Overview and Integration of Cellular Metabolism

Prof. Arindam Ghosh

Dr. B.C. Roy Multi-Speciality Medical Research Centre

Indian Institute of Technology Kharagpur

Week 01

Lecture 01: Bioenergetics: Understanding the significance in Biological Systems

Hello everyone, welcome to the inaugural lecture of your new NPTEL course Overview and Integration of Cellular Metabolism. The first lecture is about the very basic and the very generic concept of bioenergetics. As you have seen already from the course outline will be for the first couple of weeks will be dealing with the general concept, then we will delve into the deeper metabolic pathway. So, in this lecture we will be covering the following concept that will be we will learn how to define bioenergetics, we will be learning the laws of thermodynamics as well as the thermodynamic variables that is known as also known as thermodynamic quantities. We will understand the very important concept of standard free energy change and how it is related to equilibrium constant also another important concept. Also we will be learning a very important biological phenomena by which we can couple multiple enzymatic reaction using thermodynamic coupling.

So, let us start right way. So, what is bioenergetics? Bioenergetics actually deals with energy flow, how energy flows and it is transformed in various forms across biological system. This is the very basic definition of bioenergetics. Now it can include multiple things considering a living system generally we obtain energy from food, various sources plants obtain energy from sunlight and by by our various physiological processes we actually transfer this energy into various forms.

And before transferring the energy in case of storage forms it might be held in a captive state in the cells and ultimately released when there is a functional requirement. So, this is the whole concept of bioenergetics. Now giving you a few example how we can use the energy as you can see from the list it can include production of energy currency that is ATP. You can we can use the energy in multiple metabolic pathway regarding transport of various molecular ligands that is known as active transport. Energy is very important for muscle contraction, regulation of our temperature, synthesis of multiple compound reproduction the list goes on and on alright.

Also for example, in animal firefly this can be used in production of light right. So, the fundamental law of energy transformation has to I mean the fundamental phenomena of energy transformation is governed by laws of thermodynamics that is the two laws of thermodynamics and biological system are no exception right. So, let us understand the laws of thermodynamics in a simple way. The first law of thermodynamics deals with I mean is known as law of conservation of energy, it states that energy cannot be created or destroyed, but it can be converted from one form to another. So, if we consider a closed system the total energy remains constant ok.

So, this is the first law energy can either be created or destroyed it can only be converted across various forms in a closed system. So, this law is actually easy to understand. The second law may not be easier to read ok. So, we have simplified the concept for you, it states that in energy transfer or transformation ok. The total entropy of a closed system will always increase over time.

So, very important concept of entropy is introduced in the second law of thermodynamics. What is entropy? Embracing entropy is actually measurement of a randomness or disorderliness of a system how random or how the system is in disorder. So, if we look if we go inside the very atomic level we will always find out whenever an energy transfer occurs across a system ultimately if the transformation actually occurs the result the resultant product will always have a greater disorderliness or randomness ok. So, when A is transformed to B, B will always have more entropy it is more disordered ok. Now having defined these two or having known these two laws of thermodynamics we should now understand what are the thermodynamic quantities.

So, what do we mean by thermodynamic quantities? There are three thermodynamic quantities to be very precise. The first one is Gibbs free energy it is denoted by the term capital G ok. It is the amount of energy capable of doing a reaction at a constant temperature and pressure. This is the definition of Gibbs free energy. Now generally when a reaction is exergonic it always loses free energy this is the dictum ok we are defining laws here ok.

