DOCTOR 2020 | JU

METABOLISM

WRITER : Hala Zaghloul & Dana Oshroqlaban

CORRECTOR : Hala Zaghloul & Dana Oshroqlaban

DOCTOR: Dr. Nafeth Abu Tarboosh

Standard free energy change ΔG^o and Equilibrium constant K_{eq} (slide 10)

Recall that:

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

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

- **At Equilibrium**:

- there's no driving force for any reaction (forward or backward)
- no reaction is favored over the other because they have the same rate
-which means: $\Delta G = 0$
-At equilibrium concentrations of products and reactants aren't necessarily equal.

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

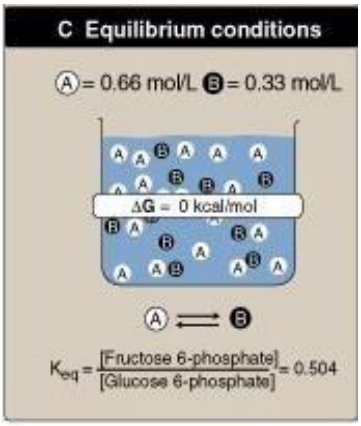
As a result, $\Delta G^o = - RT \ln (K_{eq})$
**we can use the previous equation to calculate ΔG^o at equilibrium.

- **At standard conditions**:

[products] = [reactants] = 1M
→the equilibrium constant (K_{eq}) = 1
→$\Delta G = \Delta G^o + RT \ln 1$
→$\Delta G = \Delta G^o$

Examples:
1) Equilibrium conditions:

Glucose 6- phosphate ⇌ Fructose 6- phosphate
0.66 mol/L 0.33 mol/L



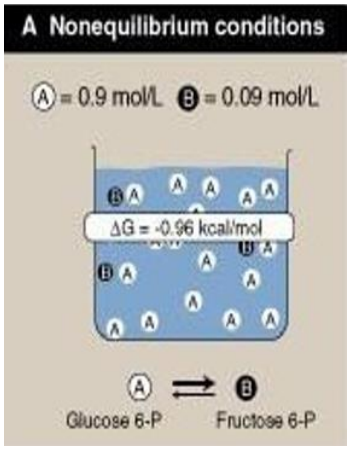
*The two equal blue arrows → indicate that the reaction is at equilibrium.
-this specific reaction is at equilibrium where the concentration of products is different that the concentration of reactants.

$\Delta G = \Delta G^o + RT \ln K_{eq}$
→$\Delta G = \Delta G^o + RT\ 2.3 \log 0.33/ 0.66$ Remember: (ln = 2.3log)
→ $\Delta G = 0$ (equilibrium)
→$\Delta G^o = + 0.4$ kcal/mol

2)Nonequilibrium conditions:

Glucose 6- phosphate ⇌ Fructose 6- phosphate

*Arrow indicates that the forward reaction is favored.
conc. of reactants [R] > conc. of products [P]
$\Delta G^o = + 0.4$ kcal/mol (calculated from the previous example)
→$\Delta G = \Delta G^o + RT\ 2.3 \log 0.09/0.9$
→$\Delta G = - 0.96$

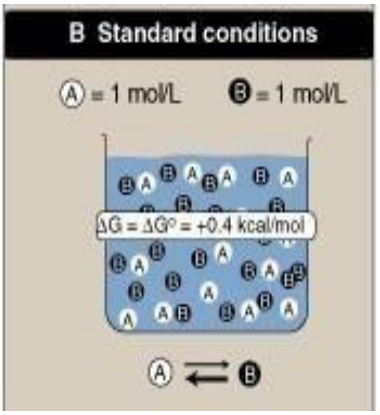


So by altering concentrations as seen in example no.2 an endergonic reaction under standard conditions (ΔG^o= + 0.4) would turn into an exergonic reaction (ΔG = - 0.96) under physiological conditions.

3) Standard conditions:

Glucose 6- phosphate ⇌ Fructose 6- phosphate

1 mol/L 1 mol/L



[reactants] = [products] = 1M

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

→$\Delta G = \Delta G^o$

ΔG^o= + 0.4 kcal/mol

→ΔG = + 0.4 kcal/mol

ΔG^o & K_{eq}

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

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

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

K'_{eq}	$\Delta G^{o'}$ 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"

- $K_{eq} = 10^4$ means that the ratio between concentrations is 10^4 [Products] = [Reactants] 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}, ΔG^o equals -23 kJ/mol accordingly.

