Bioenergetics

Energy and life

What was mentioned in the slide:

- No energy – no life
- Why do we need energy? Examples

What was mentioned in the lecture:

what do we mean by energy? Without energy there is no life. the main source of energy in this life is the sun and the sun will pass it to the plants, plants will feed animals including humans and the humans will feed on animals and plants. so the main source is the sun at the end, why do we need it? there is a lot of examples in the body of why do we need energy, like movement, pumping mechanisms across the cells, transport, blah blah blah a lot of mechanisms require energy within the body.

Energy & why do we need it?

What was mentioned in the slide:

- **Definition: Capacity to perform work**
- **What for? Mechanical, Active transport, Biosynthesis, Heat**
- **Types of energy:**
  - ✓ **1- Kinetic: Energy in the process of doing work or Energy of motion**
  - ✓ **2- Potential: Energy content stored in a matter**
- **Whether a reaction occurs or not!**
- **Stability vs. energy**

What was mentioned in the lecture:

those are the types of the need for energy, the energy as a concept can be either kinetic or potential energy, the kinetic energy was covered last semester when we talked about enzymes, the kinetic energy defines the energy during motion of many things, the second type which is a potential energy is the energy stored within materials which can be converted into kinetic energy when there is a need for it, what determines if any reaction in this world will go through or not is the potential energy, so according to the potential energy stored in the reactants and the potential energy stored in the products, we will compare them together, we will have the difference in between them and we will see if this reaction is favorable to go or it's not favorable to go through, stability is always when we compare it to energy, it's in contrast to energy when energy is high then stability is low and when energy is low -with respect to potential energy or kinetic energy- then the stability of any material in this world is high.

The major purpose of metabolism

What was mentioned in the slide:

- **Metabolism: Sum of all biochemical reactions in living organisms**
- **Mainly for energy generation**
- **Other purposes:**
  - Synthesis of building blocks
  - Synthesis of macromolecules
  - Degradation of biomolecules
  - **Bioenergetics: Energy transformations in the cell**

What was mentioned in the lecture:

Regarding the major purpose of metabolism, we've talked metabolism is all the chemical processes that occur within any living matter which can be catabolism or anabolism (breaking down or building up materials) and you can see the list.

Why Do Chemical Reactions Occur? Concept of Free Energy, *Gibbs Equation*

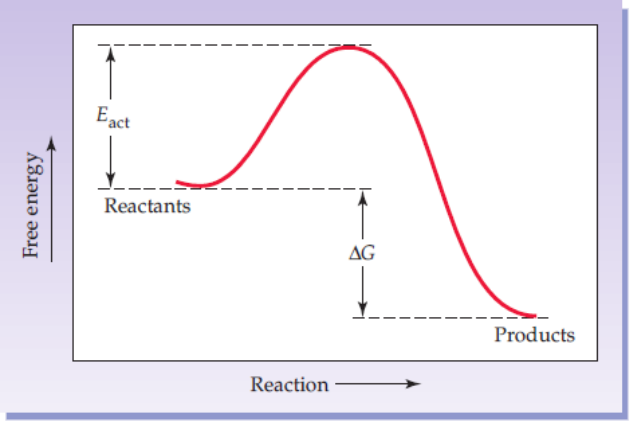
What was mentioned in the slide:

- **Free energy change: the total energy change in a system with respect to its temperature**
- **Enthalpy**
- **Entropy**
- **Exergonic vs. endergonic**
- **The value of the free-energy change determines spontaneity**
- **The concept of activation energy**

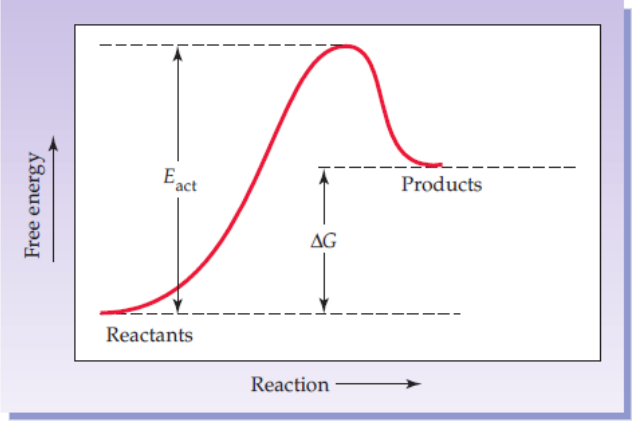
Free-energy change

$$\Delta G = \Delta H - T\Delta S$$

Heat of reaction | Temperature (in kelvins) | Entropy change



(a) An exergonic reaction



(b) An endergonic reaction

What was mentioned in the lecture:

now Gibbs came a long time before and he defined an equation: ΔG = ΔH - TΔS which defines the energy of any chemical reaction that occurs outside the body or inside the body, now we are concerned with biological systems, according to Gibbs energy, any material stores potential energy, we have the potential energy stored in the reactants here is its level and this is the potential energy in the products and the difference in between them is what defines ΔG which is the free energy difference in between the reactants and the products, here (left curve) the products are having less energy compared to the reactants which means they are more stable compared to the reactants. why do chemical reactions occur in this life? to achieve higher level of stability, this is the main goal about them, I want to achieve higher higher stability, so reactants here will pass to products spontaneously, favorably, and we call it exergonic in terms of energy. this is on the other hand (right curve) where the reactants have higher stability compared to the products (less energy compared to the products) then this reaction is non-spontaneous, unfavorable and endergonic. now with respect to the sign, how to calculate any delta in the world? its final minus initial, the final level of energy minus the initial level of energy, here (left curve) it is negative so favorable spontaneous exergonic reactions have negative ΔG sign, while the other reaction (right curve) is the opposite exactly, it has a positive ΔG because the level of energy in the products is higher than the reactants, we are taking a material from a low energy state to a higher energy state, this thing is unfavorable logic wise, any material in this world ,is trying to achieve stability (you are trying to

achieve stability, you are studying to achieve stability, after, you are working to achieve stability, after, you are marrying to achieve stability 🤣🤣🤣), and everything in this life it goes about stability, either you'll achieve it or not is something different, now although this reaction (left curve) is spontaneous, on real chemical reaction it's not spontaneous, by definition it has to go through a higher energy state which we called before in enzymes transition state, so we need what we call activation energy because reactants in any reaction are stable, yes here products are more stable compared to reactants but reactants are stable, if they are not stable, I cannot buy them, i cannot deal with them, I cannot make chemical reactions with them, so they are stable, so to convert the stable reactants into an unstable state which we call the transition state we need activation energy, and we dealt with that in enzymes, in this equation we have nothing to do from the point of reactants to the point of the products, we are dealing only with the starting state and the final state, only if there is a difference then we accordingly can predict if this reaction is a spontaneous, non-spontaneous (favorable non-favorable), exergonic or endergonic, what determines if this reaction will go through or not, spontaneous or not, according to the equation is ΔH and ΔS, T is the temperature, ΔS is the entropy change, and ΔH is the enthalpy change.

Enthalpy and entropy

What was mentioned in the slide:

- Entropy: students, hair, gas bottle, carbonic acid (pepsi), ملح ليمون وكربونات
- Plants: does not violate entropy
- G for Gibbs
- $_{\Delta G}$ deals with the system alone without caring about the surroundings
- What makes $_{\Delta G}$ negative? Enthalpy and entropy
- $_{\Delta G}$ has nothing to do about reaction rate
- $_{\Delta G}$ is a function state

What was mentioned in the lecture:

enthalpy is an energy state, it measures the actual bonding in between atoms of the material, while entropy measures the disorder between the different molecules, are they close to each other? are they far from each other? do they have a crystallized state or they are going randomly? Etc. accordingly, they defined in the past that each spontaneous natural system tries to go into more disorder, your hair will be disordered and you need energy to order it, students will be disordered unless you order them, a common example in biochemistry textbooks, they talk about your room, as a student, you need energy to order your room, but you don't need energy to make it disordered, it will become disordered with time, so mostly entropy for natural systems increases with time, it is ΔS, the enthalpy measures the bonding energy in between the different atoms in the material and between the different molecules in the material, the whole bonding energy subtracted from the that of disorder state will give you the ΔG, so accordingly ΔG actually measures only the bonding in between the different atoms of the material

The different free energy terms

What was mentioned in the slide:

- ΔG = the free energy difference of a system at any condition
- ΔG^{o} = the free energy difference of a system at standard conditions ($25C^{o}$ & 1 atmospheric pressure, 1M concentration of reactants & products, pH = 7)
- Which one of these terms determine the feasibility the reaction?
- ΔG depends only on initial state and final state of biochemical pathways

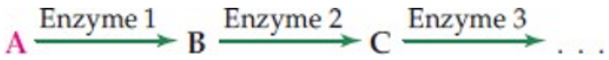
What was mentioned in the lecture:

we defined ΔG just now, ΔG^{o} which measures the difference in potential energies between reactant and products at standard state which includes 25 degrees centigrade room temperature, one atmospheric pressure, one molar concentration of reactants and products and pH seven, so if you do the reaction under all of these conditions, we term it as ΔG^{o} , if you change only one condition (if you do it at different conditions) then we call it ΔG, so because these standard conditions are defined all the time, then between any reactant that will go to a certain product ΔG^{O} is always constant, because the environment is not changing, but for ΔG as a term, each time we'll have a different value, why? because the environment is changing, which one of these terms determine the feasibility of the reaction (the favorability of the reaction)? it's always ΔG not ΔG^{o}, because ΔG^{o} is always a fixed Value, what we are concerned with is not ΔG^{o}, we are concerned with ΔG, because our body has different conditions: the first one is the temperature, it is 37 degrees centigrade, the pH is different from a place to a place, the pressure is different, and the concentrations of the reactants and the products keep changing from a place to place .

