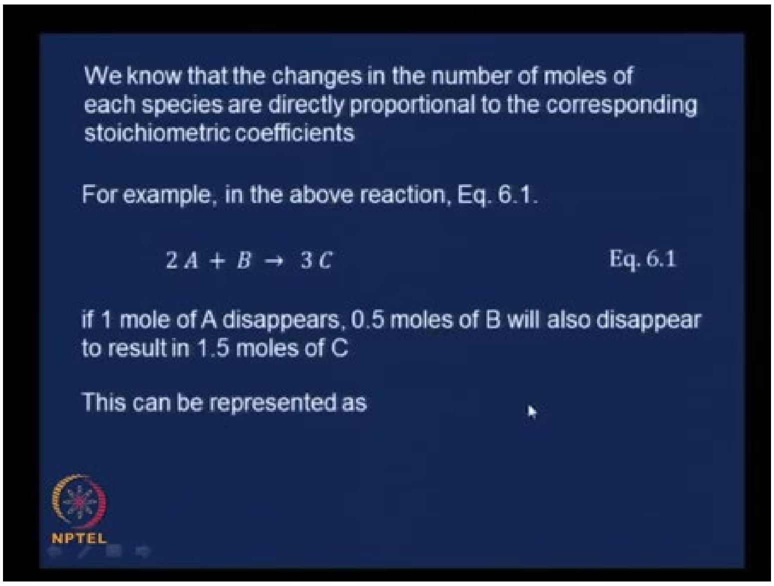
Please pause the video here. You can pause it as long as you want. The time mentioned is only a guideline

If you had followed the reasoning that we presented earlier, you can easily see that nu 1 was the coefficient of A, minus 2, nu 2, the coefficient of B, minus 1, and nu 3, the co-efficient of C 3.

$$\nu_1 = -2, \quad \nu_2 = -1, \quad \nu_3 = 3$$

And M i is the various biochemical species A, B, or C in this particular example that is considered in the reaction. Let me state this although we would not be looking at this in great detail, but it is good to state this here. If there is an inert species that is present in the system, for an inert species, that is present in the system, but does not react, the stoichiometric coefficient is taken as zero. Have this in mind. Whenever it becomes necessary to use this, please use this, and that will make things a lot more general.

(Refer Slide Time: 07:09)



We know that the changes in the number of moles of each species are directly proportional to the corresponding stoichiometric coefficients

For example, in the above reaction, Eq. 6.1.

$$2A + B \rightarrow 3C \qquad \text{Eq. 6.1}$$

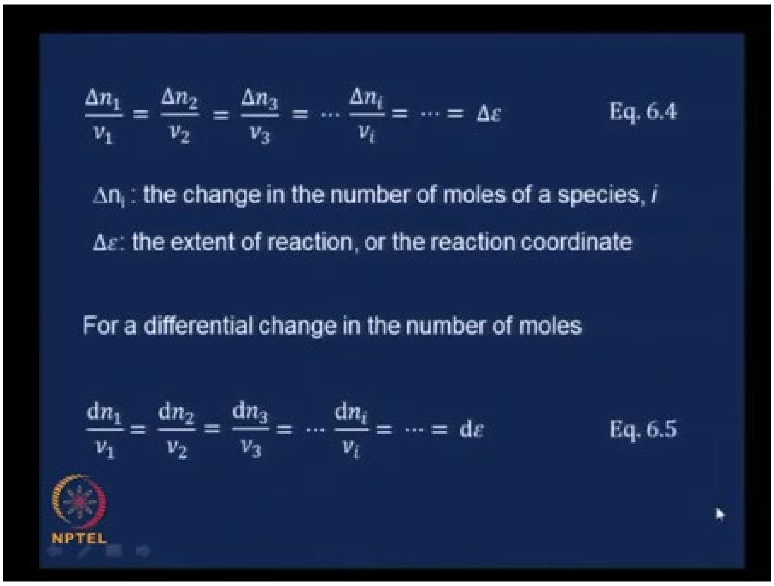
if 1 mole of A disappears, 0.5 moles of B will also disappear to result in 1.5 moles of C

This can be represented as

Now, let us go back to what we already know. We know that the changes in the number of moles of each species in a reaction are directly proportional to the corresponding stoichiometric coefficients. What do I mean by that?