- K_{eq}= 1 : [products] = [reactants], ΔG^o = 0
  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.
  ΔG^o = + 11kJ/mol

Conclusion: K_{eq} is used to find ΔG^o under the condition that states "the reaction would start with equal concentrations of products and reactants" according to the following:

- $K_{eq} = 1$, then $\Delta G^o = 0$
- $Keq > 1$, then $\Delta G^o < 0$
- $Keq < 1$, then $\Delta G^o > 0$

Side note: ΔG^o can be calculated using the unit kcal/mol as shown here, to convert kJ → kcal: 1 kcal = 4.2 kJ.

kcal

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

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, e.g., change in concentration or temperature.

  - Effect of Changes **in Concentration**:

  - when there's an increase in reactant's concentration by continuous supply, the forward reaction will overcome the backward reaction to increase product's conc. till equilibrium is achieved again.
  → same concept applies to increase in product's concentrations
  → if reactants/products got removed, the equilibrium would shift to compensate the decrease in concentrations.

- Metabolic reactions sometimes take advantage of this effect

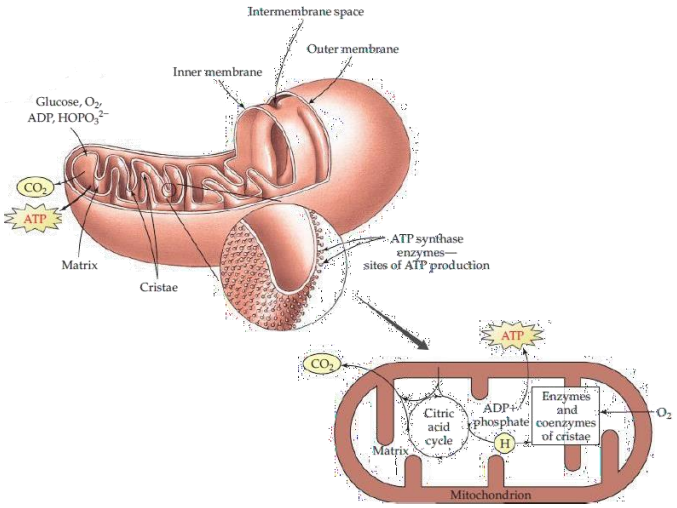
  - Effect of Changes in Temperature:

  In Endothermic reactions (+ΔH) need heat for them to occur in which heat is part of the reactants, increase in temperatures causes increase in the reactants, therefore the forward reaction would overcome the backward rxn and vice versa.

  In Exothermic reactions (-ΔH) releases heat, which means that heat is part of the products, increase in temperatures causes the backward rxn to overcome the forward rxn

Note: Catalysts (enzymes) make the reaction to reach equilibrium at a faster rate, but they have no effect on reaction favorability meaning it doesn't cause the forward rxn to overcome the backward or vice versa because it has ***no effect on ΔG.***

Energy Machinery in The Cell (Mitochondria)



Quick Bio Recap:
-**origin** of mitochondria (according to the evolution theory): it evolved from a prokaryotic (bacteria) cell that inhabited a eukaryote and formed an endosymbiotic relationship (تعايش داخلي), the cell would supply it with proteins and in return the mitochondria will supply the cell with energy.

-**Structure**: (very similar to bacteria's structure) 2 membranes inner and outer, intermembrane space, cristae which is infoldings of the inner membrane, matrix, circular DNA.

The mitochondria— singular mitochondrion:

- 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.
- mitochondrion needs around 1000 different protein types, it synthesizes (by its own mtDNA) 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.
- can replicate itself throughout **binary fission** (same as bacteria), energy demand determines mitochondrial replication rate; ⬆ demand, ⬆ mitochondria number.
  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.
  -mitochondrial replication has nothing to do with cellular replication (mitosis).
- 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.
- mutations in the cell's nuclear DNA that produces important proteins for the mitochondria would be reflected in every cell inside the body because of the cellular division mitosis where daughter cells are identical to their mother cell.
  → so you can use any cell for mutation assessment, for example u can draw a blood sample and test a lymphocyte's DNA for mutations.
- mitochondrial DNA mutations can occur at any stage and by any mutation cause (e.g., genetic diseases).

Elaborative example (مثال توضيحي)**:** during embryonic development, embryonic stem cells are directed to proliferate through mitosis and differentiate forming different tissues (skeletal muscles, smooth muscles, CNS, etc..)
mitochondrial DNA mutations can take place in the mitochondria inside these embryonic cells.
suppose that an embryonic cell has 10 mitochondria and 2 of them are mutated, when it replicates and divides into two new daughter cells the mitochondria would be distributed randomly between them.
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

→As a result, the mutated mitochondria would be present in one daughter cell and not in the other. these daughter cells are responsible for making different tissues, so the daughter cell with mutated mitochondria that's responsible for making the CNS would show a disease in the nervous tissue whereas the 2nd daughter cell would divide and form a perfectly normal muscular tissue for example.