ΔG is a state function
what does state function means? Means it cares about the initial and final states without caring about the path

What was mentioned in the slide:

- **ΔG is not affected by the mechanism of the reaction**



- $A \rightarrow B \rightarrow C$

$\Delta G_{A \rightarrow B} = GB - GA$

$\Delta G_{B \rightarrow C} = GC - GB$

$GC - GA = \Delta G_{A \rightarrow C}$

- Combustion of glucose in calorimeter

$Glucose + O_2 \rightarrow CO_2 + H_2O$ $\Delta G = -680$ kcal/mol

In the cell

$Glucose \rightarrow\rightarrow\rightarrow\rightarrow\rightarrow\rightarrow CO_2 + H_2O$ $\Delta G = -680$ kcal/mol

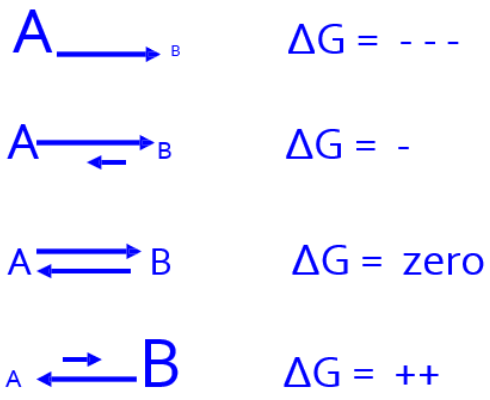
What was mentioned in the lecture:

ΔG can be summed, if we have a reaction in a pathway where material A goes to material B and material B to material C, this is what we define in the body as pathway, where every material is leading to the Other, we've defined that in enzymes and what do we mean by pathways and the different looks of the pathways, now if I want to calculate the ΔG when A goes to B, then it is the potential energy from B minus A and from B to C it equals from C minus B and if we want to calculate the total B will go with B and it proves mathematically that: the ΔG from A to C, it is C minus A, we don't care about what happens from A to C, and this is what we've said before, from reactants to products regardless of what happens in between them, (we've cared about what happens between when we talked about enzymology, here we don't care about them), we will look at the initial state and at the final state, for example glucose getting converted into pyruvate in a 10-step pathway, we will look at the potential energy in glucose and potential energy in pyruvate, and we will take the difference in between then if it's positive then the reaction is endergonic, if it's negative then the reaction is exergonic, and it's always reversible with the same amount of energy according to the laws in thermodynamics, if glucose is getting converted outside the body into CO_2 and water, it will give you -680 kilocalories per mole, when glucose goes in the body it goes into pyruvate, pyruvate will be converted into acetyl-CoA, acetyl-CoA will go into Krebs cycle and will give you NADH and $FADH_2$, and those NADH and $FADH_2$ will go into the electron transport chain to produce ATP, at the end of this process CO_2 will go out through the Krebs cycle and H_2O will go through the electron transport chain and the final amount of energy that we get, it should be the same as long as the initial material is the same and the final material is the same regardless of the pathway, however this reaction do not occur spontaneously, it happens by favor of enzymes which decrease

activation energy so the reaction can occur, most reactions do not occur by itself, because activation energy is high so random collision by itself cannot drive the reaction.

ΔG is affected by concentration

What was mentioned in the slide:



ΔG measures the tendency of the reaction to proceed towards equilibrium

What was mentioned in the lecture:

ΔG is always affected by the concentration of reactants and products, if the concentrations of the reactants are much much higher compared to the products then I expect the ΔG to be a lot negative, if the concentrations of the reactants are getting less while the concentrations of the products are Increasing (as you can see from the letter it's getting bigger) then ΔG will become less negative, and when they're equal (the concentrations) ΔG is zero, ΔG is always zero when the concentrations are Equal, when the concentrations of the products are getting bigger then ΔG will convert to positive and ΔG measures the tendency for the reaction to proceed towards equilibrium.

Standard free energy change ΔG°

What was mentioned in the slide:

- Concentrations of reactants and products = 1 mole/L
- $\Delta G = \Delta G^\circ + RT \ln \frac{[Products]}{[Reactants]}$
- $\Delta G = \Delta G^\circ + RT\ 2.3 \log \frac{[Products]}{[Reactants]}$

What was mentioned in the lecture:

Because concentrations of reactants and products can affect the value of ΔG then there should be a relation in between ΔG and the different concentrations of the products and the reactants, an equation was defined in the past as $\Delta G = \Delta G^\circ + RT \ln(products/reactants)$ R is the gas constant, T is the temperature and ln is the natural logarithm for the products concentration over the reactants concentration, when you look at this equation then you can understand a lot of things out of it now, suppose that you have a reaction with ΔG° of +4 kilocalorie, now it's plus RT ln(products/reactants), if the ratio (products/reactants) is less than one, ln will be negative great and if it is more than one it will be positive, if it is one the ln will be zero, if the products concentration are increasing and the reactants concentrations are decreasing to achieve a ratio of higher than one then the ln will be positive, and when we combine it with the ΔG, note we will have a positive ΔG (remember ΔG is assumed to be +4) now on the other hand when we will decrease the concentration of the products a lot and we are increasing the concentration of the reactants the ratio will become less and less and less where the ln will become more and more and more negative to a point where it will be more than -4 and when that happens then even if ΔG° is plus 4, because the value of ln it might reach -5, then the ΔG can be negative so for a reaction which is endergonic at standard conditions it can become exergonic at different conditions if we play with the concentrations of reactants and products. because the ln= 2.3 log, also it is the same equation it's not different.

Reversible Reactions & Chemical Equilibrium

What was mentioned in the slide:

- What is a reversible reaction?
- What is the chemical equilibrium? Chemical equilibrium is an active, dynamic condition
- At equilibrium, are concentrations equal?

$$aA + bB + \cdots \rightleftharpoons mM + nN + \cdots$$

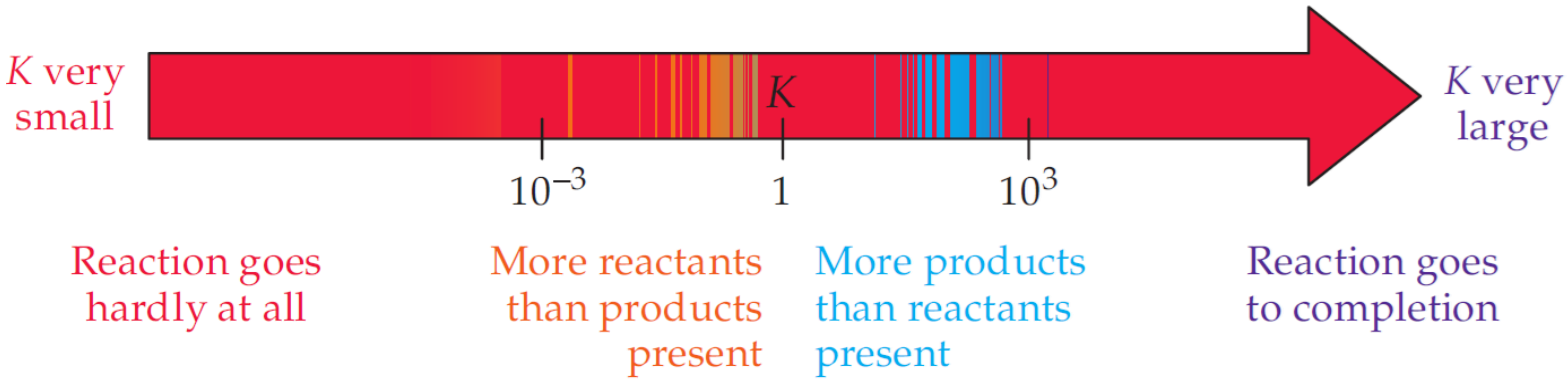
Equilibrium equation

$$K = \frac{[M]^m[N]^n \cdots}{[A]^a[B]^b \cdots}$$

Product concentrations

Reactant concentrations

Equilibrium constant



What was mentioned in the lecture:

what can we understand from that equilibrium constant? Theoretically, all reactions in this world are reversible, but essentially there are some reactions which are going into one direction only, they are not reversible essentially but not theoretically, and what does that mean is that when we look at the concentration of the products over reactants, now any reaction is trying to achieve stability in this world and stability for reversible reactions is where reactions will go into the reactants will go (into the forward direction) products will go into the reverse direction, till they achieve a state of balance, this state of balance we call it equilibrium, equilibrium is defined as when the rate that reactants is converted to products is equal to the rate of the products coming back to become reactants. it's not the concentrations, let's consider this example where you have two rooms of section one and section two,

they are different in their students numbers, section 2 250 students and section 150, now when you look at them they are different in concentration (student number), but suppose that before the meeting three students of section two asked me to go to section one and three students from section one asked me to section two and they went into the same time, did the concentration change? No, the concentration did not change because the rate is the same, but, are concentrations similar? No. can concentrations be equal? Yes, they can be. this is what we defined by the equilibrium constant, equilibrium it's not a static state, equilibrium is a dynamic state, the reactants will go into the products and products will become reactants at the same time, if this constant is one, what does that mean? It means that the concentration of the products equals the concentrations of the reactants, now when it becomes higher than one, if it is 10, what does that mean? It means that at equilibrium you'll have 10 folds products of the concentration more than the reactants. And so on, when K at equilibrium becomes large (the concentration of the products over the concentration of the reactants becomes large) what does that mean? it means that essentially the reactants are becoming products, most of what we have at equilibrium are products, and vice versa when it becomes less and less than one (when it becomes 10 to the power of minus 3 and less) what does that mean that the reaction is hardly going at equilibrium.