For example, in the above reaction given by equation 6.1, which is 2 A plus 3 B equals 3 C, if we divide this equation two throughout by 2, we get A plus half B equals three by two C. Or, if 1 mole of A disappears, half a mole of B will also disappear to result in three by two or 1.5 moles of C. Therefore, the changes in the number of moles of each species are directly proportional to the corresponding stoichiometric coefficients.

(Refer Slide Time: 08:07)



$$\frac{\Delta n_1}{\nu_1} = \frac{\Delta n_2}{\nu_2} = \frac{\Delta n_3}{\nu_3} = \cdots \frac{\Delta n_i}{\nu_i} = \cdots = \Delta\varepsilon \qquad \text{Eq. 6.4}$$

Δn_i : the change in the number of moles of a species, *i*

$\Delta\varepsilon$: the extent of reaction, or the reaction coordinate

For a differential change in the number of moles

$$\frac{dn_1}{\nu_1} = \frac{dn_2}{\nu_2} = \frac{dn_3}{\nu_3} = \cdots \frac{dn_i}{\nu_i} = \cdots = d\varepsilon \qquad \text{Eq. 6.5}$$

This particular aspect can be represented as

$$\frac{\Delta n_1}{\nu_1} = \frac{\Delta n_2}{\nu_2} = \frac{\Delta n_3}{\nu_3} = \cdots \frac{\Delta n_i}{\nu_i} = \cdots = \Delta \varepsilon$$

the change in number of moles of 1 is delta n 1. We will call this equation 6.4.

delta epsilon is the extent of a reaction. It is also called the reaction coordinate, if you recall this term from your earlier courses. Delta epsilon- the reaction coordinate, or epsilon is the reaction coordinate.

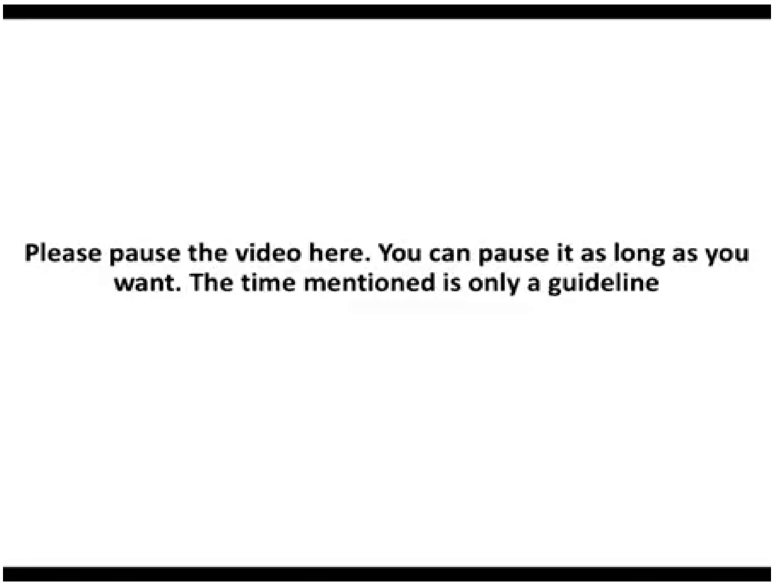
For a differential change in the number of moles, we can replace these big differences by the differential change. And therefore, we can write

$$\frac{dn_1}{\nu_1} = \frac{dn_2}{\nu_2} = \frac{dn_3}{\nu_3} = \cdots \frac{dn_i}{\nu_i} = \cdots = d\varepsilon$$