So, when in an exergonic reaction the energy change sign is always negative and we the change is denoted by a triangle delta this denotes the change. So, delta G means change in free energy and the ultimately what negative delta G means that is the system loses free energy ok. So, this is the standard of an exergonic reaction. On the contrary what is endergonic reaction in which the system gains energy the system gains Gibbs free energy and it is denoted by positive I mean delta G there is no negative sign before that. Now one thing you need to be very mindful that is the unit of delta G is in joules per mole or calories per mole depending on CGS or SI system and the conversion unit as we all know from our basic class 2 lessons or even undergraduate lessons that one calories 4.2 joules roughly and 4.18 joules to be specific. Mind it there is a term that is exothermic and endothermic that is often confused with exergonic and endergonic we will be explaining every one of them mind it if you are using it I am gonic G to remember is exergonic endergonic since it is G always remember there is a change in G or delta G or Gibbs free energy ok. So, next thing the next thermodynamic quantity is enthalpy this is also another derivative of the laws of thermodynamics. So, what is enthalpy it is denoted by capital H it denotes the heat content of the system how much heat is present in the system how do we determine how much heat is present in the system it is denoted by the total amount and quantity of chemical bonds that are present in the reactant and product ok.

Suppose one chemical or A plus B is reacting to form C. So, the amount of bonds chemical bonds that is present in A that is present in B that is present in C will actually determine the total enthalpy. So, imagine a reaction for A plus B is reacting to form C and ultimately the system is becoming hot it means what we are losing heat this reaction is losing H or heat and it is denoted by delta H being negative and this is known as exothermic reaction any reaction that becomes hot the temperature increases while the reaction proceeds is known as exothermic reaction the change in delta H is negative right. On the contrary in endothermic reaction there might be situation where system I mean compound A and compound B is reacting to form compound D and what is happening heat is gained means it is gaining heat from the surroundings and ultimately the reaction system becomes cool this type of reaction are known as endothermic reaction and delta H change is positive. So, again in contrasting with the last slide that is exergonic where the delta G was negative exothermic is delta H negative thermo means heat related to temperature ok.

So, this is the concept of Gibbs free energy and enthalpy. Now we come to a critical concept of entropy. So, what is entropy? As I told you while defining the second law of thermodynamics it is the quantitative expression of randomness or disorder in a system right and how is it translating to chemical reaction? As I told you when a chemical reaction occurs spontaneously the system gains entropy it means the change in delta S is positive ok. It was quite different from previous to reaction generally when considering delta G and delta H spontaneous reactions are exergonic spontaneous reactions are exothermic means the change in delta G and delta H is negative, but when considering entropy the change in delta S is always positive. For example, how will we measure entropy that sum total of the entropy of product minus sum total of the entropy of reactant sigma is the sign of summation.

So, this gives us the total entropy of the reaction if entropy of the reaction is positive this means and the reactant will be converted to product and the reaction will be spontaneous. There is an example where the entropy of the each and every molecule has been considered and ultimately it is found to be positive that is 103 joules per calorie because this is the unit of entropy very important. So, here simple the reaction is very simple propane C 3 H 8 combustion of propane. So, propane is combining with oxygen to get converted to carbon dioxide and water vapour or water. So, considering the total energy or total entropy of the product it is more than that of the reactant.

So, delta S is positive and the reaction will be spontaneously occurring. Mind it one thing to remember is complex molecule complex molecule will have more entropy. Why this is so? Because the more complex the compound is there are multiple bonds and they have a multiple probability of adjusting them in multiple angles. So, they can twist and turn. So, this gives rise to more disorder.

So, that is why complex compound will have more entropy. So, what is the relation between these two? So, under standard or existing biological system in considering a standard temperature and pressure standard condition the rule is delta G equal to delta H minus T delta S. So, we have introduced another new term that is T. This T capital T is the absolute temperature absolute temperature is denoted in Kelvin scale degree K ok. So, mind it this is not in centigrade or Fahrenheit this is in Kelvin.

So, delta G that is the change in Gibbs free energy delta H is the enthalpy of the system T is the absolute temperature and delta S is the change in entropy of the reacting system and this is the reaction how these three are related. Now by convention when entropy increases delta S has a positive sign, delta H has a negative sign when heat is released I told you in exothermic and delta G is supposed to be negative when the reaction is spontaneous or exergonic ok. So, equating this reaction in case of a spontaneous reaction the delta G is always negative this is the rule. So, how can it be negative if we equate the two in an exothermic reaction. So, delta H if this value is negative and this value is positive ok.