Standard free energy change ΔG^o and equilibrium constant Keq

What was mentioned in the slide:

K_{eq} is obtained by dividing [products] by [reactants] when the reaction reaches equilibrium

$$K_{eq} = \frac{[Products]}{[Reactants]}$$

- At equilibrium

$$0 = \Delta G^o + RT \ln K_{eq}$$

$$\Delta G^o = - RT \ln K_{eq}$$

- At standard conditions

$$\Delta G = \Delta G^o + RT\ 2.3 \log 1$$

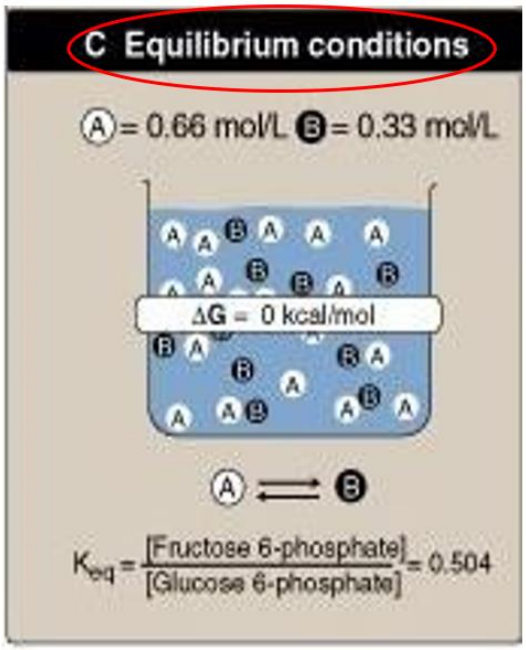
$$\Delta G = \Delta G^o$$

What was mentioned in the lecture:

ΔG determine the favorability of the reaction, because ΔG is what defines the concentration, it is what define the favorability of the reaction (will it go from reactants to products or from products to reactants) then at equilibrium what is the value of ΔG for any reaction? it should be zero all the time, at equilibrium ΔG is always zero because there is no favorability, reactants are going into the products by the same rate products are going into reactants, so if you want to look at equilibrium, at equilibrium $0 = \Delta G^o + RT \ln K_{eq}$, if we are not at equilibrium, then this ln will be concentration of products over the concentration of reactants, we replace it by k at equilibrium, so at equilibrium ΔG^o equals $-RT \ln (K_{eq})$ k_{eq} is the concentration of products over reactants and we can replace the ln by 2.3 log in mathematics.

Glucose 6- phosphate ⇌ Fructose 6- phosphate

0.66 mol/L 0.33 mol/L



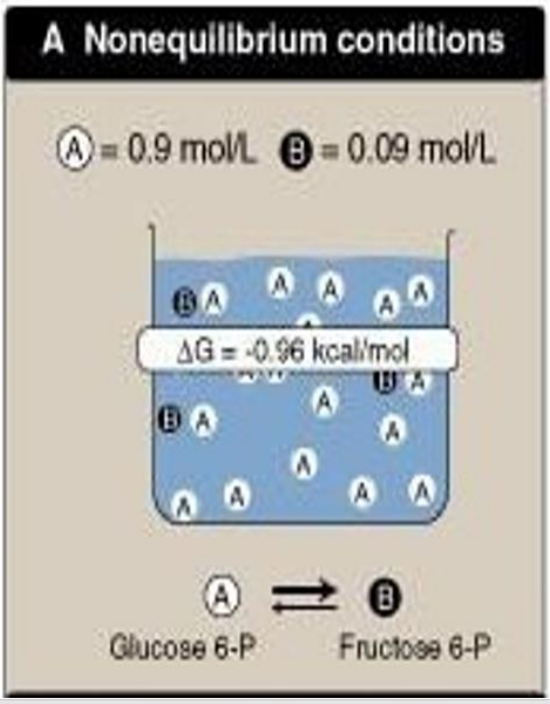
$\Delta G = \Delta G^o + RT\ 2.3 \log 0.33/0.66$

$\Delta G^o = +0.4$ kcal/mol

What was mentioned in the lecture:

look at this example, in this reaction glucose-6-phosphate is converted to fructose-6-phosphate, at equilibrium we have 0.66 mole/liter, glucose-6-phosphate, and o.33 mole/liter from fructose-6 phosphate, if you want to apply the equation at equilibrium ΔG=0 so ΔG^o equals $-RTk_{eq}$ which will become 0.4 kilocalorie per mole, this is at equilibrium because the ratio (products/reactants) is less than one, accordingly, the ln of that ratio is negative, and $\Delta G^o = -RTK_{eq}$ negative by negative it will give you a positive value, so we must play with that reaction to happen, and this is what the body does, it play with that reaction (to be continued)

Glucose 6- phosphate ⇌ Fructose 6- phosphate



$\Delta G^{o} = +0.4$ kcal/mol

$\Delta G = \Delta G^{o} + RT\ 2.3 \log 0.09/0.9$

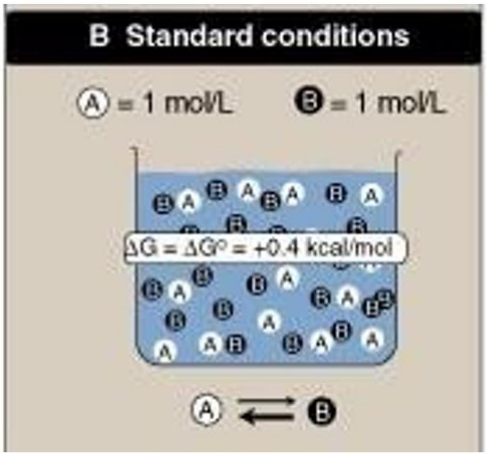
$\Delta G = -0.96$

What was mentioned in the lecture:

Let's look at different conditions (this is non-equilibrium conditions), if you have 0.9 molar of glucose-6-phosohate, and 0.09 mole per liter of fructose-6-phosphate, here we've decreased the concentration of the products and we've increased the concentration of the reactants, ΔG^{o} is 0.4 kilocalorie per mole, and the ΔG will equal 0.4 plus RT × 2.3 log of 0.09 over 0.9 and ΔG will become a negative value.

Glucose 6- phosphate ⇌ Fructose 6- phosphate

1 mol/L 1 mol/L



$\Delta G = \Delta G^o + RT\ 2.3 \log 1/1$

$\Delta G = \Delta G^o$

What was mentioned in the lecture:

this is at standard conditions, when at standard conditions, the concentrations of the reactants and the products are one molar and they are equal concentration, so log one over one is zero so the whole term is zero so ΔG equals ΔG^o.

ΔG & K_{eq}

What was mentioned in the slide:

- At equilibrium, $\Delta G=o$
- Can a reaction has a + ΔG^o & still be favorable?

For a reaction $A + B \leftrightarrow C + D$

$$\Delta G = \Delta G^{o\prime} + RT \ln \left(\frac{[C][D]}{[A][B]}\right)$$

$$\Delta G = \Delta G^{o\prime} + RT \ln \left(\frac{[C][D]}{[A][B]}\right)$$

$$0 = \Delta G^{o\prime} + RT \ln \left(\frac{[C][D]}{[A][B]}\right)$$

$$\Delta G^{o\prime} = -RT \ln \left(\frac{[C][D]}{[A][B]}\right)$$

$$\text{defining } K'_{eq} = \left(\frac{[C][D]}{[A][B]}\right)$$

$$\Delta G^{o\prime} = -RT \ln K'_{eq}$$

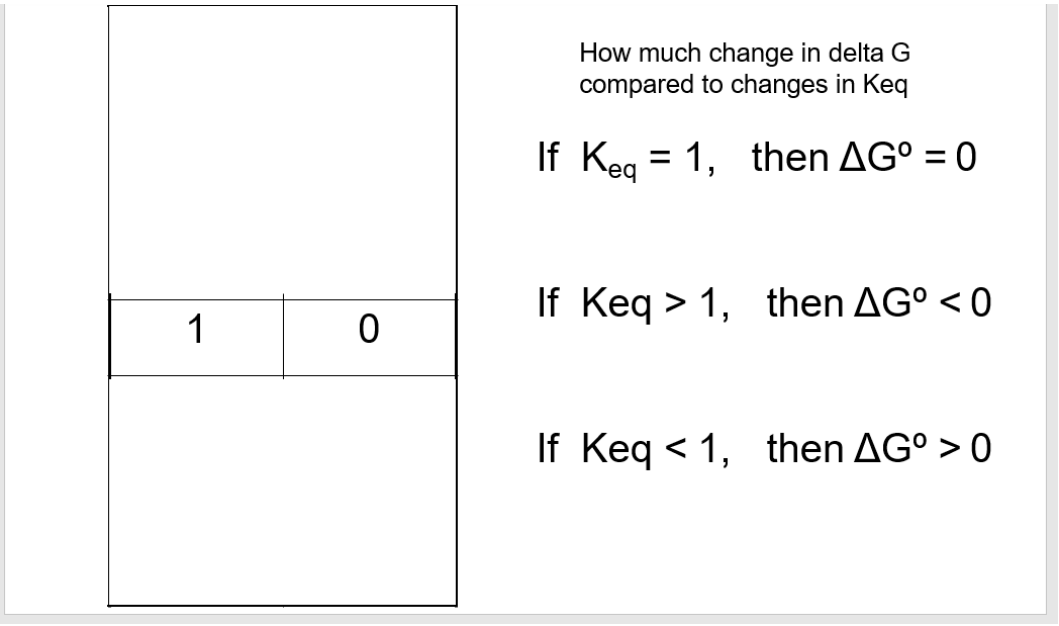
K'_{eq}	$\Delta G^{o\prime}$ kJ/mol	Starting with 1 M reactants & products, the reaction:
10^4	- 23	proceeds forward (spontaneous)
10^2	- 11	proceeds forward (spontaneous)
$10^0 = 1$	0	is at **equilibrium**
10^{-2}	+ 11	reverses to form "reactants"
10^{-4}	+ 23	reverses to form "reactants"

What was mentioned in the lecture:

This is the relation in between k_{eq} and the ΔG^o and how can we predict if the reaction will go Forward (spontaneous), if it is at equilibrium, or if it will go into the backward reaction (into the reverse reaction from products to reactants) depending on the value that we have here and this is what we've explained in the previous slides

ΔG^o and K_{eq}

What was mentioned in the slide:



What was mentioned in the lecture:

This is how value of ΔG^O and $k_{eq,}$ they are matching each other depending on what we understand outside of k_{eq}

The Effect of Changing Conditions on Equilibria

$$\text{defining } K'_{eq} = \frac{[C][D]}{[A][B]}$$

$$\Delta G^{o\prime} = -RT \ln K'_{eq}$$

What was mentioned in the slide:

- When a stress is applied to a system at equilibrium, the equilibrium shifts to relieve the stress
- Stress: any change that disturbs the original equilibrium
  - Effect of Changes in Concentration
- ✓ What happens if a reactant/product is continuously supplied/ removed?
- ✓ Metabolic reactions sometimes take advantage of this effect
  - Effect of Changes in Temperature
- ✓ Endothermic/exothermic are favored by increase/decrease in temperature, respectively.
  - Effect of a catalyst on equilibrium

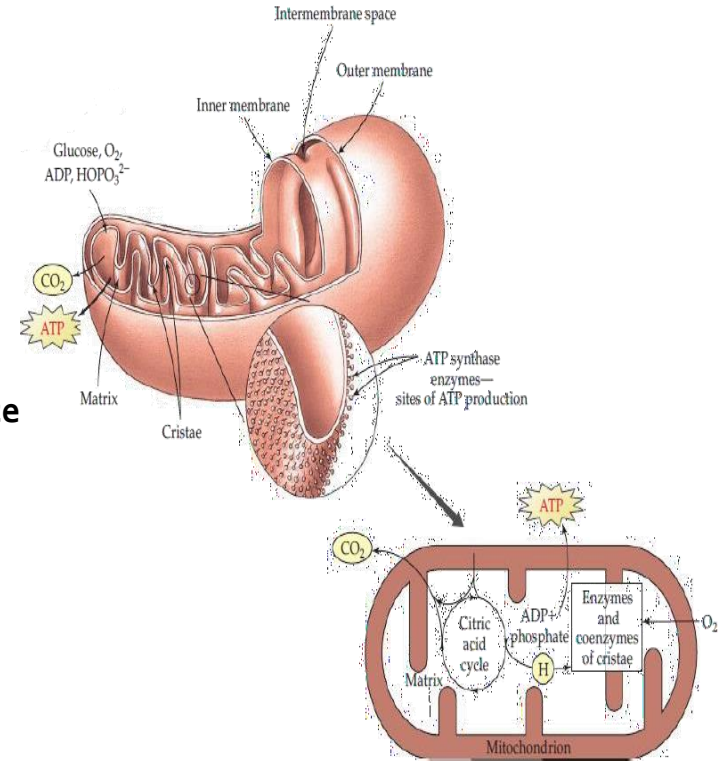
What was mentioned in the lecture:

what are the different terms that can affect the equilibria state? 1- the concentrations, if you are at equilibrium and you are increasing the concentration of the reactants then the reaction will go forward, if you are increasing products, the reaction will go backward, 2-effect of changes in temperature, to determine it, we must know if temperature is behaving as one of the reactants or one of the products, depending if the reaction is exothermic or endothermic, if we are dealing with an endothermic reaction, it absorbs heat, or if we are dealing with a reaction that releases heat (exothermic reaction), in the reaction that releases heat, heat is one of the products, in the reaction which absorbs heat, the heat is one of the reactants, so if you are increasing the temperature in an endothermic reaction you are increasing the reactants, so accordingly the reaction will proceed forward, but if you are dealing with exothermic reaction and you are increasing the temperature then you are increasing the product then the reaction will go into the reverse direction, 3-effect of the catalyst, what is the effect of a catalyst on equilibrium? Catalysts or enzymes do not affect the equilibrium by itself, it makes it faster to reach the equilibrium, but it does not make the favorable unfavorable.

The energy machinery of the cell

What was mentioned in the slide:

- Prokaryotic cells vs. eukaryotic cells
- The mitochondria (singular, mitochondrion) (90% of the body's energy ATP)
- The number of mitochondria is greatest in eye, brain, heart, & muscle, where the need for energy is greatest
- The ability of mitochondria to reproduce (athletes)
- Maternal inheritance



What was mentioned in the lecture:

90% of the body's energy is getting synthesized within the mitochondria, the remaining 10% is synthesized within the cytosol through a process that called glycolysis, in the evolution theory, they think that mitochondria came from prokaryotic cells that had invaded the eukaryotic cell, mitochondria look like bacteria, they has an outside wall, inside wall (outer membrane and inner membrane) and a space in between them which we call the intermembranous space, it has cristae and a matrix inside, where energy breakdown of all pathways for macromolecules occurs (within the matrix inside), the number of the mitochondria in each cell varies but approximately we have two thousand mitochondria per cell, regardless from this you have to know that the passage of mitochondria from the mother cell to the daughter cells is not governed by the mother cell itself, there is no rule to govern that, when the suppose you have a duplication of the mother cell to give two daughter cells, everything in the cell will go with the duplication process by the mother cell, mitochondria is outside of that process at all, it has its own numbers, it will get duplicated by a different process which is called binary fission as the bacteria, but the duplication of the eukaryotic cell goes by mitosis as everybody knows, when the cell wanna go into a duplication process (mitosis), mitochondria do not duplicate, mitochondria only duplicates in the human cells for the sake of energy production, this is the purpose why athletes get training all the time, this is why people are going into the gym, what happens is that there is more need from the muscles for energy, then mitochondria will start to duplicate more and this is why athletic people can withstand more time in doing their exercises compared to regular people, because they have more mitochondria, they can generate more energy, they can store more oxygen, compare it to other people, other peoples will get fatigue and tired in much early time, we can't change the number of mitochondria in any cell, when the mother cell duplicates into two daughter cells, the mitochondria present inside the mother cell will not be affected by that duplication, let's say we have 10 mitochondria in the mother cell, regarding the daughter cells, one of them might have the 10 mitochondria and the other will have no mitochondria (will die) or it could be nine/one, eight/two, seven/three six/four five/five, etc.any

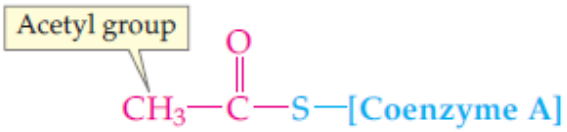
combination can occur, because mitochondria has DNA inside it and that DNA is specific for certain proteins inside the mitochondria, (not all the proteins inside the mitochondria, but few proteins inside the mitochondria, and most proteins that mitochondria need are coming from the nucleus, DNA inside the mitochondria can have a mutation, and if it has a mutation and it passes to the daughter cells, because not all mitochondria can get mutated at the same time, so this mutation can go into one of the daughter cells but not to the other cells, and if that thing happens early in embryogenesis, that daughter cells was planned to make the nervous system while the other daughter cells was planned to make the the muscular tissue then we can end up by a mitochondrial disease which affects the nervous system while the muscular system is healthy, that thing is not possible in any mutation inside the nucleus because the process is mitosis and the mutation is affecting all cells within the body, so mutate diseases that result from mutations affecting the mitochondria can be divided into two major classes: first nuclear diseases that comes from nuclear DNA and that will affect all cells in the body, and mutations which arise from the mitochondrial DNA, it might show in all cells in the body or it might show in one tissue but not the other and this thing we call it heteroplasmy, the other thing we want to discuss about the mitochondria that it has maternal inheritance, we all know about the fertilization process, the sperm will fertilize the egg by donating the nuclear material that it has but not the rest of the cellular material because it is inside the tail of the sperm, and the mitochondria are inside the tail of the sperm, so if the mother has a mitochondrial disease it will pass it to her children whether males and females, but if the father has a mitochondrial disease, it won't be passed to her to his children whether males and females.

Stages of Energy Production

What was mentioned in the slide:

- **Stage 1 (Digestion):**
  - ✓ **Mouth, stomach, & small intestine**
  - ✓ **Carbohydrates to glucose & other sugars**
  - ✓ **Proteins to amino acids**
  - ✓ **Triacylglycerols to glycerol plus fatty acids**
  - ✓ **From there to blood**
- **Stage 2 (Acetyl-coenzyme A)**

Attachment of acetyl group to coenzyme A



- **Stage 3: citric acid cycle**
- **Stage 4: electron transfer chain & oxidative phosphorylation**

What was mentioned in the lecture:

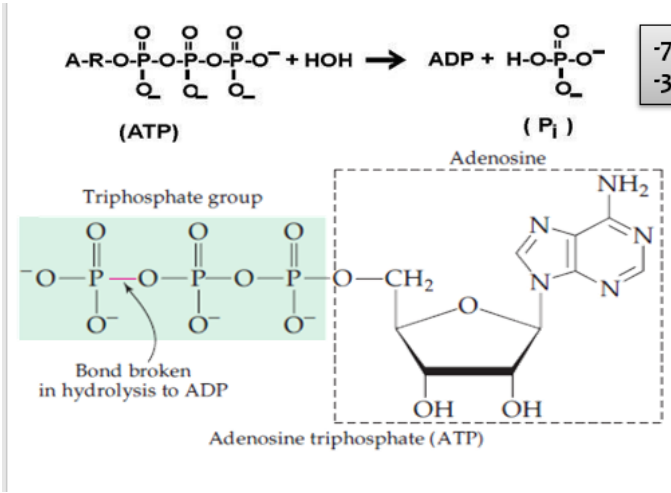
how energy passes through the body? It passes from the stage one which is called the digestion, then absorption from which all monomers of the food will go into the cells, in stage two that we will continue in

this semester, carbohydrate metabolism, lipid metabolism protein metabolism happens inside cells, in stage two, all materials either lipids, carbohydrates, or proteins, will converge to give you a common molecule that is called acetyl CoA, this acetyl-CoA will pass to the Krebs cycle that you can see here, Krebs cycle is the third stage of energy production and the fourth stage and the last stage is the electron transport chain and oxidative phosphorylation.