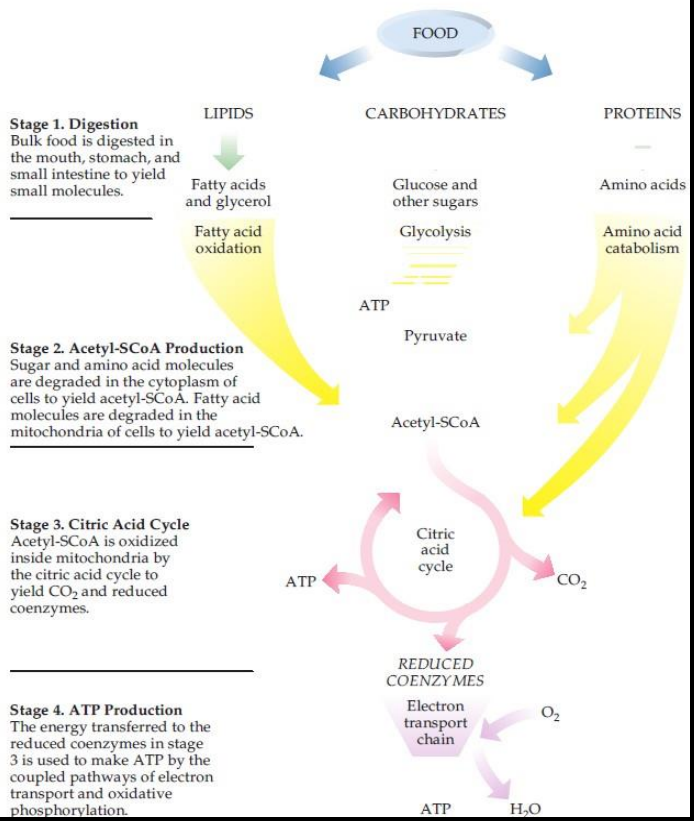
this phenomenon is known as **heteroplasmy**, where one body tissue shows a disease arising from mitochondrial DNA mutation that's not present in the other tissues, unlike nuclear DNA mutations that would show in every cell inside the body.

- mitochondrial mutations can be also maternally inherited; any mutations in the mother's mitochondria can be inherited to both female and male off springs, yet any paternal mitochondrial mutation can't be inherited.

Stages Of Energy Production

Stage 1: Digestion; food breakdown into monomers by mouth and stomach
Carbs→ glucose, other sugars
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**



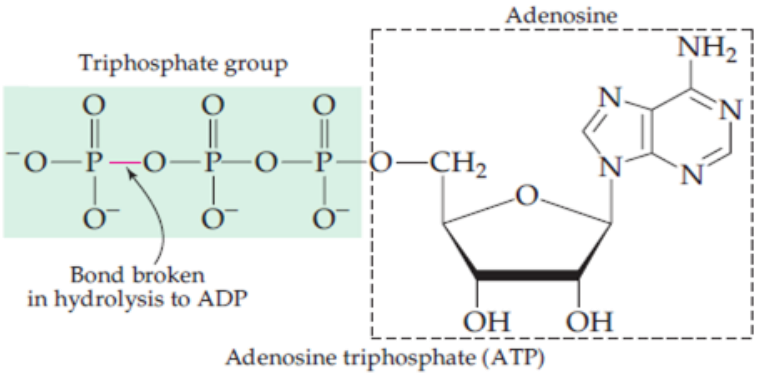
Stage 3: kerbs' cycles (citric acid cycle)
Acetyl-coenzyme A is used to produce electron carrying (NADH + FADH) molecules.

Stage 4: electron transfer chain & oxidative phosphorylation
electron carriers are used to produce ATP from the electron transport chain in the oxidative phosphorylation process.

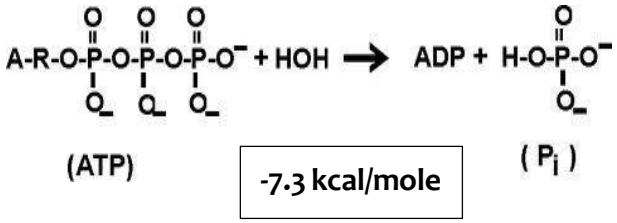
Oxidation takes place at the first 3 stages of energy production, at the 4th stage reduction reactions take place in the electron transport chain.
Redox reactions (oxidation-reduction) are coupled with phosphorylation, when redox rxns take place phosphorylation takes place.

