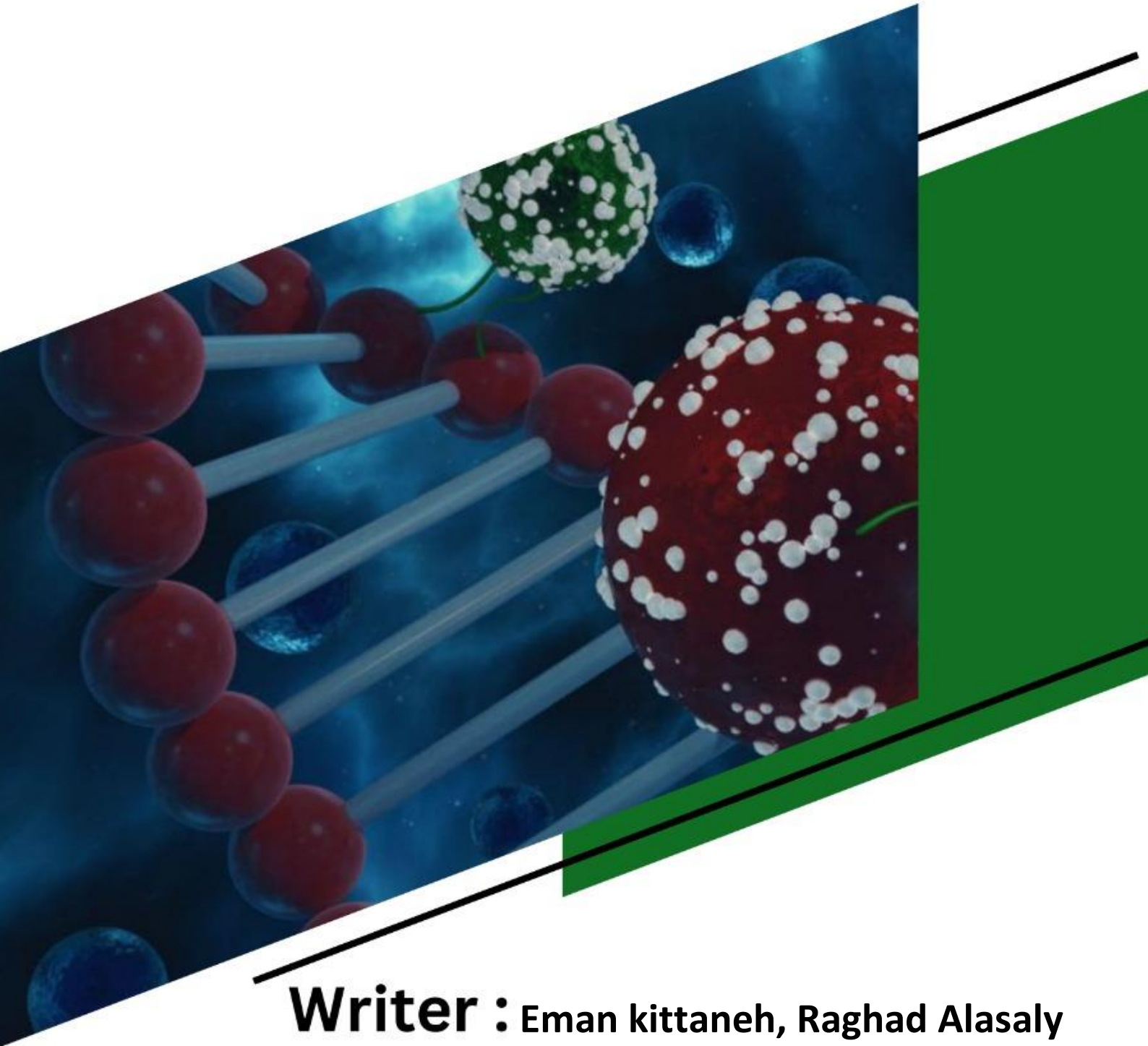




# METABOLISM

Sheet no. 2



**Writer :** Eman kittaneh, Raghad Alasaly

**Corrector :** Enjood Mhairat

**Doctor :** Nafeith abutarbosh

To remember:

- Endergonic reaction  $\rightarrow$  (positive  $\Delta G$ )/unfavorable
- Exergonic reaction  $\rightarrow$  (negative  $\Delta G$ ) /favorable

## STANDARD FREE ENERGY CHANGE $\Delta G'$

CONCENTRATIONS OF REACTANTS AND PRODUCTS = 1 MOLE/L

$$\Delta G = \Delta G' + RT \ln \frac{[\text{PRODUCTS}]}{[\text{REACTANTS}]}$$

$$\Delta G = \Delta G' + RT 2.3 \log \frac{[\text{PRODUCTS}]}{[\text{REACTANTS}]}$$

This equation describes the relation between  $\Delta G$  and the concentrations of either products or reactants.

From this equation we just need to understand the ratio between the product and reactants.

- $\Delta G$  has a direct relation to concentration
  - Con. Product increase  $\rightarrow$  ratio increase
  - Con. Reactants increases  $\rightarrow$  ratio decreases
- Any Ratio always have 3 options:
  - a. Above 1  $\rightarrow \ln \rightarrow$  positive
  - b. 1  $\rightarrow \ln \rightarrow$  zero
  - c. Below 1  $\rightarrow \ln \rightarrow$  negative
- You can have reaction at standard conditions with (-) or (+)  $\Delta G'$
- What determines the favorability in the reaction?  $\Delta G$  not  $\Delta G'$
- Playing with product and reactants concentrations allows us to change exergonic ( $-\Delta G$ ) reaction to endergonic ( $+\Delta G$ ) inside the body and otherwise which will change the reaction from favorable to unfavorable
- As we change concentrations we change number of moles, thus changing bonds and energy content, this will change the direction of the reaction so it will move from high energy content to low energy content.
- How to make a favorable reaction unfavorable?  
by Increasing the amount of products

❖ Example :

ATP hydrolysis ( $\Delta G = -7.3$ ) is an Exergonic reaction, how can I make it unfavorable (Endergonic)?

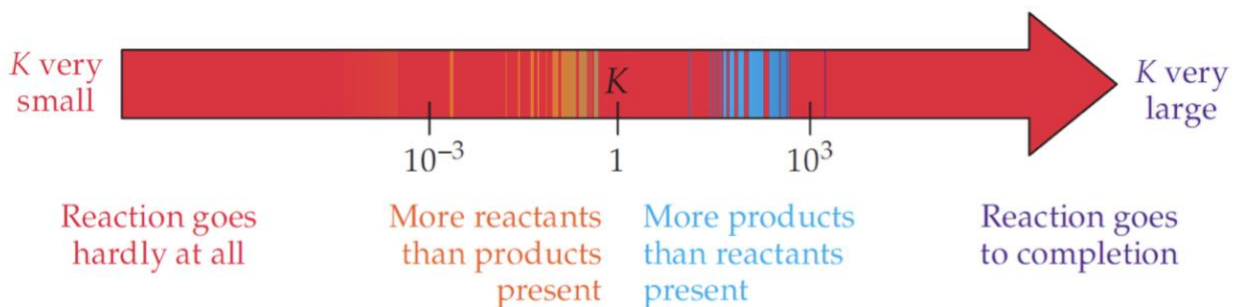
By increasing the products which are (ADP/p) which will decrease the concentration of ATP.

## REVERSIBLE REACTIONS & CHEMICAL EQUILIBRIUM

What is a reversible reaction?

What is the chemical equilibrium? Chemical equilibrium is an active, dynamic condition

At equilibrium, are concentrations equal?