ATP

What was mentioned in the slide:

- ATP is the energy currency of the cell
- What is a high energy molecule?
- Why ATP?
  - Has an intermediate energy value, so can be coupled



-7.3 kcal/mole
-3.4 kcal/mole

Compound +H_2O	Product + phosphate	ΔG°
Phosphoenol pyruvate	Pyruvate	-14.8
1,3 bisphosphoglycerate	3 phosphoglycerate	-11.8
Creatine phosphate	Creatine	- 10.3
ATP	**ADP**	**- 7.3**
Glucose 1- phosphate	Glucose	-5.0
Glucose 6- phosphate	Glucose	-3.3

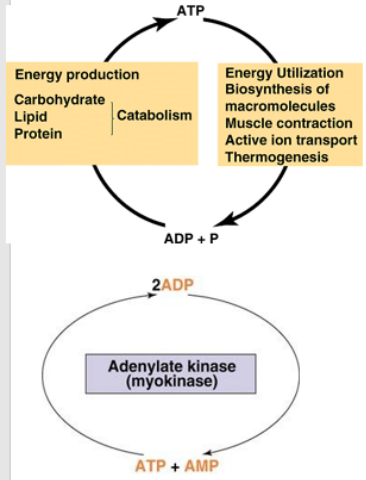
What was mentioned in the lecture:

the energy currency of the cell is ATP, ATP has been considered as the energy molecule of the cell because it has an intermediate energy value, ATP, when it is getting converted to ADP, it releases 7.3 kilocalories per mole, this is not because it has phosphate as you can see all these molecules (in the table) has phosphate, but the amount of energy is different from the release of each phosphate in these materials, ATP is in the middle, also not because it has three phosphates because in most reactions ATP is donating one phosphate only as these materials also are donating one phosphate from their structures, so why? because it has an intermediate value of energy, because when ATP is becoming ADP inside the body it has to come back and become ATP from ADP, and because energy is conserved if we are releasing 7.3 kilo calorie from ATP to ADP then we need also 7.3 to build up ATP from ADP so when that value is intermediate then we can obtain that value, so if it's very high like this we cannot obtain it from any other reaction inside the body.

Is ATP a good long-term energy storage molecule?

What was mentioned in the slide:

- As food in the cells is gradually oxidized, the released energy is used to re-form the ATP so that the cell always maintains a supply of this essential molecule.



Tissue	ATP turnover (mole/day)
Brain	20.4
Heart	11.4
Kidney	17.4
Liver	21.6
Muscle	19.8
Total	90.6

90.6 * 551 (g/mole)
=
49,920 g ATP

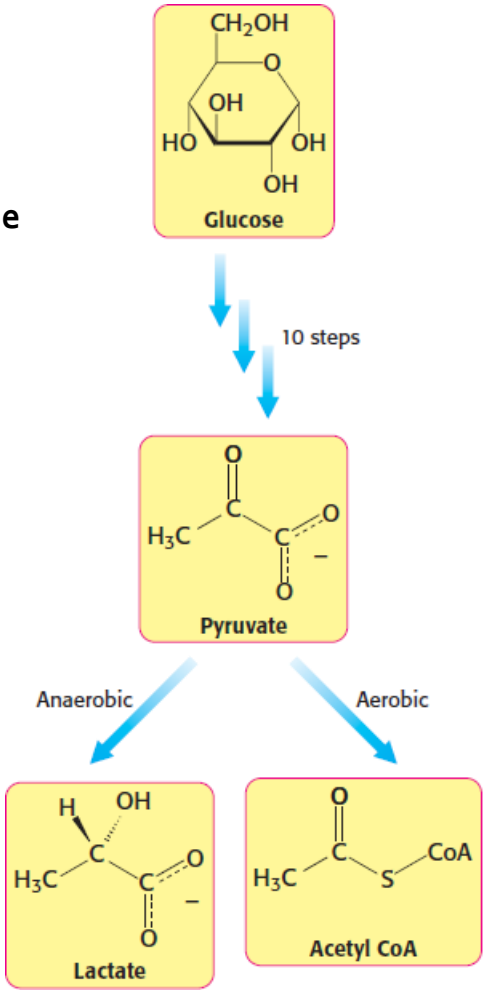
What was mentioned in the lecture:

is there a store of ATP inside the body? No. how energy is stored inside the body? as bonds in carbohydrates, lipids, proteins or whatever you have, but not as ATP. why ATP is not stored inside the body? it's not a long-term molecule to be stored for your processes, look at this table, this is the amount of ATP needed in moles per day for the main tissues and at resting state, we have brain, heart liver, muscle, etc. the total is approximately 90 to 91 moles per day of ATP and if you want to convert it to know the mass of ATP needed we will multiply it by the molecular weight and we will find that we need 50 kilograms of ATP daily which is not suitable and not logical, you need a human body beside you beside you each day of ATP😂😂 then you'll use it then another one then you'll use it, so energy is stored in different bonds inside the body when you need it then you will start breaking it down and this is why we need a constant supply of food all the time for our processes.

Metabolism & metabolic pathways

What was mentioned in the slide:

- What is the source of all energy? (autotrophs vs. heterotrophs)
- Why do we need energy?
  - ✓ (1) the performance of mechanical work in muscle contraction and cellular movements
  - ✓ (2) the active transport of molecules and ions
  - ✓ (3) the synthesis of macromolecules and other biomolecules from simple precursors
- How do we keep the energy in the body?
- Cellular metabolism: the sum of the total biochemical activities of all cells
- Mainly for energy generation
- Metabolism consists of energy-yielding and energy-requiring reactions



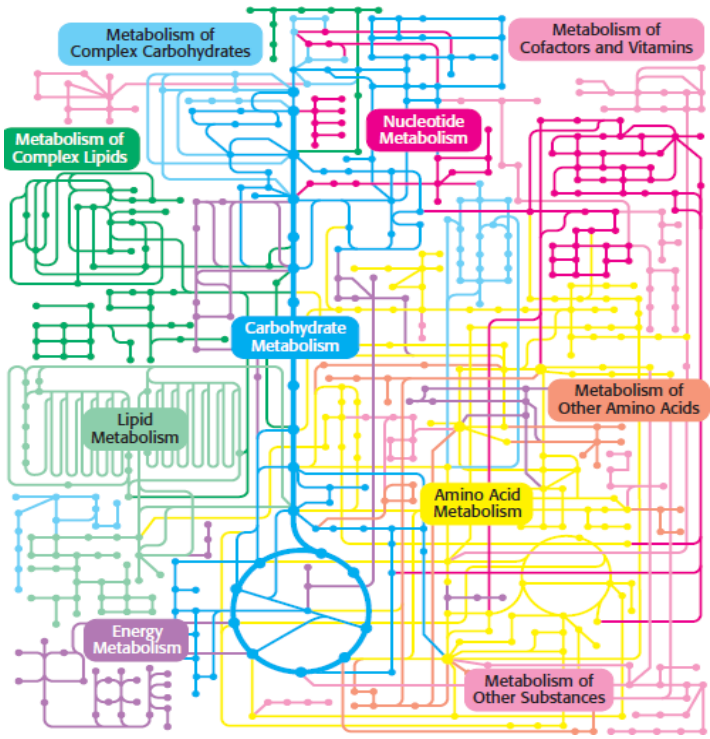
What was mentioned in the lecture:

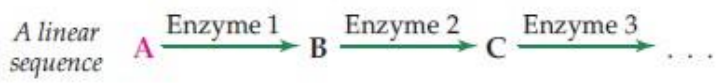
metabolism occur inside the body through pathways, it's rare to happen as single reactions and we've talked about this before when we've discussed enzymes, this is glucose and it's getting into pyruvate through 10 steps, into the anaerobic state it becomes lactate, in the aerobic it becomes as acetyl CoA, so it occurs through pathways and what applies to single reactions with respect to ΔG applies to pathways.

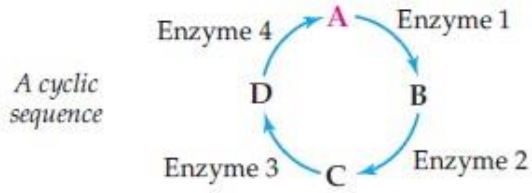
Biochemical (metabolic) pathways

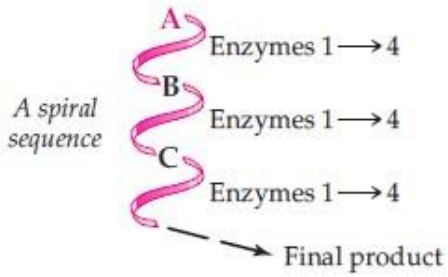
what was mentioned in the slide:

- Are <u>interdependent</u>
- Are subjected to thermodynamics laws
- Their activity is coordinated by sensitive means of communication
- <u>Allosteric enzymes</u> are the predominant regulators
- Biosynthetic & degradative pathways are <u>almost always distinct</u> (regulation)
- Metabolic pathways are <u>linear, cyclic or Spiral</u>









What was mentioned in the lecture:

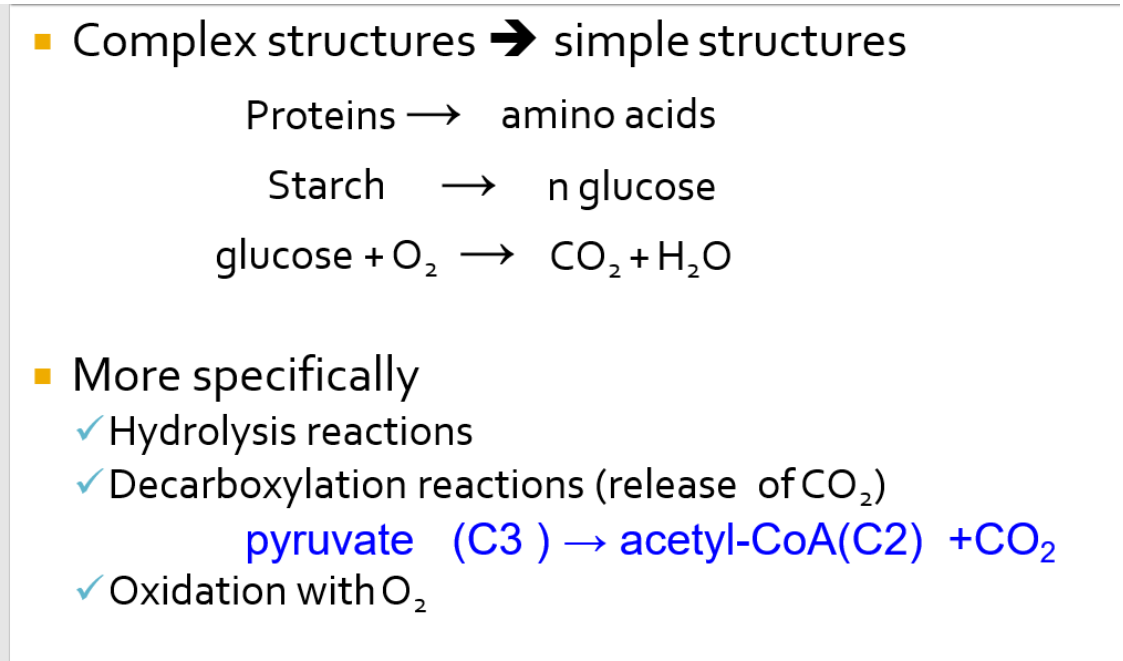
biochemical pathways are on different shapes, some of them are spiral, some of them are linear, some of them are cyclic (cyclic as Krebs cycle) where every material is leading to the other till we regenerate the first material that we started with at the end of the reaction and every step is catalyzed by a different enzyme, in linear pathway, every reaction is leading to the other till we achieve the final product and every step is catalyzed by a different enzyme, spiral the same as linear but all steps are catalyzed by the same enzymes, those are biochemical pathways inside the body (right figure) this is a real picture for the different processes that occurs within the cell, all of them are connected to each other, how do we connect them with each other? and why do we connect them? for energy saving, for the sake of energy, we do not want to lose a lot of energy, if carbohydrates does not understand what goes on with lipids, with nucleic acids, or with amino acids and how much ATP we are producing, if all of them are not communicating well, then there will be a lot of loss of energy, if we need to conserve energy well then we need to make them understanding each