ATP

- Adenosine **tri**phosphate.
- 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 (15 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_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

(Notice that all molecules mentioned above in this schedule have phosphate in their structure, which means ATP isn't favored as an energy source because it has phosphate in its structure)

- 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 in this case which equals to 3.4 kcal/mole

  ATP→ ADP + 1st P 7.3 kcal/mole
  ADP→ AMP + 2nd P 7.3 kcal/mole
  AMP→ adenosine + 3rd P 3.4 kcal/mole

  similar molecules to ATP like CTP, GTP, TTP, UTP serve as energy molecules and release the same amount of energy when the 1st and 2nd phosphates are released but energy value would differ when it comes to third phosphate because atoms orientation differ between these molecules due to differences in the nitrogenous base in each molecule.

  metabolic pathways inside in the **mitochondria** like kerbs cycle and electron transport chain use **ATP** ONLY.
  other energy molecules are distributed in different pathways for organization purposes:
  Example: in biosynthetic reactions like **protein** biosynthesis **GTP** is mainly used, **lipids** biosynthesis **CTP** is used, **UTP** is used in **carbohydrates** metabolism.

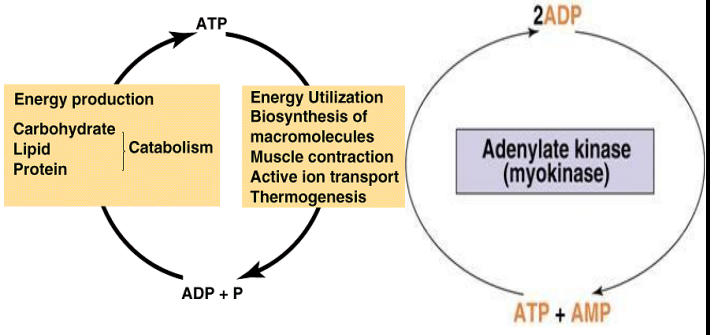
Is ATP a good long-term energy storage molecule?

- 90 moles of ATP per day is used by the main tissues at resting state.

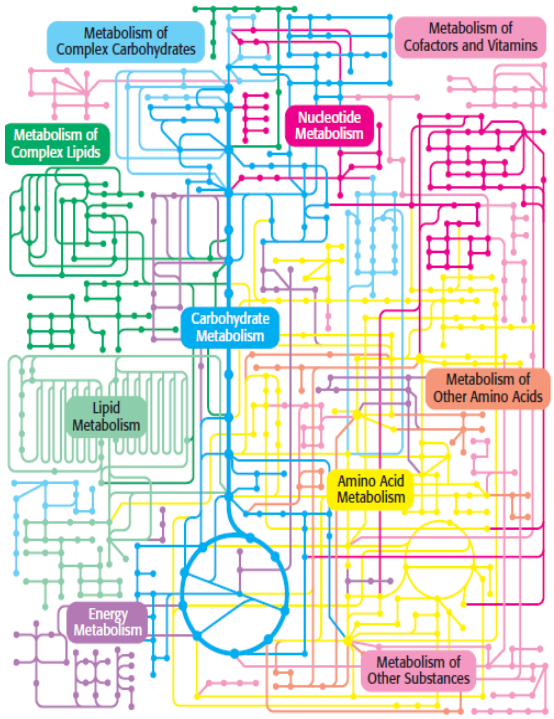
Tissue	ATP turnover (mole/day)
Brain	20.4
Heart	11.4
Kidney	17.4
Liver	21.6
Muscle	19.8
Total	90.6

- ATP's molecular weight is 551 g/mole, considering the number of consumed ATP moles daily:
  551*90 = 49,920 g = 50 kgs of ATP is consumed daily
  because of its high molecular weight, ATP isn't stored on the long term in the body, it is rather in <u>constant replenishment</u> being used and resynthesized all the time, meaning ATP would be hydrolysed in a certain pathway and then resynthesized by other pathways.

*main pathway for ATP production is the oxidative phosphorylation.
*excess energy in the body is stored in other molecules on the long term like glycogen.



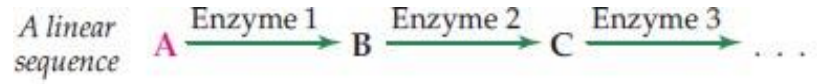
Biochemical (metabolic) Pathways



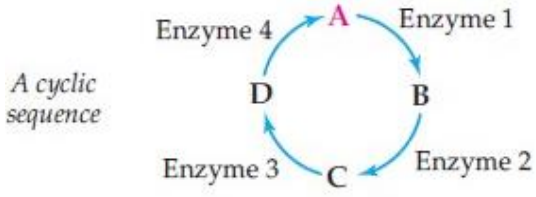
- Biochemical reactions within the body are called pathways.
- Pathways: are a series of biochemical reactions of multiple steps where one step would lead to another until the final product is formed.
- described as <u>interdependent</u>; meaning that they don't occur as single reactions.
  examples: Glucose → pyruvate is a <u>10 steps</u> process.
  - The picture is actual representation of what goes inside the body, biochemical pathways are interconnected to each other, to conserve energy as much as possible.
- Pathways communicate with each other through allosteric enzymes which have 2 subunits: **catalytic** subunits where the reaction occurs and **regulatory** subunits where other materials bind.

