Biochemistry

◉ Sheet ○ Slides

Subject:	Bioenergetics
Done by :	Abdullah AlZibdeh
Corrected by :	Mariam Hassouneh
Number :	5

The last thing we've talked about is "ATP as the energy currency of the body".

Does the body store energy in the form of ATP? Or as a long-term energy source?

- It's a big **NO** for the 1st question. As we know, energy is stored in the form of glycogen and lipids but not in the form of ATP. The reason behind that is that the body uses 50kg of ATP per day "approx. 90mol per day", which makes storing energy in the form of ATP inconvenient!

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

A lot of reactions in the body at standard conditions are endergonic in their nature so **HOW in the earth "I mean in the body :P "does the body run endergonic reactions to overcome this energy barrier?**

1. Coupling reactions

This concept can be illustrated with the idea of the "seesaw". In the seesaw, the side on which more weight is exerted will fall down. And that side can go up by exerting a force on the ground " pushing against the ground " by the person on it "opposite in direction to gravity", which will lead to move the lighter side towards the ground . Same concept with exergonic reactions being used to drive endergonic ones.

*Remember that weight is the force exerted on the body by gravity towards the ground "It varies while mass doesn't "

- Energy coupling methods

A. Phosphoryl transfer reactions:

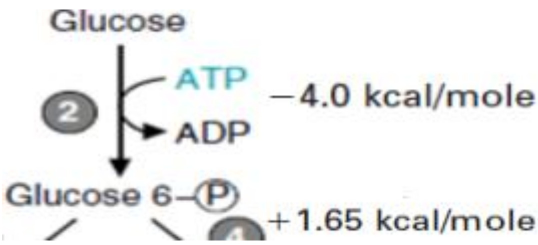
This involves a reaction of phosphorylation of a reactant. Phosphorylation process itself is endergonic so to run, it's coupled by ATP hydrolysis, which is exergonic and produces energy. So by coupling these 2 reactions, we will provide phosphate and energy to the reaction.

Take phosphate out of ATP --> This will result in release of energy --> the endergonic reaction will use that energy to proceed

By calculating the sum up of ΔG for both reactions, the result will be a negative value, assuring that the exergonic reaction provided here more than enough energy for the endergonic reaction to occur , reaching to the feature related to coupling "**ΔG^0 Values are additive** "

Example: Trapping glucose inside cells is done by phosphorylating glucose with the presence of ATP. The sum up of ΔG's = -4 kcal/mole

"-7.3 + +3.3 = -4".

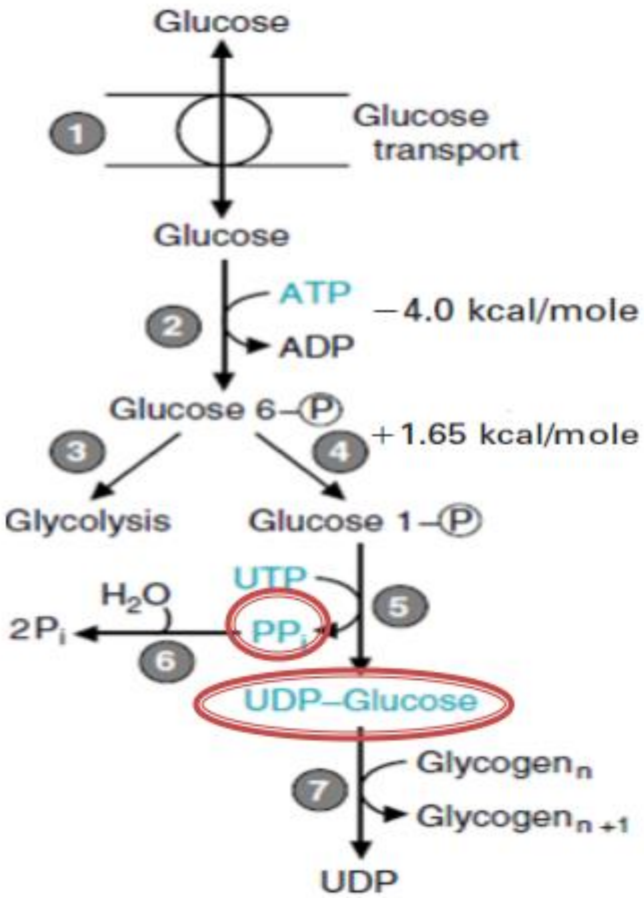


-7.3 is energy resulting of breaking down phosphate out of ATP
+3.3 is energy needed in adding phosphate to glucose