We will call this equation 6.5. …What I would like you to do is now, take some time, I will tell you how much time. Look at glycolysis, the various reactions in glycolysis, which is one of the central pathways in the cell,

Remember … glucose goes to glucose six phosphate. Glucose from outside the cell gets inside the cell first and then it will goes to glucose six phosphate, fructose six phosphate and so on, all the way down to pyruvate. Choose that pathway, which is called glycolysis. Each one of those steps as you know is catalyzed by an enzyme. Take those individual reactions and write equivalent expressions for, let us say, five of those reactions. I am going to give you about twenty minutes to do that. Take about twenty minutes; go back to your biochemistry text book, biochemistry notes. Choose five reactions that take place in glycolysis and write this down, for improving the comfort level in using this particular equation. Go ahead please.

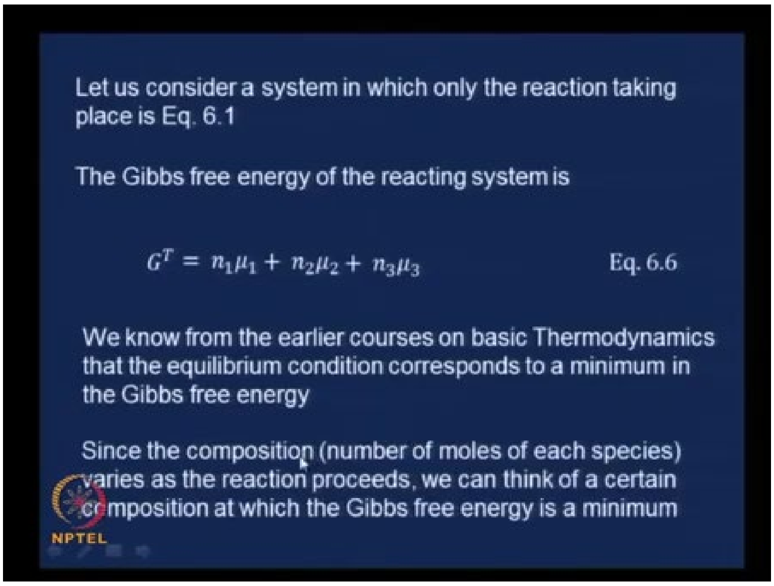
(Refer Slide Time: 11:14)



Please pause the video here. You can pause it as long as you want. The time mentioned is only a guideline

Now, hopefully, you would have gotten back the level of comfort that you had in your earlier classes while dealing with stoichiometric coefficients, by writing down the relationships between the stoichiometric coefficients for at least five reactions in glycolysis. The choice of the reactions were yours. Of course, they were reversible reactions but that does not matter.

(Refer Slide Time: 12:08)



Let us consider a system in which only the reaction taking place is Eq. 6.1

The Gibbs free energy of the reacting system is

$$G^T = n_1\mu_1 + n_2\mu_2 + n_3\mu_3 \qquad \text{Eq. 6.6}$$

We know from the earlier courses on basic Thermodynamics that the equilibrium condition corresponds to a minimum in the Gibbs free energy

Since the composition (number of moles of each species) varies as the reaction proceeds, we can think of a certain composition at which the Gibbs free energy is a minimum

Now, let us look at the condition for bio-reaction equilibrium. Let us consider a system in which the only reaction taking place is equation 6.1, which is two A plus B giving you three C; that was the reaction given by 6.1. The Gibbs free energy of the reacting system is G^T as we had seen earlier. That can be written as