- Theoretically speaking all the reaction must be reversible but essentially there are irreversible reaction and that is caused when there's a very large energy difference between the reactants and the product (very negative  $\Delta G$ )

Example: Krebs cycle is 8 steps, irreversible reaction and 3 steps of them have a very large negative  $\Delta G$

- Reversible reaction will reach at the end equilibrium state.

## STANDARD FREE ENERGY CHANGE $\Delta G'$ AND EQUILIBRIUM CONSTANT $K_{eq}$

Equilibrium

\*a state when the potential energy between products and reactants is equal.

\*Or when the rate of the convergence in the forward reaction equals the rate of convergence in the backward reaction.

\*(there are no favorability in the reaction)

$\Delta G = 0$  always at EQUILIBRIUM

$\Delta G' = -RT \cdot 2.3 \log \frac{[\text{Products}]}{[\text{Reactants}]}$

\*Concentrations of the product and reactants might or might not be equal.

\*Dynamic not static situation but the energy is preserved so we can generate a constant for equilibrium which is Keq.

**KEQ IS OBTAINED BY DIVIDING [PRODUCTS] BY [REACTANTS] WHEN THE REACTION REACHES EQUILIBRIUM.**

- AT EQUILIBRIUM**

$$K_{eq} = \frac{[\text{products}]}{[\text{reactants}]}$$

$$\Delta G = \Delta G' + RT \ln \frac{[\text{PRODUCTS}]}{[\text{REACTANTS}]}$$

$$\Delta G = \text{zero}$$

$$\text{ZERO} = \Delta G' + RT \ln K_{eq}$$

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

Q: Is there a difference between [Products] / [Reactants] (RATIO) in these two?

<div style="border: 1px solid black; padding: 5px; display: inline-block;">1</div> $K_{eq} = \frac{[\text{Products}]}{[\text{Reactants}]}$	<div style="border: 1px solid black; padding: 5px; display: inline-block;">2</div> $\Delta G = \Delta G^\circ + RT \ln \frac{[\text{Products}]}{[\text{Reactants}]}$
--	--

Yes, in 1 it represents the ratio at eq only.

In 2 it represent the ratio at any condition.

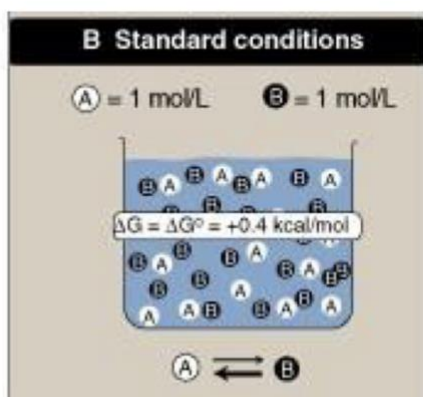
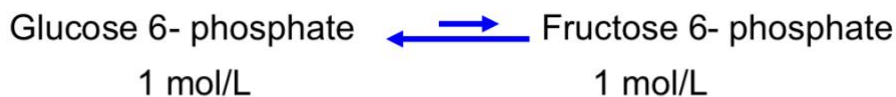
- AT STANDARD CONDITIONS**

$$[\text{products}] = [\text{reactants}]$$

$$\Delta G = \Delta G' + RT \ln \frac{[\text{PRODUCTS}]}{[\text{REACTANTS}]}$$

$$\Delta G = \Delta G' + RT \ln 1, (\ln 1 = \text{ZERO})$$

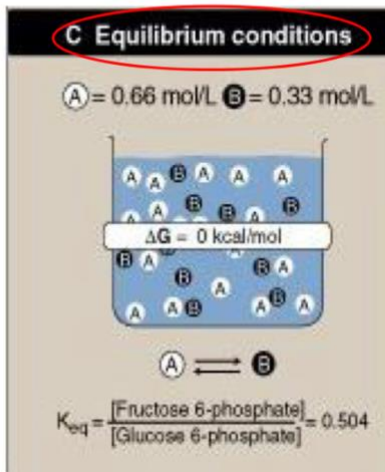
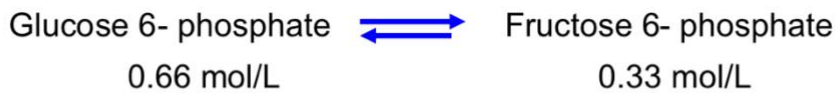
$$\Delta G = \Delta G'$$



