فريق طوفان الأقصى

METABOLISM

Modifide N. 4

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BIOENERGETICS

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Energy & why do we need it?

Definition: Capacity to perform work

Energy is very important in living organisms because it helps to do work

- **What for? Mechanical bioenergetics (if you are talking about living organisms) , Active transport of different ligands and ions , Biosynthesis, Heat, also , some degradation process.**

- **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!**
- **metabolism vs. energy**

- **In this context we will talk about energy in living cells and how they are transduced and transformed from one form to another**

The major purpose of metabolism

- **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

- **Building blocks ex: amino acids,nucleotids, sugars ,fatty acids**

- **Bioenergetics: Energy transformations in the cell**

- **some degradation process needs energy because degradation in living cells takes stepwise and those steps are different biochemical reactions and some of those biochemical reactions are spontaneous and some of them are not spontaneous.**

- **Degradation of small molecules in most of the cases it releases energy (those reactions are spontaneous),and in some cases they require energy in order to go in the direction in which the cell needs them.**

- The energy that is extracted from the fruits could be transduced or transformed from one type of energy to another depending of what cell reacquires if it reacquires chemical energy, it will convert it into chemical energy ,if it reacquires kinetic energy ……….etc.
- And this obeys the **first law of thermodynamics** which says **energy is never destroyed but could be converted from one form to another.**
- At the same time our cells obeys **the second law of thermodynamics** in which it says **the universe is going toward randomness or disorder** ,our cells <u>fight this randomness by doing metabolism</u> and producing energy in order to keep everything inside the cell under control and in order, <u>and this is the purpose of metabolism</u>.
- The transformation of different forms of energy is called the bioenergetics in biological systems.

The different free energy terms

- 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)

- **The determination of whether a reaction is spontaneous or not is primarily based on two terms in thermodynamics: ΔG (the Gibbs free energy change) and $\Delta G°$ (the standard Gibbs free energy change).**
- **ΔG: the free energy that is available in the system to do useful work .**
- **ΔG^o : same as ΔG but at specific conditions .**
- <u>Those specific conditions are not available in the living cells</u>

- Some reactions in the cell need to be spontaneous even if ΔG is positive so there are mechanisms in the cell to make them spontaneous or to make them happen
- What's provides energy for all these process is the metabolism,so the major purpose of metabolism is to provide living cells with energy for many purposes such as active transport , movement and to keep the metabolism continuous and always working.

Suppose that your heart stop working , your breath will stop and as a result no metabolism no energy produce so you will dye in seconds ,so energy production is very important as well as metabolism that provide energy ,and they must always keep working in living cells to keep them active and live .

Gibbs free energy, ΔG

$$A \rightleftharpoons B$$

this equilibrium is not determined by enzyme but determined by thermodynamics.

more equilibrium to the A, you will not change the equilibrium by adding any amount of enzyme to the reaction.

What determine the equilibrium between them? Gibbs free energy.

ΔG which is related to equilibrium constant, can be used to determine if the reaction is favorable or not:

if $\Delta G < 0$, reaction is spontaneous,

if $\Delta G > 0$, reaction is not spontaneous

if $\Delta G = 0$, reaction is at equilibrium

- ΔG will decide if the reaction is spontaneous as well as if there is releasing of energy , and if the reaction is exothermic or endothermic.

- Because we are talking about cells , the conditions in the cell is not always like the specific conditions of ΔG^o ,**so what determine the nature of the biochemical reactions is ΔG** but don't forget that there is a relationship between ΔG and ΔG^o and also between the concentration of reactants and products with the ΔG.

Standard free energy change ΔG°

Concentrations of reactants and products = 1 mole/L

$$\Delta G = \Delta G^o + RT \ln \frac{[Products]}{[Reactants]}$$

- This ratio is changeable depending on the need of the cell

- ΔG° is constant for a specific reaction

$$\Delta G = \Delta G^o + RT\ 2.3 \log \frac{[Products]}{[Reactants]}$$

- R: gas constant

- T: Temperature in Kelvin

- If I give you ΔG° for any reaction if it is negative(-) most probably the reaction is spontaneous but, in some cases, it is not the only determinant of the direction of the reaction ,in addition to it the log products/reactants , and the cell changes this ratio in order to reach the equilibrium according to the need of the cell if it want the reaction to have(-)or(0)or(+) ΔG.