So, the sum becomes negative that is why if we incorporate or consider a spontaneous reaction where the delta value of delta H is negative and delta S is positive by equating this relation it always becomes negative and thus the reaction is spontaneous. So, considering how this whole thing is maintained in a living system mind it living system is not a closed system we are not a closed system because we continuously react with our surrounding. So, if we just look at one organism and the laws might be might appear to be violated, but please remember living system also follows these two laws of thermodynamics it has to follow because the corollaries we always react with the surroundings. If we consider our system and the surrounding the exchange then it becomes a closed system ok. So, how we gain energy we gain energy from our surroundings in the form of nutrients of light that is either food or sunlight and we also return continuously the energy to the system in the form of heat maybe you are not feeling hot, but micro perspiration heat is constantly lost from our system from the skin ok.

But cell a cell is always isothermal means the milieu internal milieu of a cell is fixed the temperature is always fixed. So, generally we can consider a cell to be an ideal system where a constant temperature and pressure is maintained. So, the only energy with which the cell has to deal with all its function is actually the Gibbs free energy ok. So, now let us look I mean let us find out what the Gibbs free energy allows the cell to do it allows the cell to predict many things ok. Number one whenever a chemical reaction is happening I told you when change in delta energy is negative the reaction is spontaneous it is always occurring, but when this change in delta energy stops it means the cell has reached its equilibrium means a reaction will not proceed in either direction ok.

Next the amount of work the cell can perform also depends on the total Gibbs free energy the and how does the cell at individual level how do they gain the Gibbs free energy there are multiple sources there are nutrient molecule from solar radiation considering a plant they are gaining energy from photosynthesis ok. And what the they do they transform this free energy into some form with which they can readily use by which they can readily use and this is actually ATP adenosine triphosphate this is the ready made energy currency that can be used by a biological cell for performing multiple reactions multiple phenomena and since the biological cell is at the constant temperature the laws of thermodynamics will also hold true. Now let us learn a concept of equilibrium constant. So, what is equilibrium constant or how is it denoted suppose a two reactants A and B are reacting to form product C and D. The concentration of any reactant or product is denoted by a third bracket or a square bracket.

So, if something is x if I write x in a square bracket it means this is the concentration or amount per unit volume ok. So, considering the concentration of the reactant and product the equilibrium constant is denoted by this formula. The product of concentration the product of concentration of the product by one product I mean multiplication and the one product I mean the reactants and products. So, do not get confused between words like it is the multiplication of the concentration of the products divided by the multiplication of the concentration of the reactant or product of the concentration of product divided by product of concentration of the reactant. This is the equilibrium constant and we can assign any digit conventionally k is assigned to any equilibrium constant for a this reaction.

So, we can see k 1 is the specific equilibrium constant equilibrium constant for this reversible reaction, ok. Now another concept that is standard free energy change. So, what is standard free energy change? We will see how what is the exact mathematical formula. Now first thing to something to know about standard free energy change often these are used interchangeably with the equilibrium constant, but they are not they are actually closely related, but they are a bit different, ok. So, what the standard free energy change tells us? It tells us the composition of a tells us that a reacting system will continue to react till equilibrium is reached and it will gain or lose a amount of free energy.

This is very specific for a reaction and this is known as the standard free energy change. We know at equilibrium so, how considering this reaction if this reaction is at an equilibrium means neither the reaction is going in any direction. It means what? It means concentration of the reactant and product will remain constant. The rate at which the reaction is occurring in forward direction is absolutely same the rate that is absolutely same to the rate in which the reaction is occurring in the reverse direction. So, basically what happens? No net further change occurs in the system, ok.