$$\Delta G = \Delta G^\circ + RT \ln 1/1$$

$$\Delta G = \Delta G^\circ$$

**Q:calculate  $\Delta G'$  for this reaction: (equilibrium)**



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

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

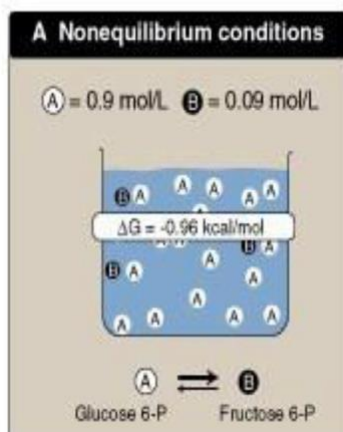
, At Equilibrium conditions

$$\Delta G = \text{Zero}$$

- We calculated  $\Delta G'$  so in any other condition I can find  $\Delta G$

\*The two equal blue arrows  $\rightarrow$  indicate that the reaction is at equilibrium.

**Q:calculate  $\Delta G$  for this reaction :(non equilibrium condition)**



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

$$\Delta G = \Delta G^\circ + RT 2.3 \log 0.09 / 0.9$$

$$\Delta G = - 0.96$$

- This reaction is Endergonic ( $+\Delta G'$ ) at standard conditions but when I played with concentrations it became exergonic ( $-\Delta G'$ ) at physiological conditions.

\*Arrow indicates that the forward reaction is favored.

Q:Why do we need to convert glucose to fructose in this reaction?

2<sup>nd</sup> step in glycolysis always is transferring glucose to fructose by isomerase enzyme ,Because Phosphorylation happens twice, we need 2 carbons.And since glucose is hexagonal ring structure (has 1 carbon outside the ring) and fructose is pentagonal ring structure (has 2 carbons outside the ring) hence



glucose is transferred to fructose so phosphorylation could happen to the 2 carbons outside the ring.

-comparing the previous two examples, we notice a decrease in concentration of products and an increase in the concentration of reactants and that resulted in converting this reaction from a non-favorable endergonic one to favorable exergonic one.

To sum up:

We can change a reaction whether it is exergonic or endergonic by changing the concentration of reactants and products since it changes its free energy.

## $\Delta G'$ & $K_{eq}$

if a reaction started with equal concentrations of reactants and products, and then reached equilibrium.

$\Delta G = 0$ , therefore  $\Delta G'$  can be calculated from the equation:  $\Delta G' = -RT \ln K_{eq}$

$K_{eq}$  would have different possible values as the following schedule suggests:

$K'_{eq}$	$\Delta G'^{\circ}$ 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 <b>equilibrium</b>
$10^{-2}$	+ 11	reverses to form “reactants”
$10^{-4}$	+ 23	reverses to form “reactants”

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

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

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

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

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

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

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

$K_{eq} = 10^4$  means that the ratio between concentrations is

$10^4 [\text{Reactants}] = [\text{Products}]$  at equilibrium, which means that at the beginning before equilibrium, the forward reaction was favored and gave more products than reactants.

using the value of  $K_{eq}$ ,  $\Delta G'$  equals -23 kJ/mol accordingly.

at the beginning, neither forward nor backward reaction was favored, products and reactants were produced at the same rate.

$K_{eq} = 10^{-2}$  means  $[Products] = 10^{-2} [Reactants]$  at equilibrium

at the beginning before equilibrium, the backward reaction was favored and gave more reactants.