Standard free energy change (ΔG^o) and equilibrium constant Keq

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

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

- **This ratio is not changing at equilibrium, independent of the concentrations.**

At equilibrium **ΔG is zero:**

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

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

- **In this case ΔGº is related to K_{eq} so ΔGº will give us the idea about the dissociation constant of equilibrium constant of the reaction.**
- **While total ΔG will give us other information other than K_{eq}**

ΔG & Keq

- The relation between ΔG and keq is logarithmic

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

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

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

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

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”

- When keq>1, ΔGº is negative (-) and the reaction proceed forward and happen spontaneously.
- When keq=1,no reaction it is equilibrium
- When keq<1, ΔGº is positive (+) ,and the reaction proceeds backward, but it does not happen spontaneously

- So, what determines the spontaneity of the reaction is this ΔG that depends on ΔGº plus this log of this ratio. The equation

ΔG^o and K_{eq}

K_{eq}	ΔG^o
10^3	- 4.08
10^2	- 2.72
10^1	- 1.36
1	0
10^{-1}	1.36
10^{-2}	2.72
10^{-3}	4.08

How much change in delta G compared to changes in Keq

If $K_{eq} = 1$, then $\Delta G^o = 0$

If $Keq > 1$, then $\Delta G^o < 0$

If $Keq < 1$, then $\Delta G^o > 0$

Gibbs free energy conditions & ΔG`0

ΔG depends on conditions: equilibrium & concentration

A↔B at equilibrium, [A] and [B] are not changing. ΔG=0.

If we add more A, leads to production of B,

ΔG A-B <0, until you establish the equilibrium.

If we add more B, leads to production of A, ΔG B-A <0, until you establish the equilibrium, or ΔG A-B >0.

Does not matter how much A or B added, **the equilibrium** depends on the ratio of [B]/[A] not the absolute concentration of each species. The ratio will stay the same.

In the reaction of A to B

if we change the concentrations of A and B what will happen to ΔG^o ? Nothing

What will happen if we change the concentrations of A and B to ΔG ? Depends

Now we are at equilibrium, the ratio is not changing , if we add more A this reaction will go to more production of B , ΔG will be –ve , so changing concentrations of A and B affects ΔG, if we add more B – more A will be produced and ΔG is +ve (A to B),

So ΔG is affected by the changing concentrations of products and reactants.

So, concentration of products and reactants has to do with the value of ΔG and as a result it will determine the directionality of the reaction.

Direction of a reaction

If $\Delta G_{A-B} = 0$, $\Delta G`0 = -RT \text{ lin } [B]/[A]$, so you can calculate the equilibrium constant if you know the ratio or the concentrations of A and B.

A→ B

If $\Delta G`0 < 0$, then B is favored over A at equilibrium

If $\Delta G`0 > 0$, then A is favored over B at equilibrium

So $\Delta G`0$ is the convenient way to determine the direction of the reaction

ΔG depends on conditions: $\Delta G`0$ and the concentration of B &A

If $\Delta G < 0$, then, the RX is spontaneous, energy is released,

If $\Delta G > 0$, then, there is no RX without energy input

- **The complement in this slide:**

A lot of biochemical reactions in metabolism , they obey this role of thermodynamics , depends on their total ΔG to determine to what direction the reaction goes for (toward products or reactants) and that depends on the cell , sometimes when the cell requires A to go towards B (consuming energy reaction) and ΔG is +ve what will happen ?

In a specific mechanism we do ''coupling'' with –ve ΔG reaction , keep in mind that ΔG is additive .