  Example on pathway communication:
  materials from the carbohydrate metabolic pathways would bind on a specific allosteric enzymes of lipids metabolic pathway.
  the resulting regulatory effect would: activate/inhibit pathways, rates and molecule concentration regulations.
- Types of pathways:

1)linear pathways e.g., glycosis

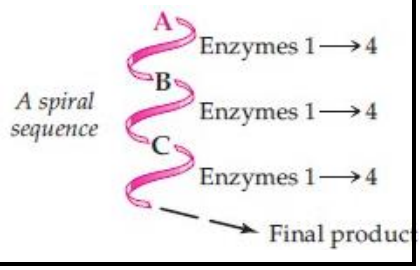


2)cyclic pathways series of reactions that lead to the first reactant regeneration; the first material the reaction started with would be regenerated at the end e.g., urea cycle, Krebs cycle.



*each step in metabolic linear and cyclic pathways is catalyzed by different enzymes

3)spiral pathways: each step is interconnected with the next, but all of them are catalyzed by the same set of enzymes



Exergonic Reactions in Biochemistry

Breaking down all molecules:

Releasing energy by breaking the bonds

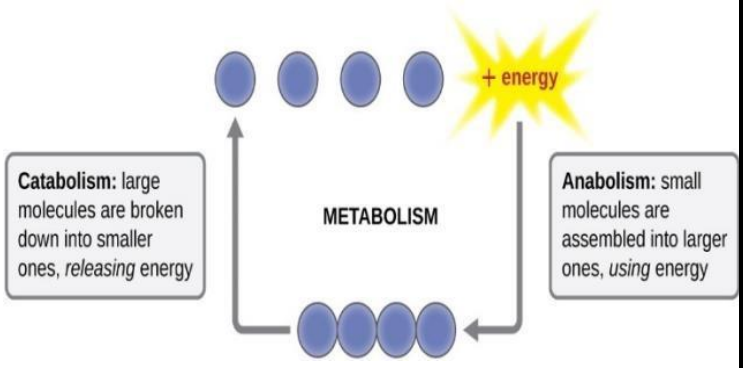
energy-producing reactions within the body:

1) **Hydrolysis** (molecules breakdown by H_2O)

2) **Decarboxylation** (removal of carboxylic group → CO_2 release)
Example: pyruvate (C3) → acetyl-CoA(C2) +CO_2

3) **Oxidation** with O_2 e.g., glucose using molecular oxygen

-in metabolic pathways:
Complex structures→ Simple structures
proteins → amino acids
starch → n (glucose)
glucose + O_2 → CO_2 + H_2O



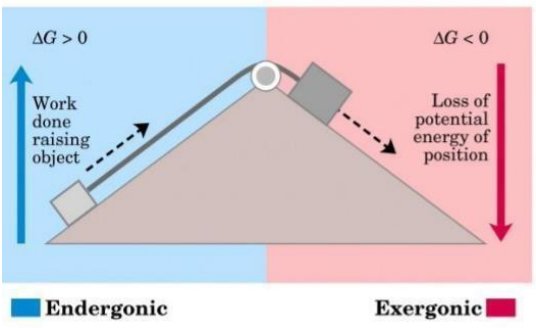
How do our cells get energy for unfavorable biochemical work?

We know that endergonic reactions need energy, so what are the sources or strategies to do that?

*The concept of coupling

On seesaw, the person with a higher weight will fall down and pushes the lower weight person up, this is what happens in biochemical reactions inside the body, to run endergonic reactions, the body uses the energy produced from exergonic reactions and couple it with endergonic reactions. Both reactions run at the same time!

meaning that both reactions are merging with each other and not running separately; the products of exergonic reactions are reactants in the endergonic reaction its coupled with.



Example: Conversion of Glucose⟶Glucose-6-phosphate
It's an endergonic rxn that needs two things: a 1phosphate group and 2energy to form the glucose-phosphate bond.
So it will be coupled with an exergonic rxn that serves **both** energy and a phosphate group.