And as I already told you the concentration of the reactant and product at equilibrium define the equilibrium constant. So, what is the standard free energy change? This standard as I told you free energy is always capital G, ok. And change in free energy is delta G. So, we have defined K, we have defined delta G. So, let us see how these two are related.

Whenever we are saying standard free energy it means this has got a specific symbol, it has got a 0 not sign. So, delta G not sign, ok. So, is an alternative mathematical way of expressing the equilibrium constant. If we state a standard free energy change of a reaction and if we state the equilibrium constant of a reaction we will get roughly the same idea as to when the reaction will attain equilibrium at what time the reactant and product will be at the same concentration. But there is a mathematical relation which is standard free energy change or delta G not is equal to negative R absolute temperature and natural log of K that is the equilibrium constant.

So, what are these variables? Delta G 0 is actually the standard change in Gibbs free energy, R is the universal gas constant, its value is fixed 8.31 joules per Kelvin per mole, ok. And T is the temperature, ok and K is the natural log of this natural log of the equilibrium constant. So, we can have an idea looking at the chart that if the equilibrium constant of a reaction is greater than 1, then delta G is negative. Why we are giving delta G prime sign? Because we are considering a specific reaction, ok.

So, delta G not prime is a specific standard free energy change for a reaction. So, why this is happening? See whenever we are considering the natural log of K, if the equilibrium constant is less than 1, the value of delta G will automatically becomes positive because the log will be negative and the product of negative will become positive. And what if the equilibrium constant is 1 means the product of the reactants and the product of the concentration of the product is same means equilibrium has reached. Then what is it what does it mean? It means the standard free energy change is 0.

So, reaction is not proceeding in either way. If the delta G is negative, reaction has to proceed in forward direction. If the delta G is positive, reaction has to proceed in the reverse direction. So, this is basically the rule between equilibrium constant and the standard free energy change. Mind it a small since both are exponentially related, a small change in delta G will have massive changes in the equilibrium constant, ok. So, again the unit of specific I mean standard free energy change is kilojoule per mole.

So, here is a table where we can see the standard free energy change of various compounds. This is very important and will come handy at the later stage of the lecture and in the entire course of the I mean entire like course lecture because it is very fundamental to understand the concept of thermodynamic coupling of the reactions. But for now we can remember some value that is delta G prime of adenosine triphosphate or the dissociation the reaction where ATP dissociates to form ADP and Pi is 30.5 kilojoule per mole.

I already told you the conversion factor. So, that is the homopho you can work it out what is the value in the CGS scale, ok. So, considering this thing we can see the compounds above ATP that is phosphocreatine acetyl phosphate again I mean dissection of ATP into adenosine monophosphate and pyrophosphate it has got a huge amount of negative delta G. So, this reaction is much more spontaneous and favorable compared to dissociation of ATP to adenosine diphosphate and inorganic phosphate. The terms ATP is adenosine triphosphate ADP is adenosine triphosphate Pi is inorganic phosphate so on and so forth, ok. And according to this chart phosphoenol pyruvate the dissociation of phosphoenol pyruvate will release the maximum amount of free energy.

So, this is highly favorable. So, phosphoenol pyruvate always tries to dissociate and compared to so the compounds which are lower down the order will have less free energy change, ok. This ATP as it is dissociating some bond is breaking this is actually phosphate bond. Since the breakage of phosphate bond is liberating so much high amount of energy. So, these few compounds are known as these few bonds in actually these compounds are actually known as high energy phosphate bonds. We actually use the dissociation of high energy phosphate bond to utilize our own means of making a reaction or unfavorable reaction spontaneous.

So, this is a common example of firewood that we have studied in our NCERT books, textbook, physics textbooks in 5, 6, 7 nowadays, right. So, what is this? Basically we are considering a concept of burning firewood that is in our fireplace. So, the normal reaction we already know when wood burns what happened it gets converted to carbon dioxide and water vapor because wood is a form of carbon, right. And is delta G change is large and negative means wood always the one started wood will always continue to burn till the whole reaction is completed, right. It is a exergonic reaction, it is highly spontaneous reaction.