E.g. when we have a +ve ΔG reaction and another super –ve ΔG reaction , since ΔG is additive we will have a total –ve ΔG reaction → A will go towards B

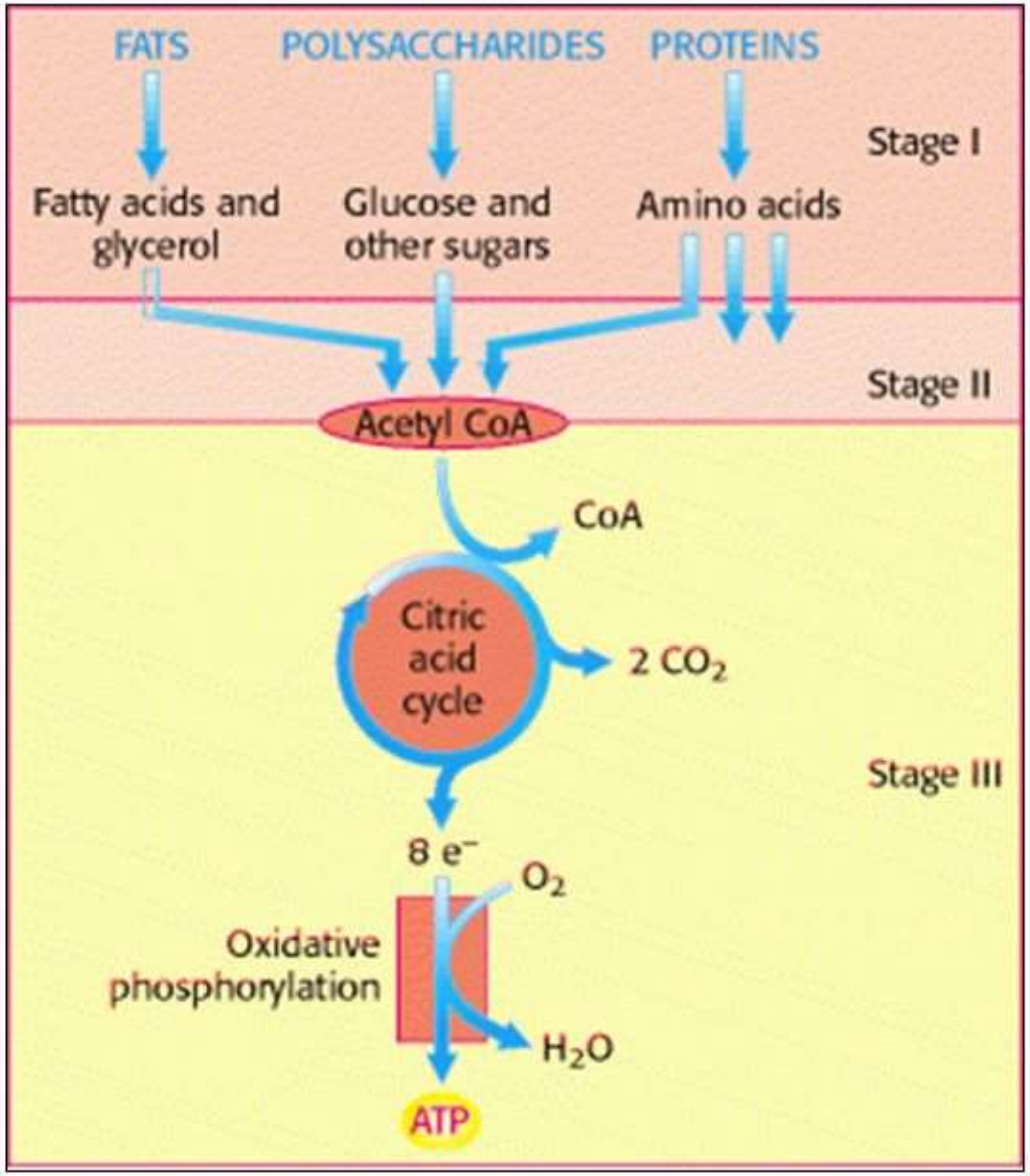
- **Additional information:** coupling means using an exergonic reaction (releases energy) as a driving force to complete an endergonic reaction (consumes energy)

- ΔG depends on conditions which are : ΔGº and the concentration of products and reactants.