$\Delta G' = + 11 \text{ kJ/mol}$

Conclusion:

If the reaction started with 1mol/L concentration for reactants and products (standard conditions) and you knew  $K_{eq}$  could you know which way the reaction will move? Yes by  $K_{eq}$  value

If:

- ( $K_{eq}=1$ )  $\rightarrow$  it's already at equilibrium,
- ( $K_{eq}>1$ )  $\rightarrow [Products]>[Reactants] \rightarrow$  moving forwards.

Explanation: (they started with the same concentrations then the product concentration become higher so it's moving forward to reach equilibrium)

- ( $K_{eq}<1$ )  $\rightarrow [Products]<[Reactants] \rightarrow$  moving backwards.

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

If  $K_{eq} > 1$ , then  $\Delta G^\circ < 0$

If  $K_{eq} < 1$ , then  $\Delta G^\circ > 0$

## THE EFFECT OF CHANGING CONDITIONS ON EQUILIBRIUM

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
- ❖ Concentration change effect:

What happens if a reactant/product is continuously supplied/ removed?

- If you increases the product reaction moves backwards.
- If you increases the reactants reaction moves forwards.

▪ **Metabolic reactions sometimes take advantage of this effect**

❖ **Temperature change effect:**

**Endothermic/exothermic are favored by increase/decrease in temperature, respectively.**

\*conceder temperature as one of the reactants or product.

If the reaction is:

- Exothermic→release's heat, temperature is considered as a variable in product.

Ex:exothermic reaction in eq ,temperature increases →product increase  
→reaction moves backwards.

- Endothermic →consume's heat ,temperature considered as a variable in reactants.

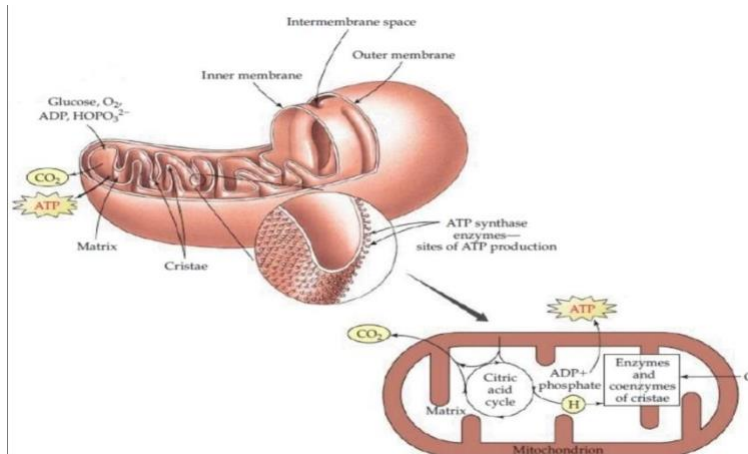
Ex:endothermic reaction in eq ,temperature increases→ reactants increases  
→reaction moves forward.

❖ **Effect of a catalyst on equilibrium (enzymes):**

- Enzymes have nothing to do with  $\Delta G$
  - They just help in reaching the eq faster ,but don't change anything in the eq state.
- So NO EFFECT.

## ENERGY MACHINERY IN THE CELL

**(MITOCHONDRIA)** The mitochondria- singular mitochondrion:





-**origin** of mitochondria (according to the evolution theory): It was prokaryotic and formed an **تعايش داخلي** (bacteria) cell that inhabited in a eukaryote **endosymbiotic relationship**

the cell would supply it with nutrients and in return the mitochondria will supply the cell with energy .

What support this theory is :

1-Structure: (very similar to bacteria's structure): 2 membranes inner and outer, inter-membrane space, circular DNA.

**2-can replicate by itself throughout binary fission** ,it does not depend on the replication of the mother cell , and there is no regulation from the mother cell on it . for example , If there are 10 mitochondria in the mother cell and it want to replicate into two daughter cell, the mitochondria well be randomly distributed (1,9) ,(10,0) .....

So the possibilities are :

1)one daughter cell would have all the 10 mitochondria and the other would have none which causes it to die.