DONE BY AHMAD AYMAN | DOCTOR 2019 | JU

other, how do we make them understand each other by the use of allosteric enzymes, and all of us remember from the last semester what allosteric enzymes do, they have multiple binding sites for different molecules, from different areas and from different pathways that come to this enzyme and tell him, this molecule is coming from the carbohydrates on this allosteric enzyme of the lipid to tell him that i increased in my concentration you should do this or you shouldn't do this blah blah blah

Exergonic reactions in Biochemistry

what was mentioned in the slide:



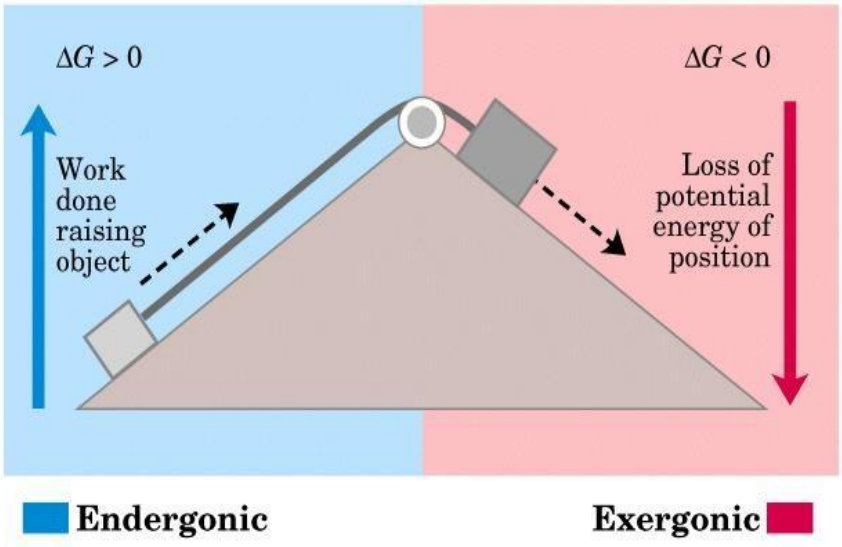
What was mentioned in the lecture:

reactions and pathways are either exergonic or endergonic, now when you look at pathways, consider this all degradative (breakdown) pathways, breaking down pathways are exergonic by nature, if you are breaking bonds you are having energy, if you need to build up molecules you need energy, so exergonic pathways and reactions by definition and by logic are exergonic in nature and those are examples of them, hydrolysis reactions, decarboxylation reactions, oxidation in the presence of oxygen.

How do our cells get energy for unfavorable biochemical work?

what was mentioned in the slide:

- The concept of coupling



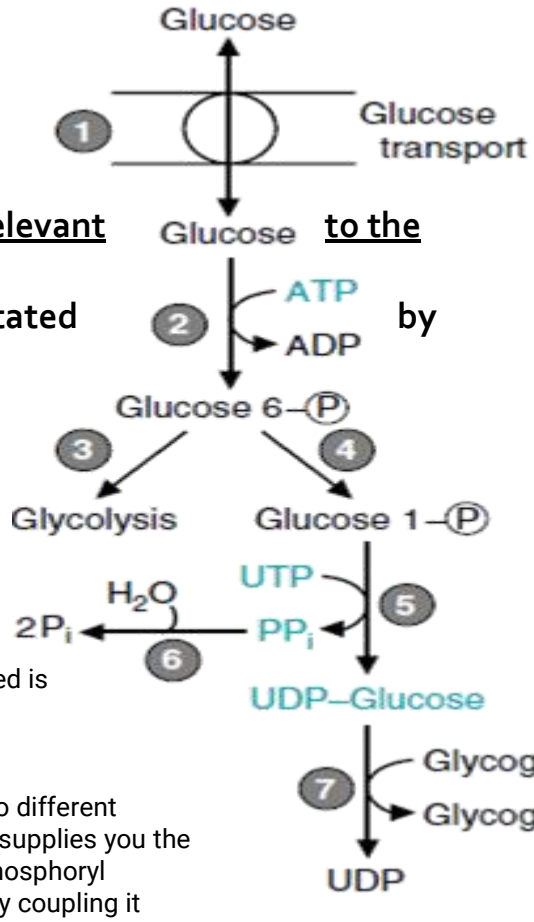
What was mentioned in the lecture:

on the other hand, endergonic reactions need energy to occur, how do we manage that inside our bodies? there is a concept of coupling, what do we mean by coupling? It means that we will couple a reaction that needs energy with a reaction that that gives us energy to go at the same time, that thing by by itself is not that smart, it is nice to couple both reactions together, but what is really smart is for that reaction needs energy, because it needs this material, that reaction needs energy because of the use of a certain material (of addition of a certain material) now what is really smart it is to couple it with a reaction to the energy and that material and this is what is defined by the phosphoryl transfer reactions (to be continued).

How do our cells get energy for unfavorable biochemical work?

what was mentioned in the slide:

I. **ΔG° Values are additive**
   i. **Through phosphoryl transfer reactions:**
      - ✓ **Step 2 (+3.3 vs. -4 kcal/mole)**
      - ✓ **Step 2 + 4 = -2.35 kcal/mole**
      - ✓ **The net value for synthesis is irrelevant to the presence or absence of enzymes**
   ii. **Activated intermediates (step 4 is facilitated by steps 5&6)**
   iii. **ΔG Depends on Substrate and Product Concentration (step 4 has a ratio of 6/94; +1.65 kcal/mol, if 3/94; -0.4kcal/mol)**



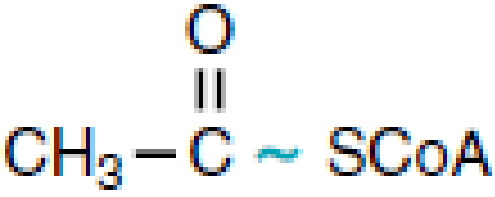
What was mentioned in the lecture:

now ATP and glucose is getting converted to glucose 6-phosphate in any cell inside the body, the addition of phosphate on glucose on carbon number six needs energy and the amount of energy needed is 3.3 kilo calorie per mole, from where to get that phosphate? you'll get it from ATP, ATP will give you the energy and the phosphate at the same time this is how coupling will become a unit , it's not becoming as this two different reactions going at the same time it will become as a unit because it supplies you the material and supplies you with the energy and this is what we call phosphoryl transfer reactions, so you can pass a reaction which is endergonic by coupling it with a reaction that gives you energy and the materials, you can use high energy intermediate as you can see here, glucose with UDP coupled to it, this is a high energy intermediate, the separation between glucose and the UDP will release energy that will make you add glucose to the glycogen stores, you can use high energy molecules ATP, UTP, CTP, GTP, TTP any of them has the same amount of energy, and that energy will be released, also pyrophosphate can be broken down to give you more energy

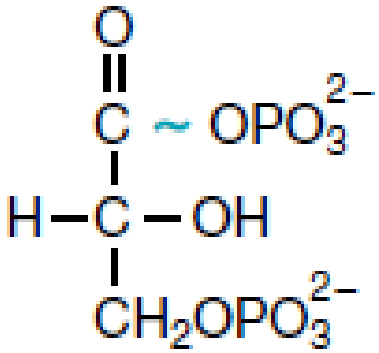
How do our cells get energy for unfavorable biochemical work?

what was mentioned in the slide:

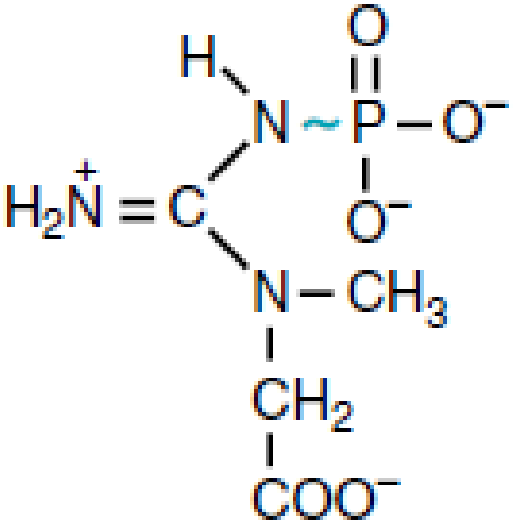
Activated Intermediates other than ATP; UTP is used for combining sugars, CTP in lipid synthesis, and GTP in protein synthesis