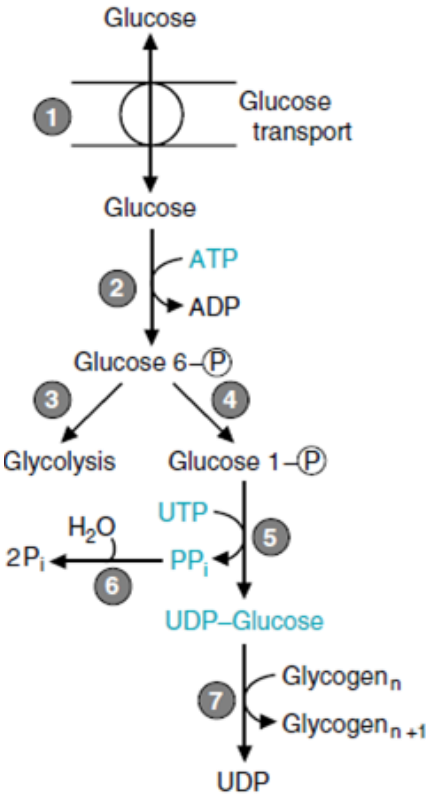
ATP is the perfect candidate for this specific reaction; releases energy by hydrolysis of the phosphoanhydride bonds between phosphates in ATP which releases energy and donates a phosphate group:
ATP⟶ADP + P (exergonic rxn: ATP hydrolysis)

This chemical proess is known as phosphoryl-transfer reactions.

An example to illustrate this is glycogen synthesis, which is an endergonic pathway that needs energy.

Glucose→glucose-6-phosphate → glucose-1-phosphate→ UDP-glucose → Glycogen

in Step 2: Glucose is always converted to glucose-6-phosphate that need energy = 3.3 kcal/mol So , the ATP can supply that reaction with (material (phosphate) + energy needed. Notice that ATP hydrolysis provided 4 kcal/mole as an excess energy (this excess energy can be used during the pathway or in other reactions or heat).



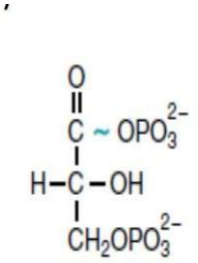
Step 4 gets its energy by **playing with the concentrations**. As ΔG Depends on Substrate and Product Concentration. The original (products/reactants) ratio is 6/94 so ΔG= +1.65 kcal/mol but if we can withdraw some of the products out then the ratio will become 3/94 and ΔG= -0.4kcal/mol so the reaction will become exergonic.

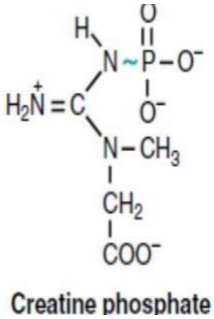
Some pathways generate high energy intermediate like in step 5 where UDP- Glucose is produced which means that its separation will supply the energy needed for the pathway. So here in step 7, separation of UDP from glucose gives the energy to attach the glucose to glycogen.

In conclusion, playing with concentrations, high energy intermediate, Phosphorylation transfer reaction (coupling) are all strategies used by the body to provide energy for endergonic reactions.

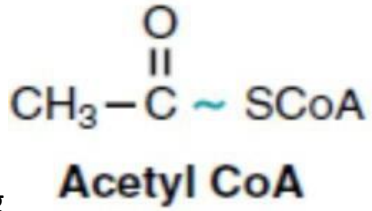
Activated Intermediates other than ATP;
UTP is used for combining sugars, CTP in lipid synthesis, and GTP in protein synthesis (as mentioned in page 8)

* 1,3-bisphosphoglycerate and Creatine phosphate have a high energy phosphate bond in their structure.





* **Coenzyme A** is a universal carrier (donor) of Acyl groups:
→Forms a thio-ester bond with carboxyl groups
→used in acetyl choline synthesis; a neurotransmitter that binds to receptors on nerves endings to contract the muscles, it gets broken down by the enzymeacetyl choline esterase causing muscle relaxation.



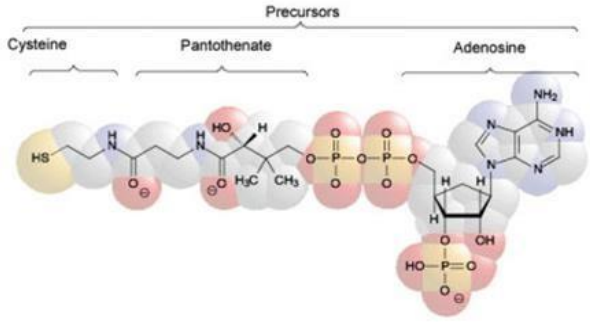
Acetyl choline is made of choline + acetate