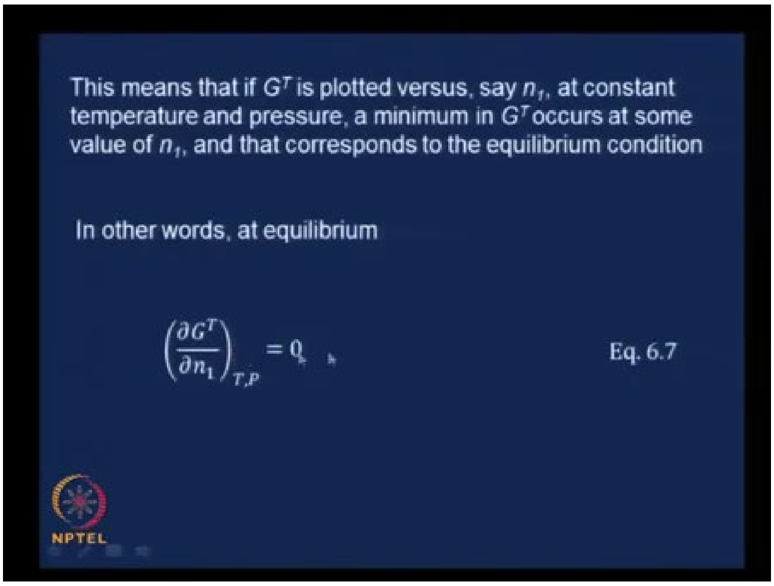
$$G^T = n_1\mu_1 + n_2\mu_2 + n_3\mu_3$$

Let us call this equation 6.6.

Now, we know from either chemistry courses, the thermodynamic aspects of chemistry courses, or some specific courses that you would have take earlier that the equilibrium condition corresponds to a minimum in the Gibbs free energy. I am just going to take this directly from whatever we know earlier that a minimum in Gibbs free energy occurs at equilibrium. Since, the composition or the number of moles of each species varies as the reaction proceeds, we can think of a certain composition at which the Gibbs free energy is a minimum.

You know the reaction is going to take place, when the reaction takes place, with time, the number of moles of each species is going to change. We already know from earlier that equilibrium occurs when the Gibbs free energy is a minimum. In other words, there must be some combination of moles of these species involved in the reaction at which the Gibbs free energy turns out to be a minimum. That is the whole basis of the argument here.

(Refer Slide Time: 14:42)



This means that if G^T is plotted versus, say n_1, at constant temperature and pressure, a minimum in G^T occurs at some value of n_1, and that corresponds to the equilibrium condition

In other words, at equilibrium

$$\left(\frac{\partial G^T}{\partial n_1}\right)_{T,P} = 0 \qquad \text{Eq. 6.7}$$

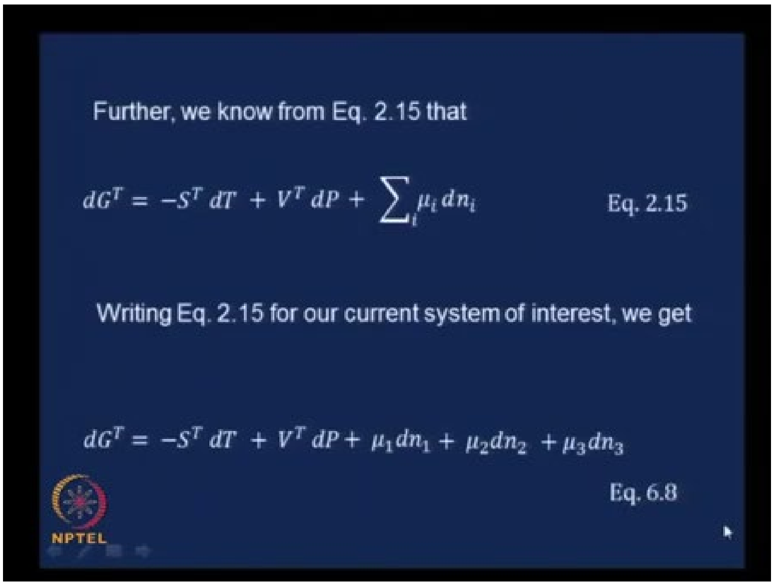
This means that if G^T, the total free energy, is plotted as a function of let us say n1, the number of moles of species 1 – that is the only thing that we can represent on one co-ordinate. That is only reason for taking n 1. At constant temperature and pressure, a minimum in G T occurs at some value of n 1, and that corresponds to the equilibrium condition. If we write it mathematically, at equilibrium,

$$\left(\frac{\partial G^T}{\partial n_1}\right)_{T,P} = 0$$

This is just a mathematical statement of the fact that we knew from earlier classes that the free energy, Gibbs free energy, of a system is minimum at equilibrium.