Acetyl CoA



1,3–Bisphosphoglycerate



Creatine phosphate

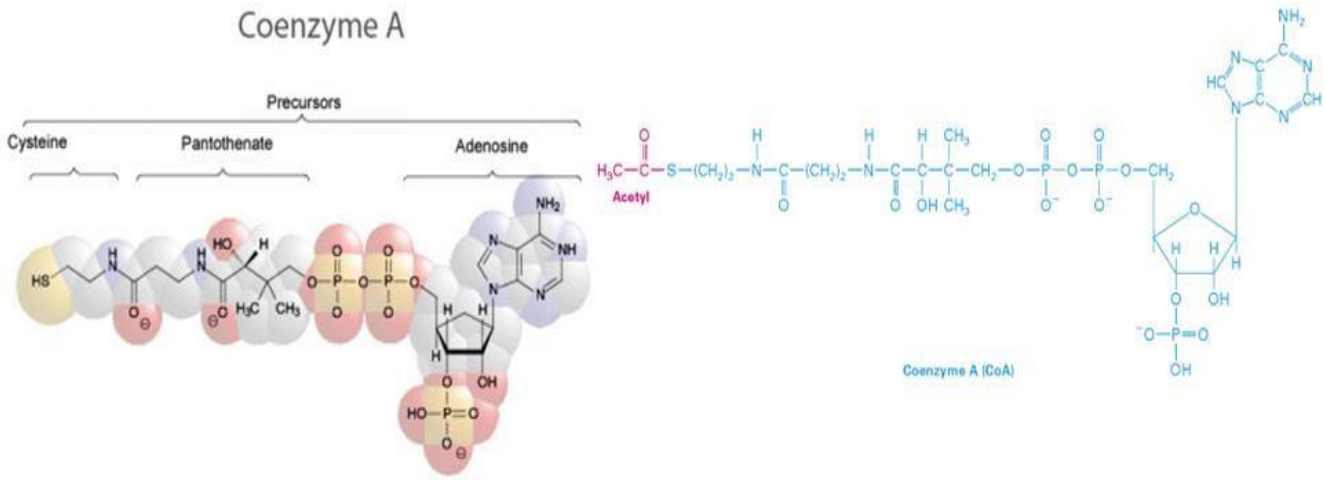
What was mentioned in the lecture:

you can use other materials as you can see here you can use 1,3-bisphosphoglycerate because it has the phosphate and breaking down the phosphate will release energy, creatine phosphate the same thing, and acetyl CoA, remember always that acetyl CoA provides energy why? because it's connected with coenzyme A, coenzyme A has sulfhydryl group because it has modified cysteine, so the sulfhydryl group when sulfur is always connected to carbon breaking down of that bond will release energy which is comparable to the ATP or more, so phosphate bonding breaking down of phosphate all the time releases energy, sulfur bonding to carbon all the time or to oxygen all the time releases energy when it is it gets broken down.

The acetyl CoA as an example

what was mentioned in the slide:

- **Coenzyme A is a universal carrier (donor) of Acylgroups**
- **Forms a thio-ester bond with carboxyl group**



- $Acetyl\ CoA + H_2O \longrightarrow Acetate + CoA \quad \Delta G^o = -7.5kcal$
- $Acetylcholine + H_2O \longrightarrow Acetate + Choline \quad \Delta G^o = -3\ kcal$

What was mentioned in the lecture:

this is the acetyl-CoA as an example in coupling reactions, now all of you know the acetylcholine, how do we make the acetylcholine? by having the acetate and the choline with each other, so from where to get the acetate? We get the acetate from acetyl-CoA, so if you'll couple acetyl-CoA with choline what happens is that the acetate from acetyl-CoA will join choline and the the energy needed for joining them will come from the separation of coenzyme A.

THERMOGENESIS

what was mentioned in the slide:

- The first law of thermodynamics
- Heat production is a natural consequence of "burning fuels"
- Thermogenesis refers to energy expended for generating heat ($37^{\circ}C$) in addition to that expended for ATP production
- Shivering thermogenesis (ATP utilization): responding to sudden cold with asynchronous muscle contractions
- Non-shivering thermogenesis (ATP production efficiency)

The body stores only 90g of glycogen , less that a piece of bread

What was mentioned in the lecture:

thermogenesis is as the name implies it the process of synthesis for heat within the body, 37 degrees (more or less) Centigrade is the optimum temperature within the body, temperature is regulated by thermogenesis, It's not as byproduct for other reactions No, It is a very regulated process.

what we want to deliver out of this slide is that the temperature is fixed, It's 37 degrees centigrade in all people, yes it varies (plus minus), but that plus minus has a lot of reasons, it varies by plus minus fractions, very small fractions and those very small fractions, one of the reasons of these fractions is the machine (thermometer) accuracy, the other reason is instant changes on the human, as a human might make it Vary by fractures (very little fractions) otherwise it's fixed, how to make it fixed in that way? We have two processes in the, which fits under thermogenesis, one of them We call it shivering thermogenesis, and the other is non-shivering thermogenesis, And the concept of thermogenesis is the production of heat for things to be at 37 degrees centigrade., why at 37 degrees? because it is the optimum temperature for the metabolism to play around, playing with temperature makes it worse for the reactions, it plays with the metabolism itself, And we've discussed the effect of temperature on enzymes before and on proteins, on lipids, blah, blah, blah.

DONE BY AHMAD AYMAN | DOCTOR 2019 | JU

people vary in their length, in their gender, in their weight, in the place they are living in, in the diseases that they have, in medicines they are taking, their age etc. So there is a huge amount of differences, which keep changing some of them daily and some of them from a time to a time, but still the body's temperature is 37 degrees centigrade, This is a controlled process, If there is a sudden change in the temperature, the body will shiver unconsciously, what does that imply? when you are shivering
You are moving muscles and there is a heat generation out to movement of muscle but that's not the goal. To keep the temperature, what happens in shivering thermogenesis (the main thing) that when you are shivering, muscles are contracting, they're using ATP, they send a message for the body that muscles need more ATP because I'm consuming this ATP. And the process of making ATP has a byproduct of. Heat generation, so the heat loss will be replaced instantly. And the other type is non-shivering, thermogenesis, which we call it adaptive thermogenesis, Now we eat food. All of us eat food for the sake of ATP production at the end, which is either proteins, carbohydrates, lipids, nucleic acids, blah, blah, blah. Everything is at the end for the sake of generating ATP., Now, producing ATP has a by-product of making heat, but how much heat?, how much percentage of that energy which is designed to make ATP is going for regeneration? This is the thing that differs from each human to another human, depending on his height, weight, gender, age, place living in, diseases, Medicines, the whole metabolism, which occurs inside his body, for example, you are eating 100 gram of carbohydrates, How much you'll specify out of that 100 for the sake of heat generation? This what the body specifies for you to keep your temperature at 37 degrees centigrade.

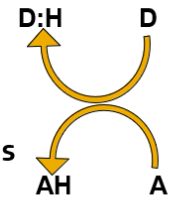
ATP is made through a process called oxidative phosphorylation, This is the main process of making ATP, This process is defective, God made it defective by having some of the energy, not directed to make ATP but directed to make heat.

Oxidation-Reduction reactions (Redox)

what was mentioned in the slide:

- **Oxidation:**
  - ✓ Gain of Oxygen
  - ✓ Loss of Hydrogen
  - ✓ Loss of electrons
- ***Reduction:***
  - ✓ Gain of Hydrogen
  - ✓ Gain of electron
  - ✓ Loss of Oxygen

- ***E*= redox Potential: it is a POTENTIAL ENERGY that measures the tendency of oxidant/reductant to gain/lose electrons, to become reduced/oxidized**



- **Electrons move from compounds with lower reduction potential (more negative) to compounds with higher reduction potential (more positive)**
- **Oxidation and reduction must occur simultaneously**

What was mentioned in the lecture:

Now we will come fast discussing oxidation reduction reactions, Why these specifically? because in energy metabolism we are dealing with oxidoreductases, we are dealing with oxidation reduction reactions because after the Krebs cycle, the goal behind Krebs cycle is to extract the electrons. and Load them on electron carrying molecules as NAD^+ and FAD to become NADH and $FADH_2$ and deliver them to the electron transport chain.
So we need to discuss how these electrons are moving .
ΔG is the difference in bond energies, here we are discussing about reactions which involve electronic transfer. We have studies enzymes that are called oxidoreductases, like dehydrogenases which transfer hydrogens with their electrons and heme that shuffles between oxidized and reduced heme forms depending on an electron which is passing between Fe^{+3} to become Fe^{+2} and vice versa, if we were given a reaction which involves a movement of electrons from this point to this point, like when FAD becomes $FADH_2$ or NAD^+ becoming NADH, Do you think that the bond energies will differ in between them to make such a driving force for the reaction to occur? How do these reaction occur if the difference in their potential energies, which is defined as bond energies, is not that difference? electronegativity might be the answer for atoms, but here we are dealing with molecules whose molecular wight is very huge. We have defined ΔG as the amount of potential energy stored, it is true that most reactions it is a bond energy, but when we come to the oxidation reduction reactions (the redox reactions) we've said that the bonds are not that different in between the reactants and the products, however, the stored energy is different. And what is different in between them? It is The electrons and the tendency for that molecule to give that electron or to accept more electrons, it is like electrons move from the electricity company (where there is high potential) to the street wires, then to the house wires, then to your phone battery where there is low potential, for electrons to move from one point to another point, then there should be a difference in what we call potential . Otherwise electrons will never move, The same thing, you should apply it to proteins and to every material inside the body that has the capacity of accepting electrons or donating electrons. (like NAD^+, FAD, heme, copper, zinc, metals and proteins that have metal in their structure) regardless of what form of these electrons, are they single electrons moving, or are they loaded on hydrogen atoms, or are they loaded on what we call hydride ion blah, blah, blah. We can reverse the direction of movement of electrons by reversing the potential.

To summarize, the purpose of Krebs cycle is to generate electrons to be transported to electron transport chain, electron transport chain is a chain of enzymes, where electrons will keep passing from one molecule to another, (from one enzyme to another), until they reach their final destination, They are moving according to difference in potential, if that difference in potential is not there, The electrons won't move.