Stages of catabolism

صحيح هتشوف الكلام الي تحت طويل لكن فعليا كله فهم
وان شاء الله بسيط (:

- **1st stage:** Large molecules in food are broken down into smaller units. Preparation stage without capture of energy.
  - Proteins -> amino acids,
  - Polysaccharides -> monosaccharides (glucose, ...)
  - Fats -> glycerol, fatty acids.
- **2nd stage:** Molecules are degraded to simple units that play a central role in metabolism. Most of them are converted into the acetyl unit of acetyl CoA. Some ATP is generated in this anaerobic stage, but amount is small compared with 3rd stage.
- **3rd stage:** ATP is produced from the complete oxidation of the acetyl unit of acetyl CoA. Acetyl CoA brings acetyl units into the citric acid cycle, where they are completely oxidized to CO_2. Four pairs of electrons are transferred (three to NAD^+ and one to FAD) for each acetyl group that is oxidized. Then, a proton gradient is generated as electrons flow from the reduced forms of these carriers to O_2, and this gradient is used to synthesize ATP.



- **The complement in this slide:** to give you an overview on components of metabolism and where energy is released .

Metabolism could be oxidation or degradation and that part of metabolism is called catabolism (releases energy) and polymerizing building blocks of macromolecules is called anabolism (requires energy).

Anabolism uses the released energy (of catabolic reactions) it must be high energy in order for anabolism takes a place .

What are the stages of metabolism ? Simply metabolism is a collection of biochemical reactions obey thermodynamic rules

($\Delta G = \Delta G^{o} + RT * Ln$ (products/reactants)

What happens in these stages that we eat food to produce energy , what form of energy ? That what we are going to learn during this slide (:

■ **The complement in this slide:**

How do we extract energy , in what form ? , from the food we eat .

We eat lipids , carbohydrates , proteins .

By the first stage of metabolism which is the (Digestion and absorption) using some enzymes lipids are converted to fatty acids and glycerol , carbohydrates → glucose and simple sugars (galactose fructose ,,,.) , proteins → amino acids

There is no produced energy in the first stage of metabolism .

■ **The complement in this slide:** طيب احنا حكينا انه عمليات الهدم بتنتجلنا طاقه ليش هدول عمليات هدم والدكتور بحكي انه ما في انتاجيه للطاقه ؟

ارجعو لكلام الدكتور بسلايد

the major purpose of metabolism 4 سلايد رقم

- **The complement in this slide:** the next stage (2^{nd})is the oxidation or degradation (**the reversible stage**) anabolic and catabolic **but not at the same time .**

Meaning that whenever cell requires to build the blocks (polymers for storage) , the reverse reaction happens , but during energy release fatty acids are oxidized in specific metabolic pathways called **β-oxidation** in which fatty acids are converted to acetyl coA and it is a high energy molecule , each acetyol coA is composed of 2 carbons , **if you have a fatty acid of 16 carbons then how many acetyl coAs ? ANS : 8 acetyl coAs will be produced from degradation of 16C fatty acids**

Glucose via a process called glycolysis it will be degraded or oxidized into pyruvic acid a 3 carbons molecule

How many pyruvates will be produced from glucose ? ANS: 2 pyruvates

And amino acids that come from proteins upon oxidation , some of them will be converted to pyruvate , and some to acetyl coA and some of them to other intermediates to be further oxidized.

- **The complement in this slide:** in this stage which the small molecules (fatty acids , glucose , amino acids) are degraded all and converted into acetyl coA , there will be a production , releasing of energy in this stage .

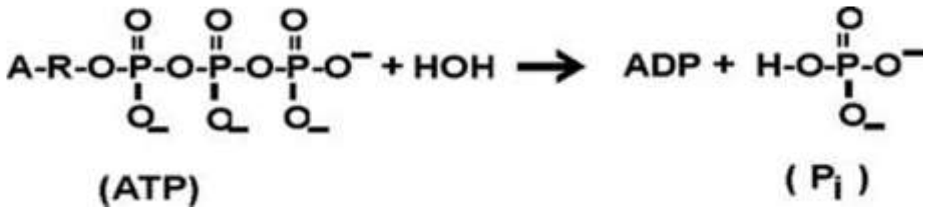
If you are talking about anabolism , synthesis of amino acids , fatty acids , sugars consumes energy (E.g., you need energy to convert a pyruvate to acetyl coA).