Therefore, the slope of the GT versus n1 curve goes to zero at that particular point. You know it is a minimum and therefore, this slope goes zero. Let us call this equation 6 7.

(Refer Slide Time: 15:57)



Further, we know from Eq. 2.15 that

$$dG^T = -S^T\,dT + V^T\,dP + \sum_i \mu_i\,dn_i \qquad \text{Eq. 2.15}$$

Writing Eq. 2.15 for our current system of interest, we get

$$dG^T = -S^T\,dT + V^T\,dP + \mu_1 dn_1 + \mu_2 dn_2 + \mu_3 dn_3$$

Eq. 6.8

Further, we know from equation 2.15 that

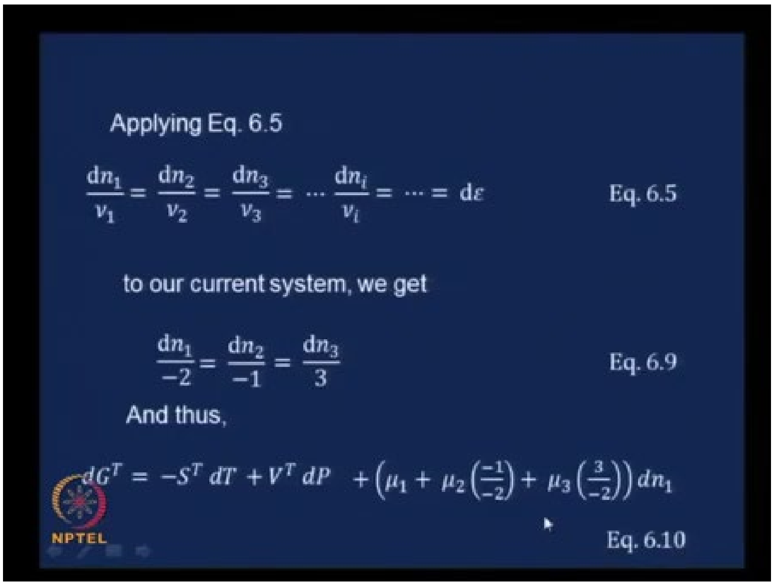
$$dG^T = -S^T\,dT + V^T\,dP + \textstyle\sum_i \mu_i\,dn_i$$

you recall this equation? This equation we have used many times. If we write equation 2.15 for our current system of interest, which is the system that consists of that only reaction taking place, we can write

$$dG^T = -S^T\,dT + V^T\,dP + \mu_1 dn_1 + \mu_2 dn_2 + \mu_3 dn_3$$

Let us call this equation 6 8.

(Refer Slide Time: 17:02)



Applying Eq. 6.5

$$\frac{dn_1}{\nu_1} = \frac{dn_2}{\nu_2} = \frac{dn_3}{\nu_3} = \cdots \frac{dn_i}{\nu_i} = \cdots = d\varepsilon \qquad \text{Eq. 6.5}$$

to our current system, we get

$$\frac{dn_1}{-2} = \frac{dn_2}{-1} = \frac{dn_3}{3} \qquad \text{Eq. 6.9}$$

And thus,

$$dG^T = -S^T\,dT + V^T\,dP + \left(\mu_1 + \mu_2\left(\frac{-1}{-2}\right) + \mu_3\left(\frac{3}{-2}\right)\right)dn_1 \qquad \text{Eq. 6.10}$$