Reduction potential

what was mentioned in the slide:

- A-P + B ⟶ A + B-P

  Type of reaction

  What determine the direction of the reaction?

- $A^{++} + B^{++} \longrightarrow A^{+} + B^{+++}$

  Type of reaction

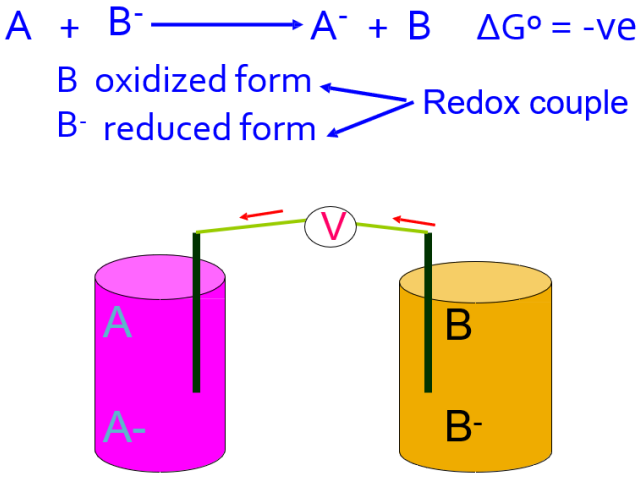
  What determine the direction of the reaction?

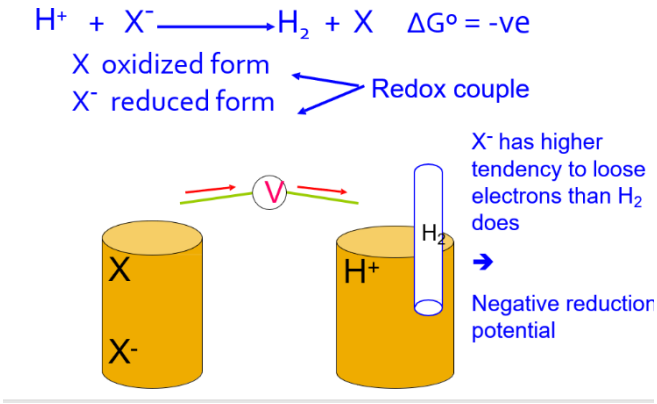
What was mentioned in the lecture:

because all materials differ in their chemical structure, regardless of they are single atoms or they are molecules, huge or small molecules, they should differ in their ability to accept electrons to be reduced And because they are different from each other, they want to measure their tendency of accepting the electrons and this measure of tendency because it's a potential, it can be measured in volts or milli-volts, Now, if you put many molecules together or two molecules together to measure their tendency of giving or accepting electrons, Then you'll see that this material can give electrons to other material or vice versa, but how much is the actual value for this one to make the values standardized? (to be continued).

Reduction potential and direction of the reaction

what was mentioned in the slide:





What was mentioned in the lecture:

So they've said as in any science in the past and nowadays, that we must have standardized values, like ΔG^{O} which We use to compare reactions together because ΔG can vary with each reaction, here also the same. They needed a reference for each material to compare it well, and the reference was used in the past is the hydrogen electrode, electrodes will move from any area to any area depending on that reduction potential. So they put the hydrogen electrode in one chamber and they've put the other material in the other chamber and they've seen how electrons will move. And how much is that tendency, which can be measured and volts because this tendency can be injured in volts, depending on that potential difference, we can tell that electrons will move from which point to which point.

So ΔE determines the direction of the reaction, the feasibility and the favorability of the reaction, and also ΔG determines this and this and this. Accordingly, there should be a relation between these two concepts with now other variables, (to be continued)

Calculation of ΔG° from ΔE°

what was mentioned in the slide:

- $\Delta G^\circ = - n f \Delta E^\circ$
  - F = Farady constant = 23.06 kcal/*Volt*
- Calculate ΔG° of the following reaction

$NADH + 1/2O_2 \longrightarrow NAD^+ + H_2O$

$NADH \longrightarrow NAD+ + 2e^-$ $\quad \Delta E^\circ = +0.32V$

$O + 2e^- \longrightarrow O^{2-}$ $\quad \Delta E^\circ = +0.82V$

$\Delta G^\circ = - 52.6$ kcal/mol

What was mentioned in the lecture:

This is the relation between ΔE and ΔG, $\Delta G^O = n*f*\Delta E^o$ n is the number of electrons moving and f is the faraday constant, ΔE is the difference in reduction potential, How much is the ability for me to be reduced? And how much is the ability for you not to be oxidized for you or to be reduced? So its comparing the variable between two substances.

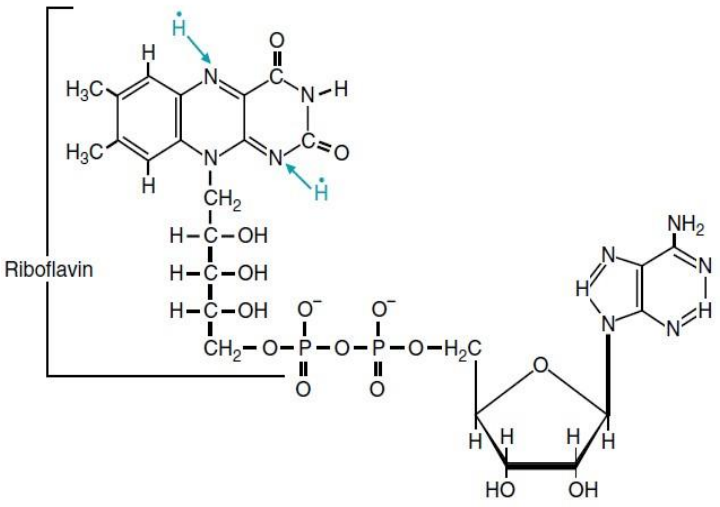
Reduction potential: Ability to accept electrons

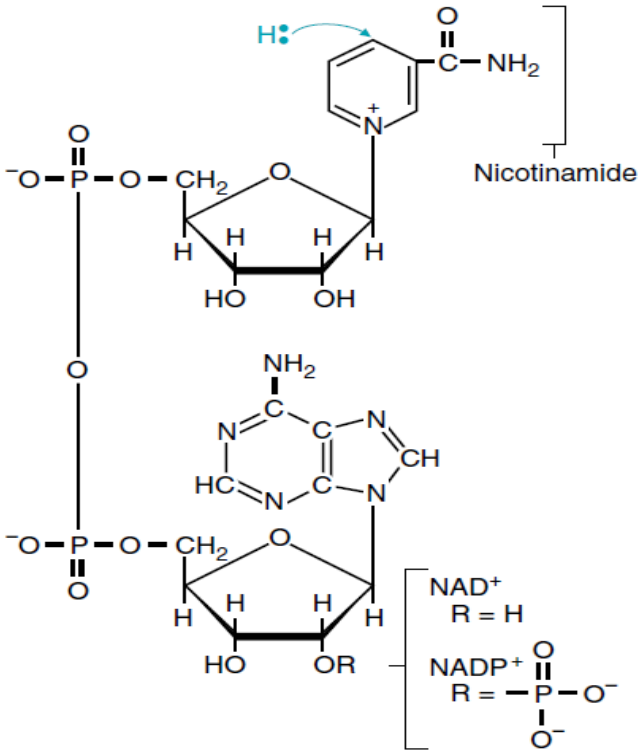
Oxidized + e^-	➔ Reduced	*ΔE° (V)*
Succinate	α ketoglutarate	- 0.67
Acetate	Acetaldehyde	- 0.60
NAD^+	**NADH**	**- 0.32**
Acetaldehyde	Ethanol	- 0.20
Pyruvate	Lactate	- 0.19
Fumarate	Succinate	+ 0.03
Cytochrome^{+3}	Cytochrome^{+2}	+ 0.22
oxygen	**water**	**+ 0.82**

Oxidation-Reduction reactions (Redox)

what was mentioned in the slide:

- $\Delta E = E_A - E_D$
- ΔE = Redox difference of a system in any condition
- ΔE^o = Redox difference of a system in standard condition ($25C^o$ and 1 atmosphere pressure, pH = 7)
  - <u>Does ΔE determine the feasibility of a reaction?</u>
    - $\Delta G^o = -nf\Delta E^o$
- In other words; energy (work) can be derived from the transfer of electrons Or
- Oxidation of food can be used to synthesize ATP
- Always involve <u>a pair</u> of chemicals: an electron donor and an electron acceptor (Food vs. NAD^+)
- NAD^+ vs. FAD
- NAD^+ vs. $NADP^+$ (fatty acid synthesis and detoxification reactions)





What was mentioned in the lecture:

We must understand Why we are going through the redox reactions, redox reactions are occurring

after food degradation, from Krebs cycle we are taking electrons. So those electrons are coming from acetyl-CoA, which is a product for protein, carbohydrate, and lipid metabolism that we ingest. so we need food to break it down to extract electrons, to synthesize ATP. So oxidation of food, breaking down a food can be used to synthesize ATP,

this is the structure of NAD^+ and how it accepts two electrons in a form of hydride ion and becomes NADH, and this is the $NADP^+$ where this R will be replaced by phosphate, both of them are doing the same action, however, in different places for different organization purposes, this is the structure of a FAD (Flavin adenine dinucleotide.), if it is FMN (flavin mononucleotide) its structure will be without the phosphates and the adenine. both of the molecules accepts two electrons in a form of hydrogen atoms. FAD one goes sequentially, not like NAD^+ and because it goes sequentially, it can generate free radicals. This is why it's all the time. bound to a protein or enzyme, it's hidden inside it, And because NAD^+ can be found swimming in the solution, it is not connected to any other molecule. Then it has a fixed potential It is -0.32 millivolt, However, there is no fixed value for FAD because all the time it's bound to a protein or an enzyme, and because of the protein or the enzyme, the environment around it affects the value.
So in one protein, you will find it. A numer and in another a different number, so you cannot give a number unless you specify the enzyme or the protein where FAD is hidden inside, The same thing applies to the heme because heme is always down to a protein or to an enzyme. So its electric potential differ from one place to another place.