WHERE can we use the excess 4.0? Remember that the body treats the pathway as a single reaction "sum up of ΔGs' values" , and so considering the steps additive to each other " transferring energy from one step to another " , so excess energy will be used to run the next ENDERGONIC step .

B. Activated intermediates:

High energy molecules are ones that yield energy equal to or higher than 7 kcal/mole" like ATP, UTP, CTP. Break down of such intermediates results with energy to facilitate the pathway steps. "Again, remember that pathways are treated as single reactions with additive ΔG values". See exergonic steps 5 and 6 which facilitate the 7th endergonic step.



As we can see, glucose when using UTP will end up binding to a high energy molecule like UDP, this will result in releasing energy if the complex broke down, and it will in turn run the reaction of adding glucose to glycogen to become

PP is pyrophosphate, if broken it gives 2 phosphates in addition to energy

2. Manipulating Substrates and Products Concentrations:

So the body may alter concentrations of materials involved in the pathway "such as removing products constantly"; which results with lowered ΔG value "more exergonic". In the previous photo, notice that in step 4, if the ratio of [product]/[reactants] = 6/94, then ΔG = +1.65 kcal/mol, but when the ratio = 3/94, ΔG = -0.4 kcal/mol, less, more negative, spontaneous.
So by continuous taking of products out, the body will force reactants to transform into products and so changing the reaction nature into spontaneous.

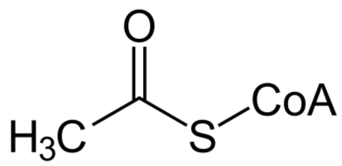
3. Activated Intermediates other than ATP

For example UTP is used for combining sugars, CTP in lipid synthesis, and GTP in protein synthesis.

"The specificity of the intermediates used in the pathways is for better regulation."
These molecules have the same energy values of their bonds between the first and the second phosphate groups, and the second and the third phosphate groups. Since energy levels are dependent on atoms of bonds and the spatial arrangements of atoms around the bond; which are the same for the mentioned bonds except for the third, the energies are different between the third phosphate and the ribose linked to the rest of the molecule in each type "since the molecules are different in nitrogenous bases".

EXAMPLE TO MAKE IT SIMPLER : Galaxy jewels chocolate box contains lots of chocolate types , ALL jewels share the outer plastic paper , the smooth melting chocolate but differ inside , some contain crispy , some contain vanilla , some contain coconut , they're ALL the same on the outside but each flavor inside gives you a different sense of happiness .

- *Example: Acetyl coA*



Acetylcholine is a very important neurotransmitter. It is made by reacting the acetate with choline "Anabolic pathway; energy requiring". Acetate has to be produced from a high energy molecule to produce the energy needed to complete the reaction (same as phosphoryl transfer reaction), and this molecule is acetyl coA. Coenzyme A is a universal carrier (donor) of Acyl groups, and it Forms a thio-ester bond with carboxyl group "high energy bond" (any molecule that binds with CoA through thiol group will produce high energy when breaking down)

Acetyl CoA + H_2O ⟶ Acetate + CoA $\Delta G^o = -7.5$kcal

Acetylcholine + H_2O ⟶ Acetate + Choline $\Delta G^o = -3$ kcal

- + Choline ⟶ Acetylcholine + $\Delta G^o = +3$ kcal
- Acetyl CoA + ⟶ + CoA $\Delta G^o = -7.5$ kcal

- Acetyl CoA + Choline ⟶ Acetylcholine + COA

ΔG= +3 + -7.5= -4.5 "negative, spontaneous".