Now, if we apply 6.5, equation 6.5, which is

$$\frac{dn_1}{\nu_1} = \frac{dn_2}{\nu_2} = \frac{dn_3}{\nu_3} = \cdots \frac{dn_i}{\nu_i} = \cdots = d\varepsilon$$

In our current system , we get

$$\frac{dn_1}{-2} = \frac{dn_2}{-1} = \frac{dn_3}{3}$$

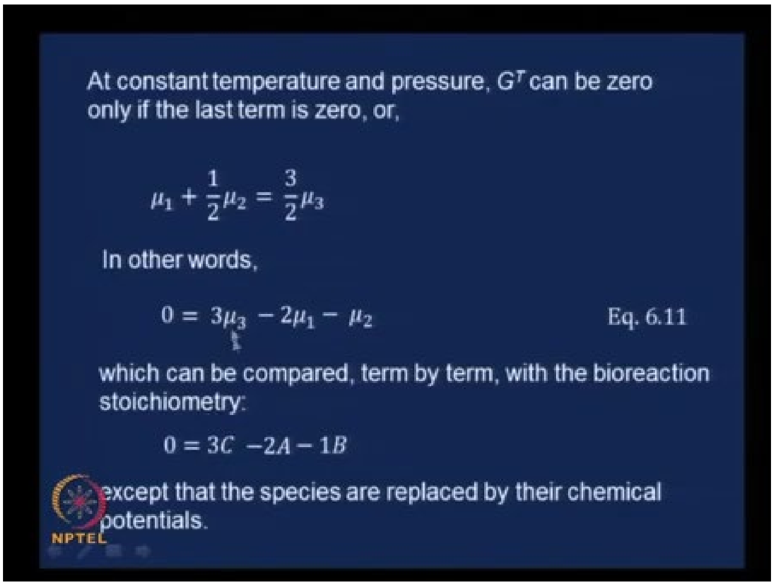
Since it is a reactant, this becomes minus one. Similarly, here also 2 was a stoichiometric co-efficient of A, and since it is a reactant, by our convention, this becomes minus 2; equals d n 3 by this stoichiometric coefficient of the product C, and since it is a product we have a positive terminology here, plus 3. So, dn1 by minus 2 equals dn2 by minus 1 equals dn3 by 3.Let us call this equation 6.9.

Therefore,

$$dG^T = -S^T\,dT + V^T\,dP + \left(\mu_1 + \mu_2\left(\frac{-1}{-2}\right) + \mu_3\left(\frac{3}{-2}\right)\right)dn_1$$

Let us call this equation 6 10.

(Refer Slide Time: 19:17)



At constant temperature and pressure, G^T can be zero only if the last term is zero, or,

$$\mu_1 + \frac{1}{2}\mu_2 = \frac{3}{2}\mu_3$$

In other words,

$$0 = 3\mu_3 - 2\mu_1 - \mu_2 \qquad \text{Eq. 6.11}$$

which can be compared, term by term, with the bioreaction stoichiometry:

$$0 = 3C - 2A - 1B$$

except that the species are replaced by their chemical potentials.

And at constant temperature and pressure, G^T can be zero. It can be zero, only if the last term is zero, because at constant temperature and pressure as dT is zero, dP is zero anyway at constant temperature and pressure. Therefore dG^T can be zero, only if this term goes to zero. Therefore,