However, it does not occur at room temperature, right. Why? Because it needs something that is known as activation energy. This is the very important concept just because when a substance A in this case wood will react with oxygen to form will react with oxygen to form the next product that is carbon dioxide and water it does not mean it is spontaneous. So, we need something known as activation energy. This activation energy is actually provided by the match light, ok. So, once we give a match light it will catch fire and the whole reaction will spontaneously occur.

This concept is actually used in enzymes. So, enzymes are biocatalyst whenever a product two reactants are reacting it might not be spontaneous. So, we provide some means by which the activation energy is lowered. We will see within with an illustration. Just know this for a reaction for a product A to be converted to B or for a product A to B to be converted to C and D the delta G change is independent of the pathway.

The path does not matter. Ultimately the final product and reactant matter and it depends on the initial concentration nature of the reactants as the product. So, this is what an enzyme does. Enzyme actually see this is an illustration where a ball will ultimately roll from higher point to lower point, but it cannot overcome this bump it does not have that energy. So, enzyme does what it lowers the bump now the ball can easily roll over. This is the role of role that an enzyme actually does they lower the activation.

Energy. So, how we can actually use this concept in our biological system? We can use it very beautifully because standard free energy change is actually additive. Suppose a compound has to transform from A to B and B to C ultimately when we look at the bigger picture when the compound is converted to A to C there is a delta G for each of the reaction. When we combine the two reaction the delta G value will add up. So, let us see how it is beneficial for our system ok.

It is the algebraic sum of the total reaction. So, this principle is used for the very important concept that is the crux of learning of today's class that is a thermodynamically unfavorable or endergonic reaction can be driven forward by coupling it to highly exergonic reaction through a common intermediate these are few key terms. Unfavorable coupling with highly exergonic and through a common intermediate. So, this is a very classical example mind it glucose plus phosphate that is converted to glucose and inorganic phosphate that is converted to glucose 6 phosphate and water. The standard free energy change is 13.

8 kilo joule per mole positive not at all favorable. However, we couple this reaction with the common intermediate that is inorganic phosphate. So, what does what do we do? We utilize ATP hydrolysis. So, when adenosine triphosphate combines with water to form ADP and PI the reaction is highly spontaneous the total delta G change is minus 30.5 kilo joule per mole. So, since these two reaction have got a common intermediate that is inorganic phosphate these two can easily be combined and now the beauty of the law of thermodynamic is this the resultant free energy change is negative the reaction is exergonic and now we can easily convert the reaction we can easily go forward with the reaction.

So, this principle has been used is actually used in multiple steps in multiple reactions that we will read in detail where any endergonic reaction can be thermodynamically coupled with an exergonic reaction and ultimately the final reaction can be done is possible in the biological system. And if the reaction 1 and 2 may be different, but net result is all that is matters and if you look at the equilibrium constant if you look in the terms of equilibrium constant not free energy again the product of the equilibrium constant is actually very high. So, generally 2 to 10 to the power 5 times it actually increases and as we know when equilibrium constant is in the positive side the reaction is spontaneous. So, whether we equate it by equilibrium constant or we equate it via the standard free energy change we can use the thermodynamically couple of reaction in all living cells and the key possibility of this to happen is if ATP or the energy currencies available if you can use the later reaction then only we can utilize the former or the thermodynamic coupling of the reaction. So, the concepts to few facts to remember in this lecture is ATP is except actually very useful for the basic as a basic energy source as we saw how it can help in coupling of various reaction how do we produce ATP if oxygen is present it is produced by cellular respiration if oxygen is absent we produce it via the fermentation and for quick burst of energy body already utilizes the ATP that is present that is made in the muscle by the lactic acid formation as well as very other metabolic steps that makes ATP.

So, these are the few concepts that have been cleared in lecture 1 these are my references. Thank you for your attention.