Thermogenesis

- It is the heat generating way in the body "thermo; heat, genesis; generating".
  NOTE: There is no specific pathway or process the body follows to make heat, it's always a BY-PRODUCT
- It keeps the body temperature constant.
- Very regulated. It also can be altered by drugs. inducing changes in this process can be fatal.
- Heat is produced from lost energy in the process of producing ATP in the mitochondria "respiration by-product". So the ATP production process is not efficient perfectly; since some of the energy is produced as heat. Any process that generates ATP also generates heat.
- It has 2 types :

1. Shivering

Associated with muscle activity, ATP is used to produce kinetic energy "muscle activity", so energy is produced, and heat is the by-product.
The most famous example you know is when getting out of bath, you always feel cold and shiver to feel warmer, WHY? Because your body moves your muscles to generate more ATP so more heat as by- product for the body to become warm until wearing your fancy clothes or pajama : P

2. Non-shivering "adaptive"

Adapting process to the surrounding environment, to a lifestyle, to a disease or to a drug, to determine the amount of the ingested food which will be used to produce heat to maintain the normal body temperature "37^{0}", this is why we find differences between people in energy used to make heat, some uses 60%of their energy, others use 30% and others use 15%. This process occurs in infants in brown adipose tissue.

Oxidation-Reduction reactions "redox":

- Reactions involve ONLYYYY transfer of electrons.
- Oxidoreductases "Dehydrogenases, oxidases, oxygenases, peroxidases "are the group of enzymes which catalyze such reactions.
- Redox potential "E": it is potential energy that measures the tendency of oxidant/reductant to gain/lose electrons, to become reduced/oxidized.
- Redox potentials have been given a numeric scale that shows the order of reactions from the most positive to the most negative.

Table 19.4. Reduction Potentials of Some Oxidation-Reduction Half-Reactions

Reduction Half-Reactions	$E^{0'}$ at pH 7.0
$1/2\ O_2 + 2H^+ + 2\ e^- \rightarrow H_2O$	0.816
Cytochrome a-Fe^{3+} + 1 e^- → cytochrome a-Fe^{2+}	0.290
$CoQ + 2H^+ + 2\ e^- \rightarrow CoQH_2$	0.060
Fumarate + $2H^+$ + 2 e^- → succinate	0.030
Oxalacetate + $2H^+$ + 2 e^- → malate	−0.102
Acetaldehyde + $2H^+$ + 2 e^- → ethanol	−0.163
Pyruvate + $2H^+$ + 2 e^- → lactate	−0.190
Riboflavin + $2H^+$ + 2 e^- → riboflavin-H_2	−0.200
$NAD^+ + 2H^+ + 2\ e^- \rightarrow NADH + H^+$	−0.320
Acetate + $2H^+$ + 2 e^- → acetaldehyde	−0.468

- Electrons move from compounds with lower reduction potential (more negative /more willing to give) to compounds with higher reduction potential (more positive / more welling to gain).
- Oxidation and reduction must occur simultaneously " together "
- Always involve a pair of chemicals: an electron donor and an electron acceptor (ex. Food vs. NAD+).

- All energy source molecules (in other words all types of food) are transformed into molecules "mainly acetyl coA" that enter mitochondria for respiration and ATP generation. After that, citric acid cycle occurs to extract electrons and load them on carriers like NAD^+ to become NADH or FAD to become $FADH_2$. And then, electrons are transferred to oxygen "final electron acceptor" through electron transport chain. This is why you breathe, to get O_2 necessary to be last electron acceptor then to transform mostly into water.
  - By knowing this mechanism, we can predict that reduction potential for oxygen is the highest value of all electrons acceptors in the respiration pathway "since it is the final electron acceptor".
- Because we can predict the spontaneous direction "related to ΔG" of the redox reaction by knowing the E value of reactants " $\Delta E = E_A - E_D$ ", then a relation must connect between E & ΔG.