$$\mu_1 + \frac{1}{2}\mu_2 = \frac{3}{2}\mu_3$$

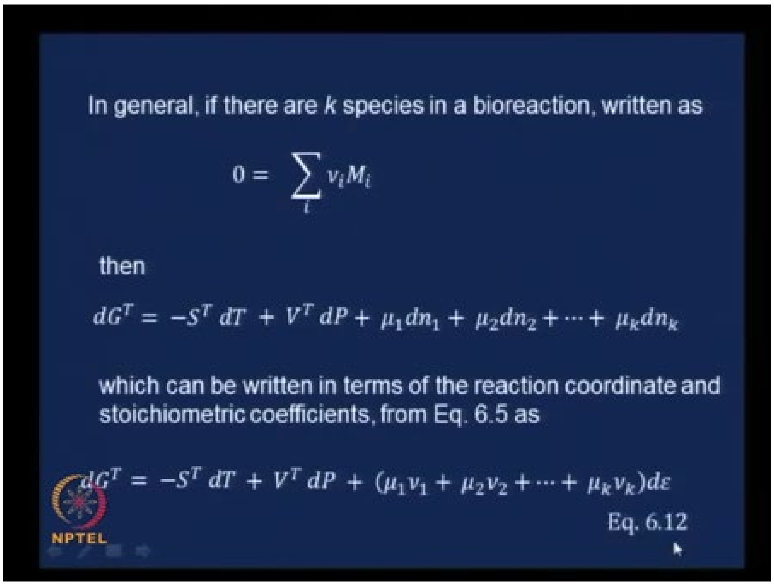
$$0 = 3\mu_3 - 2\mu_1 - \mu_2$$

We will call this equation 6.11, which can be compared, term by term with the bio-reactions stoichiometry as

$$0 = 3C - 2A - 1B$$

except that, this species are replaced by their chemical potentials. Can you see this here? 3 C minus 2 A minus 1 B, whereas here for the condition of equilibrium, we got 3 mu 3 minus 2 mu 1 minus mu 2.

(Refer Slide Time: 20:41)



In general, if there are *k* species in a bioreaction, written as

$$0 = \sum_i v_i M_i$$

then

$$dG^T = -S^T\,dT + V^T\,dP + \mu_1 dn_1 + \mu_2 dn_2 + \cdots + \mu_k dn_k$$

which can be written in terms of the reaction coordinate and stoichiometric coefficients, from Eq. 6.5 as

$$dG^T = -S^T\,dT + V^T\,dP + (\mu_1 v_1 + \mu_2 v_2 + \cdots + \mu_k v_k)d\varepsilon$$

Eq. 6.12

Therefore, in general, if there are k species in a bio reaction written as

$$0 = \sum_i v_i M_i$$

Then,

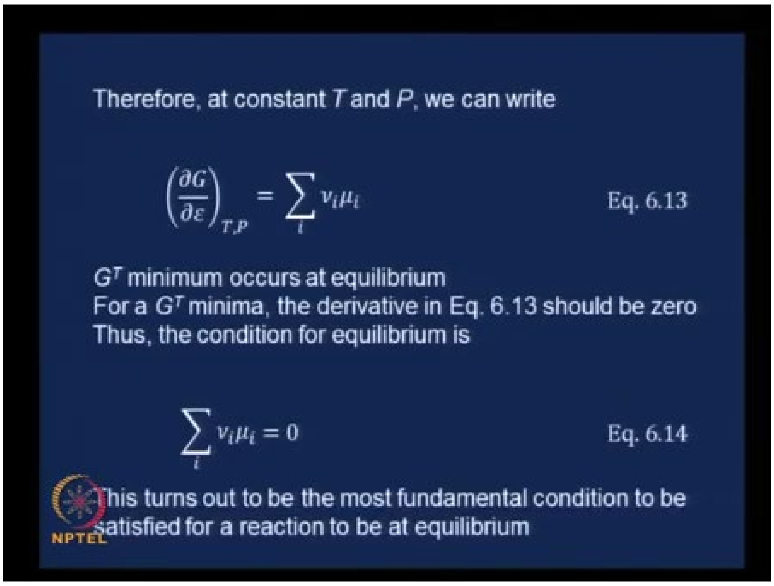
$$dG^T = -S^T\,dT + V^T\,dP + \mu_1 dn_1 + \mu_2 dn_2 + \cdots + \mu_k dn_k$$

We can write this in terms of e reaction coordinate and the stoichiometric coefficients from equation 6.5, we get

$$dG^T = -S^T\,dT + V^T\,dP + (\mu_1 v_1 + \mu_2 v_2 + \cdots + \mu_k v_k)d\varepsilon$$

I hope you are able to see this please go back to Equation 6.5 if you are unable to see this. This will drop out from there. You know the relationship between the various d ns and d Epsilons will drop out from there and from that we will get this expression. We will call this equation 6.12.