2) mitochondria would be distributed in different ratios between the two cells respectively: 9:1, 8:2, 7:3, 6:4, 5:5

**To sum up** : mitochondrial replication has nothing to do with cellular replication .

- **It produces 90% of the cell's energy. 10% are produced in the cytoplasm by glycolysis. cells that lack mitochondria (e.g., RBCs) are supplied with ATP through glycolysis in their cytoplasm.**

- **on average the number of mitochondria per cell is 2000, the number of mitochondria is greatest in the eye, brain, heart, & muscle, where energy need is the greatest.**

**What is the only factor that determines the mitochondrial replication rate ?**

- energy demand determines mitochondrial replication rate; demand increases , mitochondria number will be increased ,e.g : athletes regularly exercise; therefore, they have energy demand which increases numbers of mitochondria in their muscle cells which aids in building up muscles and increases their endurance.

-mitochondrion needs more than 1000 different protein types, it synthesizes (by its own DNA) 13 protein subunits of its own, and the cell fulfils the other protein supply by synthesizing them in the nucleus and translocating them to the mitochondria.

**Finally , mitochondrial mutations are maternally inherited; any mutations in the mother's mitochondria can be inherited to both female and male off springs, while any paternal mitochondrial mutation can't be inherited.**

(the sperm donated by the father forming the fertilized egg contains mainly the DNA, it has mitochondria in the tail but it is mainly for movement, so if the father's sperm has a mutation it won't be passed )

## Stages of energy production:

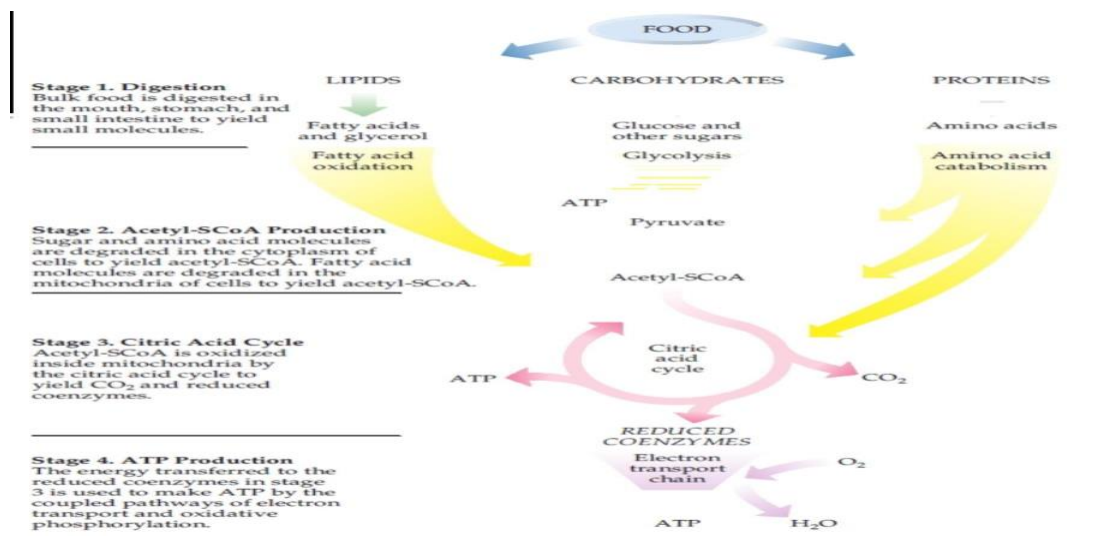
**Stage 1: Digestion;** food breakdown into monomers by mouth and stomach

Carbs → glucose, other sugar

Proteins → amino acids

Triacylglycerols → glycerol + fatty acids monomers

then are absorbed by the small intestines, delivered to cells by the blood.