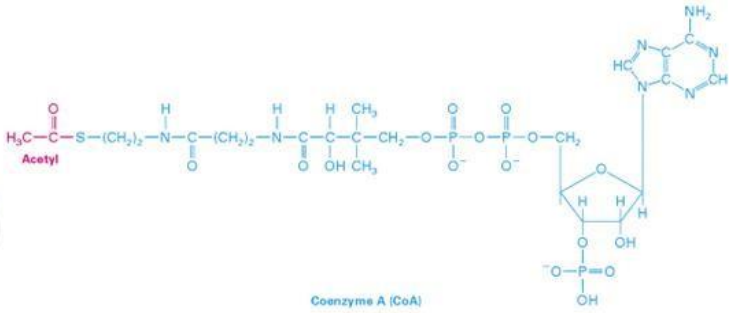
Hydrolysis of acetyl coA will result in energy and acetate to be used as reactants in acetyl choline synthesis.

Breaking down

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

Coenzyme A





THERMOGENESIS : first law of thermodynamics

It is the energy expended for generating heat (37oC) in addition to that expended
for ATP production

Shivering

(ATP utilization)

asynchronous muscle contraction due to sudden change in the body temperature

More ATP and generate heat

(Heat production is a natural consequence of "burning fuels")

Non-shivering ((adaptive))

the percentage of energy that you are ingesting inside your body to make heat (ATP production efficiency)

Oxidation reduction reactions: (we are studying them now because they exist in most of the metabolism of energy reactions.)

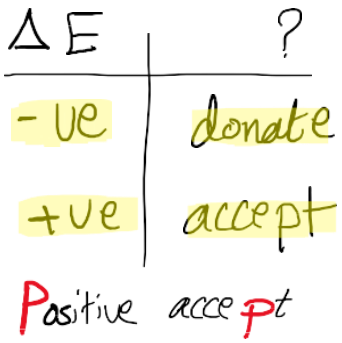
✓ Oxidation reduction reactions include moving of electrons <u>without changing the chemical structures.</u>

ΔG: the difference in bond energies between materials

when electrons move between molecules we can't identify the change in energy content therefore we can't calculate ΔG using the original equation.

redox potential (E) (THE POTENTIAL ENERGY): the driving force of moving the electrons from one atom to another, these electrons are hold on chemical structures which has the ability to donate its electrons or accept its electrons.

✓ redox Potential 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)

#Or there is a difference in the ability of accepting donating-electrons between any 2 chemical materials

✓ The electrons move from the material that has a higher ability to donateelectrons to the one which has a lower ability to donate electrons.

✓ Oxidation and reduction must occur simultaneously

Oxidation:

Gain of Oxygen Loss of Hydrogen Loss of electrons

Reduction:

Gain of Hydrogen Gain of electron Loss of Oxygen

*What makes an enzyme to function as redox enzyme is that it has a specific structure that can accept or donate electrons such as heme group, NAD ,FAD,..

 A- P + B —> A + B- P

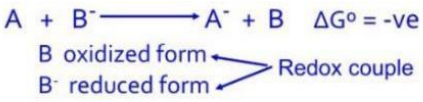
Type of reaction: transfer of phosphate

What determine the direction of the reaction?**delta G**

 A++ + B++—> A+ + B+++

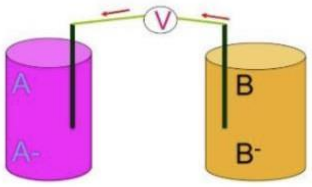
Type of reaction: **redox**

What determine the direction of the reaction? **delta E**



Now look at this redox couple: (A) accepts electrons and is converted to the reduced form A- so we have a redox couple (A , A-).

Another redox couple is shown in the illustration.



Now, can we measure redox potential experimentally?

The answer is **yes**. Scientists were able to measure reduction potential for a wide variety of materials with respect to hydrogen electrode (as a standard electrode Eo=0) and they arranged these values from the more negative to the more positive value in a large scale. **The more negative value has high capacity to lose electrons while the more positive value has high tendency to gain electrons.**

For example, if we have 2 reduction potentials: the first equals -600mv while the second equals -500mv then electrons move from the first to the second material.