(Refer Slide Time: 22:17)



Therefore, at constant T and P, we can write

$$\left(\frac{\partial G}{\partial \varepsilon}\right)_{T,P} = \sum_i \nu_i \mu_i \qquad \text{Eq. 6.13}$$

G^T minimum occurs at equilibrium
For a G^T minima, the derivative in Eq. 6.13 should be zero
Thus, the condition for equilibrium is

$$\sum_i \nu_i \mu_i = 0 \qquad \text{Eq. 6.14}$$

This turns out to be the most fundamental condition to be satisfied for a reaction to be at equilibrium

Therefore, at constant temperature and pressure, we can write

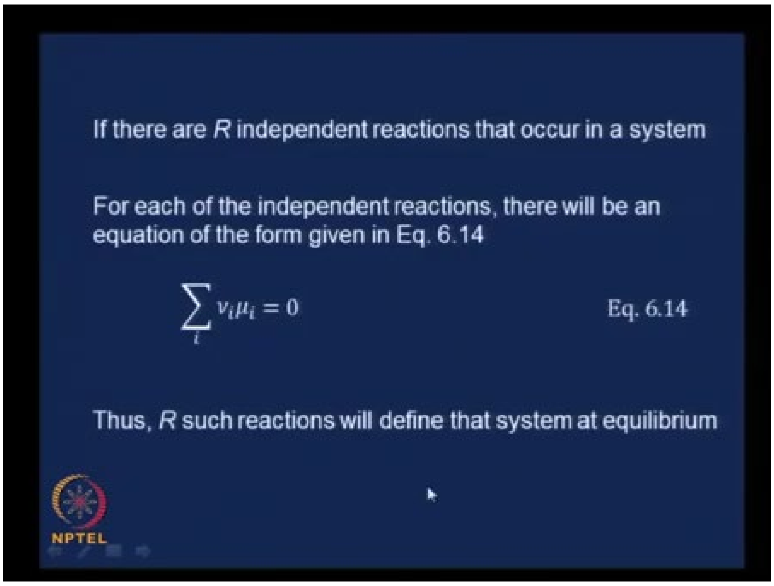
$$\left(\frac{\partial G}{\partial \varepsilon}\right)_{T,\,P} = \sum_i \nu_i \mu_i$$

That is equation 6.13. We know that GT minimum occurs at equilibrium and for a minima to occur the … derivative given here must be equal to zero. And therefore, the condition for equilibrium is

$$\sum_i \nu_i \mu_i = 0$$

equation 6.14. This happens to be the most fundamental equation to represent chemical equilibrium, or equilibrium of a system in which chemical reactions take place. So, please remember this. I think we are almost out of time.

(Refer Slide Time: 23:42)



If there are *R* independent reactions that occur in a system

For each of the independent reactions, there will be an equation of the form given in Eq. 6.14

$$\sum_i \nu_i \mu_i = 0 \qquad \text{Eq. 6.14}$$

Thus, *R* such reactions will define that system at equilibrium

Therefore, when we come back, in the next class or let me see whether we can go further a little bit. If there are R independent reactions that occur in a system, for each of those independent reactions, there will be an equation of the form 6.14. $\sum_i \nu_i \mu_i = 0$ Thus, R such reactions will define that system at equilibrium. Therefore, we will have, for a multi-reaction system, also the condition for equilibrium remains the same. But, we will have R such equations that specify the equilibrium. We will stop here and when we start the next class, we will continue with other aspects of reaction equilibrium.