### Stage 2: Metabolism

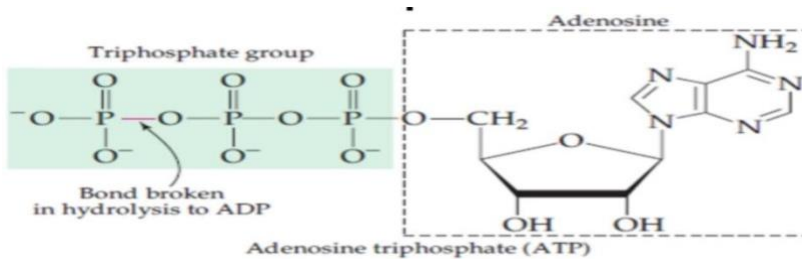
different monomers regardless of their nature are broken down into a common molecule Acetyl-coenzyme A

**Stage 3: kerbs' cycles (citric acid cycle)** Acetyl-coenzyme A is used to produce electron carrying (NADH + FADH<sub>2</sub>) molecules. **Stage 4: electron transfer chain & oxidative phosphorylation.**

electron carriers are used to produce ATP from the electron transport chain in the oxidative phosphorylation process.

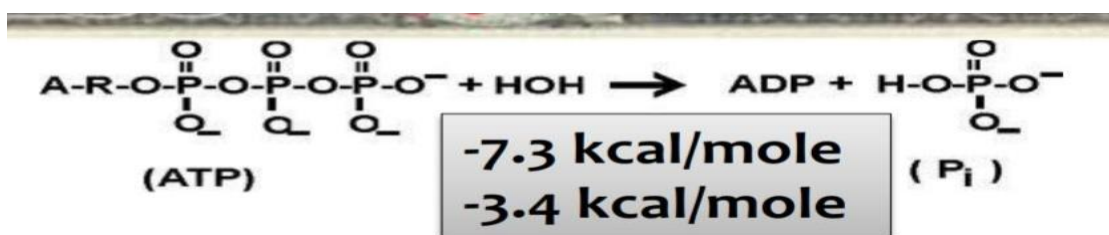
## ATP

- Adenosine triphosphate



- energy currency of the cell
- used as an assessment for cell's energy content.
- why is ATP specifically chosen as the main source of energy?

because it has an intermediate energy value, it can be broken down and resynthesized easily by coupling it with body reactions. ATP hydrolysis produces energy of a value 7.3 kcal/mole, ATP resynthesis would be coupled by a reaction that has energy value around 7.3 kcal.



So any molecule that gets broken down inside the body must be resynthesized, it is inconvenient to use a high-energy molecule like phosphoenol pyruvate (14.8 kcal/mole) or low energy molecule like glucose-6 phosphate (3.3 kcal/mole) as an energy source because when broken down it would be hard to find another reaction in the body that has the same amount of energy resource to resynthesize them again

Compound +H <sub>2</sub> O	Product + phosphate	$\Delta G^\circ$
Phosphoenol pyruvate	Pyruvate	-14.8
1,3 bisphosphoglycerate	3 phosphoglycerate	-11.8
Creatine phosphate	Creatine	- 10.3
<b>ATP</b>	<b>ADP</b>	<b>- 7.3</b>
Glucose 1- phosphate	Glucose	-5.0
Glucose 6- phosphate	Glucose	-3.3

- the value of released energy upon ATP hydrolysis is determined by:

- 1) the amount of energy between the oxygen and phosphate in their **P—O bond**

- 2) **orientation** of other atoms around the bond.

- when the first phosphate is released from ATP, 7.3 kcal/mole is released, same thing applies to 2nd phosphate release because the atoms forming the bond and the orientation around the bond didn't change, but when it to the 3rd phosphate the energy value differs because atoms distribution is different(close to the suger ) in this case which equals to 3.4 kcal/mole.

ATP → ADP + 1<sup>st</sup> P.                      7.3 kcal/mole

ADP → AMP + 2<sup>nd</sup> P.                      7.3 kcal/mole

AMP → adenosine + 3<sup>rd</sup> P    3.4 kcal/mole