The importance of this standard electrode is to obtain the exact value of reduction potential because if we used 2 materials of unknown reduction potential, then we will not be able to find the exact value for both since they are different. Another advantage of using hydrogen is that **most materials can gain/lose hydrogen.**

Reduction potential: Ability to accept electrons

Oxidized + e^-	→ Reduced	ΔE^o (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**

From the table, we notice 2 important points. Firstly, **oxygen** is the final electron acceptor for electrons (electrons from different nutritional materials are trapped by oxygen) thus it has the most positive reduction potential. Secondly, **NADH** has a reduction potential (Eo) of -320 mv thus it gives electrons to oxygen with Eo =+820mv. This direction of electron movements fits the science since we already know that **electron carriers like NADH after produced from Krebs cycle donate their electrons for materials with higher E.**

As we talked before about ΔG and its relation to bond energy, we can say the difference in energy caused by reduction potential is another diameter of what ΔG measures. So, ΔG is not only concerned with bond energy. The reduction potential, not bond energy, is the driving force for electrons movement. Therefore, **if we inverted the sign of reduction potential value then electrons will move in the backward direction**. There must be a mathematic relation that governs the direction of electrons movement. Moreover, it should not contain any variable other than ΔG and ΔE.

$$\Delta G^o = - n f \Delta E^o$$

- F = Farady constant = 23.06 kcal/*Volt*

(n) constant: the number of electrons moving

Also, the following relation can be used:

$$\Delta G = - n f \Delta E$$

For a reaction to be favorable, spontaneous and exergonic (-ve ΔG) then ΔE must have a +ve value. The following example supports the previous statement.

NADH has a reduction potential Eo= -320 mv thus it gives electrons to oxygen with Eo = +820mv.
ΔEo = Eo (final oxygen) – Eo (initial NADH) = +820 – (-320) = +1140 mv (positive value and spontaneous reaction)

As we seen before, the sign of ΔE o is +ve thus when scientists wrote equation, they inserted the -ve sign to fit the real situation.

Question:

Calculate ΔG^o of the following reaction

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

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

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

Solution: ΔE o =1140 mv

= 1.14 volt

ΔG o = -nf ΔE o

= -(2) (23.06)(1.14) ➔ $\quad \Delta G^o = - 52.6$ kcal/mol

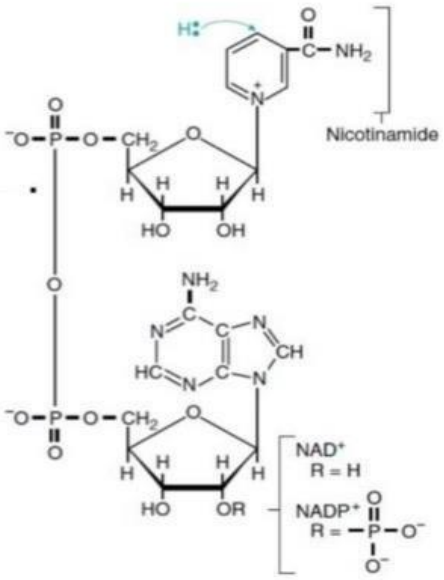
Now, let us talk about **electron carriers** (that transports electrons to ETC).

There are 2 main electron carriers:

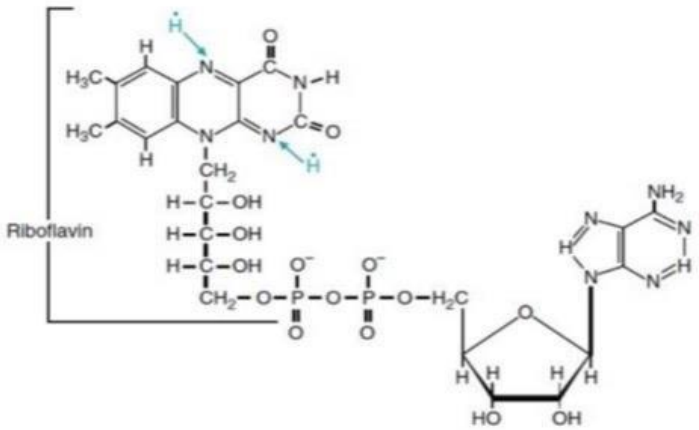
- ✓ NAD+ (niacin, B3) & FAD (riboflavin, B2).

NAD+ accepts a single hydride ion H - (2 electrons) on nicotinic ring with one step, so it does not form a radical (will not be harmful) and thus can be found free as both NAD+/NADH in mitochondria/cytosol, as a result, it has a fixed reduction potential.

-NADP+ is different from NAD+ only by **a ssphosphate group** instead of **a hydrogen atom** as shown in the previous figure. Both of them carries 2 electrons but NAD+ participates in **catabolism** while NADP+ participates in **anabolism**. So, different structures that do the same function for better organization and regulation.



- ✓ FAD accepts 2 protons (2 electrons) sequentially since there are 2 Hatoms thus it forms a radical intermediate and passes through (one electron/free radical state) that is harmful. Therefore**, it cannot be found free in the cytosol** and is always bound to proteins. Also, its reduction potential depends on the protein it is bound to. **FMN** also carries 2 electrons sequentially, but for better organization: one works in anabolic reactions while the other in catabolic reactions.



اخر 3 صفحات من شيت 019********

THANK YOU