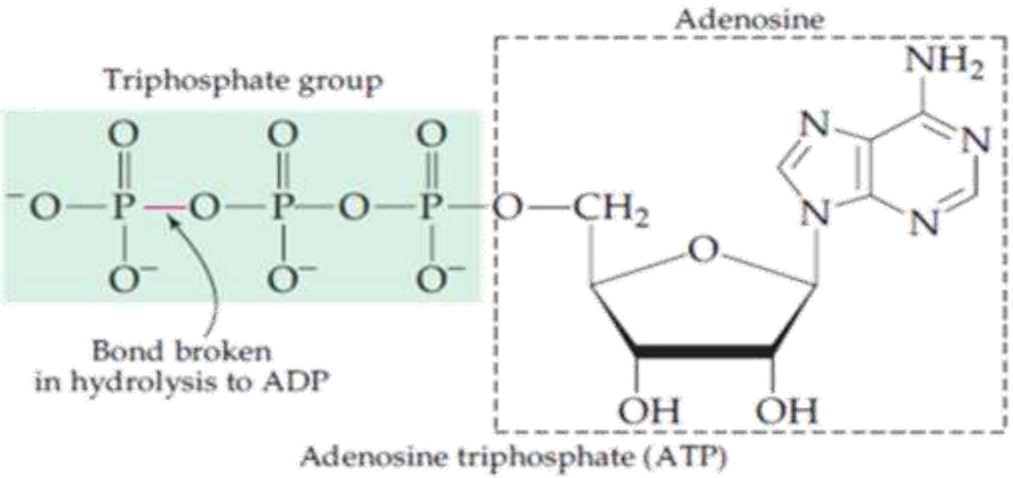
Acetyl coA that is produced in the 2nd stage of metabolism is going to be oxidized into 2 molecules of CO_2 and one molecule of water .

In addition to that , some energy currency molecules such as ATP , GTP and many reducing powers or co factors such as NADH +H and $FADH_2$, these reducing powers are loaded with electrons and protons as result of the oxidation of acetyl coA , and they will go to the electron transport chain and transfer their electrons via different carriers .

While those electrons are being transferred via ETC (electron transport chain) between carriers , energy will be released and that energy will be used in the synthesis of ATP by an enzyme in the inner mitochondrial membrane called ATP synthase ,a lot of ATP molecules will be produced here from those protons and electrons that passed between carriers , so indeed you are converting your food into electrons and protons used in oxidative phosphorylation of ADP into ATP and those protons and electrons are accepted by oxygen that will be reduced into water . **Long story sry (:**

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





- **NOTE:** phosphoenolpyruvate to pyruvate is spontaneous

- **NOTE:** phosphoenolpyruvate is one of the intermediates of glycolytic pathway and its energy is used to synthesize ATP in glycolytic pathway in a process called " substrate-level phosphorylation" , easier to produce ATP than synthesizing it details later (; .

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

- **The complement in this slide:** ATP is composed of a nucleoside called adenosine , Adenosine = adenine + pentose sugar , this nucleoside is connected with 3 phosphate groups

In each of these phosphate bonds , upon hydrolysis energy will be released from them , it was found that when ATP is converted into ADP one of the energy bonds is hydrolyzed and this amount of energy is released (-7.3)

If you look at this table you will see other compounds that produce more energy in their metabolism than ATP , but ATP is used as the currency for energy in metabolism not these high energy compounds

ATP is easier to be reproduced than being synthesized , glucose and phosphoenolpyruvate carry more energy than ATP

Another reaction in glycoses when 1,3-bisphosphoglycerate is converted into 3 phosphoglycerate by enzyme 3 phosphoglycerate dehydrogenase , also at this step an ATP could be produced in a glycolytic pathway , and it is easier to the cell to produce it during substrate level.

- **The complement in this slide:** creatine phosphate vs creatine, when some cells are in sudden shortage of ATP like muscle cells , creatine phosphate will be converted to creatine, creatine will produce ATP in seconds and let the muscle contract (when the muscle is unable to produce ATP)

تم بحمد الله تعالى
اللهم احفظ أهلنا في غزة
شافي جرحاهم وتقبل شهداءهم وصبّر أهلهم وانصرهم على
عدوهم يا عزيز يا جبار

V2: slide N.12

ΔG^{o} Instead of ΔG

Keq=1 instead of Keq=0