  This relation is this equation:

$$\Delta G^{o} = -nf\Delta E^{o}$$

"Where n= number of electrons transferred; f: faraday's constant"

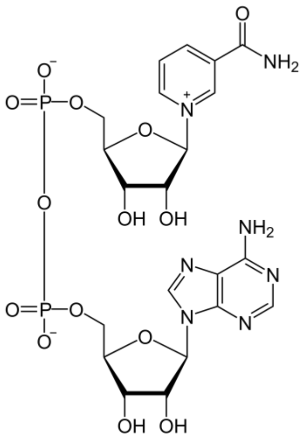
According to the equation:

Spontaneous	ΔE is +	$E_{donor} < E_{acceptor}$
Non-spontaneous	ΔE is -	$E_{donor} > E_{acceptor}$

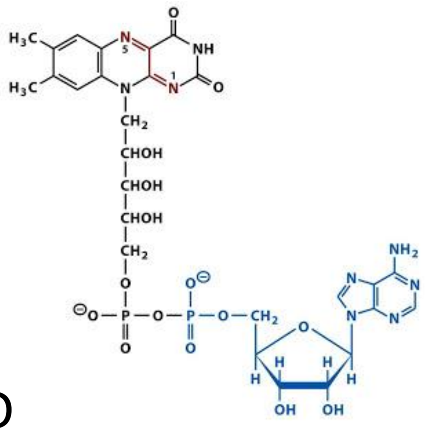
BEWARE : You can't measure difference for example between ability of O_2 to accept and NADH to give , if you're willing to measure the difference in reduction potentials , you must measure the difference between O_2 ability to accept and NADH ability to accept , or measure differences in ability to give , and this makes sense ; since we want positive and negative values .

- **NAD^+ vs. FAD:**

Structural differences are required" you have to know their structures and be able to distinguish between them "



NAD+



FAD

Notice the Flavin ring of FAD and the nicotine ring of NAD^+. These adenosine based molecules can be mono- or di- nucleotides. Notice also that FAD is always bound to a protein or an enzyme; since it can enter the free radical state "which is dangerous to the cell", but NAD^+ can be free. NAD^+ can accept 2 electrons at the time, and FAD can accept one electron at a time. Reduction potential value of NAD^+ is fixed; since it is a free molecule and it either accepts a hydrogen or loses a hydrogen with electrons, whereas FAD reduction potential value is not constant; depending on the protein to which it is bound "just like the difference in the heme group activity in myoglobin, hemoglobin, cytochrome C…etc., because of the difference in the environment in each case which affects the value of how much this structure is able to give you electrons ".

By reading the reduction potential values of NADH and $FADH_2$, we can notice that the process of electrons transfer from NADH to oxygen yields more energy than from $FADH_2$ "The more negative the reduction potential, the greater is the energy available for ATP generation".

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

$$NADH \longrightarrow NAD^+ + 2e^- \quad \Delta E^o = +0.32$$
$$O + 2e^- \longrightarrow O^{2-} \quad \Delta E^o = +0.82$$

$$\Delta G^o \approx -53 \text{ kcal/mol}$$

$$FADH_2 + 1/2O_2 \longrightarrow FAD + H_2O$$

$$FADH_2 \longrightarrow FAD + 2e^- \quad \Delta E^o = +0.20$$
$$O + 2e^- \longrightarrow O^{2-} \quad \Delta E^o = +0.82$$

$$\Delta G^o \approx -41 \text{ kcal/mol}$$

quote

"If you believe
Within your soul
Just hold on tight
And don't let go
You can make it
Make it happen"

MUCH THANKS to reach this page while you're still strong and hopefully not sleepy: P

Who wrote and corrected this sheet are both humans , incomplete and so are their actions , if you found any mistake or extra info we missed don't hesitate in informing us with , and we'll be more than glad to add :D

Best of luck SWEET PEOPLE OF CURE *.*