ALQUSOUR ACADEMY

أكاديمية القصور

BIOCHEMISTRY

Subject: Second Exam - Chapter Fifteen

للاستفسار والتسجيل

عمان – 078 570 6006
إربد – 078 570 6008
079 533 9934

للضـــرورة

مدير الأكاديمية
أ. إبراهيم الشواهين
0795 74 74 45

ساعات الدوام الرسمي

	اربد	عمان
الأحد - الأربعاء	11:00 -12:30	10:00 -12:30
الخميس	11:00 -12:30	8:00 -12:30
الجمعة	11:00 - 2:00	8:00 - 2:00
السبت	11:00 -12:30	8:00 -12:30

ALQUSOUR ACADEMY
خاص للفصل الدراسي الثاني
2012 - 2013

Prod. Date	3/4/2013
Pages	12
Price	35

The Importance of Energy Changes and Electron Transfer in Metabolism

In this chapter we are going to discuss the major energy changes and electron movements in different biochemical reactions.

☒ **Free-Energy Changes:**

Any reaction is accompanied by a ***free-energy change*** ***(ΔG)***, which can be taken up by the reaction or generated from the reaction. The free-energy change is dependent on different factors among which the concentration of reactants and products plays a key role. In order to make comparisons between different reactions we have to workout some forms of standards so that reactions can be compared to each other.

- For this reason scientists have worked what we call ***Standard States*** for reactions, in which case we can say that substances are at ***unit activity***:

1. For solids and liquids, standard state is the pure substance itself.
2. For gases, the standard state is the presence of gases at a pressure equal to 1 atmosphere.
3. For solutes, the standard state is usually taken as 1 molar concentration.

The free-energy change under standard states is given the symbol ΔG^o.

- Now in the following discussion you only have to keep in mind the 2 following equations:

$$aA + bB \longrightarrow cC + dD$$

- We can write the following equation to relate the free-energy change (ΔG) for the reaction under any condition to the free-energy change under standard conditions, this equation would be:

$$\Delta G = \Delta G^o + RT \ln \frac{[C]^c [D]^d}{[A]^a [B]^b}$$

- Where, **ΔG** is the free-energy change.
  ΔG^o is the free-energy change under standard states.
  R is the gas constant. ($R = 8.31\ J\ mol^{-1}\ K^{-1}$).
  T is the absolute temperature. (T = T in C +273).
  [A] [B] [C] [D] are the molar concentration of these substances.
  ln is the natural logarithm (to the base *e*) rather than logarithm to the base 10 (log).

☒ *Concepts*

In order to understand the different biochemical reactions you have to understand the following concepts:

1. When ΔG is negative this means that the reaction gives energy, whereas when it is positive this means that the reaction needs energy.
2. A spontaneous (occurs spontaneously without added energy) or exergonic (exerts energy) reaction is a reaction that releases energy, which means that ΔG is negative.
3. A non-spontaneous (does not occur spontaneously) or endergonic (needs or sucks energy) is a reaction that absorbs energy, which means that ΔG is positive.
4. The most important thing is to determine the sign and amount of ΔG which is dependent on ΔG^o and the concentration of reactants and products for a given temperature.

5. If any reaction reached equilibrium, then the generated energy ΔG will be zero as the reaction has stopped, so the original equation will be:

$$\Delta G = \Delta G^o + RT \ln [C]^c [D]^d / [A]^a [B]^b$$
$$0 = \Delta G^o + RT \ln [C]^c [D]^d / [A]^a [B]^b$$

And since the equilibrium constant $K_{eq} = [C]^c [D]^d / [A]^a [B]^b$ then the equation will become:

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

Given this equation we can calculate the amount of ΔG^o for any reaction by finding the concentration of reactants and products at equilibrium and substituting them in the equation.

6. Given the previous discussion we can calculate ΔG by calculating ΔG^o from point number 5 and then substituting it along with the concentration of reactants and products in the original equation, and then we can determine whether the reaction will absorb energy (non-spontaneous/endergonic) or it will generate energy (spontaneous/exergonic) and the exact amount of energy generated or absorbed.

7. As we said, if for a reaction $A + B \rightarrow C + D$ ΔG is negative ($- \Delta G$) then the reaction is exergonic (it will generate energy), if ΔG for the reverse reaction ($C + D \rightarrow A + B$) is the same in amount but has a positive sign then the reaction is termed a **reversible reaction**, that is, if you add reactants or remove products the reaction will continue in the first direction, but if you add products or remove reactants then the reaction will go in the second direction.

Note: [Many of the reactions in the human body are of this type, in fact many of them are even done by the same enzyme, and the human cell controls these reactions by either adding or removing reactants or products].

8. At last we can see that the standard states implies that the concentration of solutes be equal to 1 M. Now if the $[H^+]$ of a solution is 1M, then the pH is zero, but as we know the pH of the human body is 7 which means that H^+ concentration is equal to 1×10^{-7} so the ***Modified Standard State*** applies this fact in the equation for calculating ΔG for biochemical applications in the human body, which is termed $\mathbf{\Delta G^{o'}}$.

☒ ***The Nature of Metabolism:***

Metabolism is defined as the biochemical basis of all life processes in the organism. It can be divided into 2 major categories:

1. ***Catabolism*** which is the breakdown of large molecules to smaller ones; it is an oxidative process that releases energy.

2. ***Anabolism*** which is the process by which the body builds up large molecules from smaller ones; it is a reductive process that requires energy.

☒ *The Role of Oxidation and Reduction in Metabolism:*

Oxidation-reduction reactions also referred to as ***redox*** reactions are those reactions that involve the transfer of electrons from a donor to an acceptor.

- **Oxidation** is the loss of electrons from a donor and usually involves the release of energy; the electron donor (the substance that is oxidized) is termed a reducing agent or a reductant because it reduces (gives an electron to) another substance.

- **Reduction** is the gain of electrons; the electron acceptor (the substance that is reduced) is termed an oxidizing agent or an oxidant because it oxidizes (accepts an electron from) another substance.

❖ In aerobic oxidation, the ultimate oxidizing agent (the one that receives all the electrons from large molecules while they are broken down) is ***Oxygen***.

NOTE: There is no oxidation without reduction, that is, when a molecule loses electrons another one has to accept them. For simplicity in the following reactions we are going to divide redox reactions into their original 2 parts.

Let's take for example the following reaction:

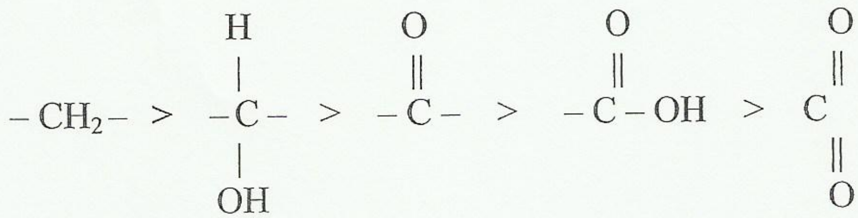
$$Zn(s) + Cu^{+2}(aq) \longrightarrow Zn^{+2}(aq) + Cu(s)$$

- In this reaction we can see that Zn (Zinc) has lost 2 electrons and changed from the solid form to ionic (aqueous) form, this is oxidation, and since Zn has been oxidized it is a reducing agent for Cu. On the other hand, Cu^{+2} (Copper ions) has gained 2 electrons and has changed from the ionic (aqueous) form to the solid form, and since Cu^{+2} has been reduced, it is an oxidizing agent for Zn.

- From this we can write 2 separate equations, one for oxidation and called half reaction of oxidation, while the other one for reduction and called half reaction of reduction:

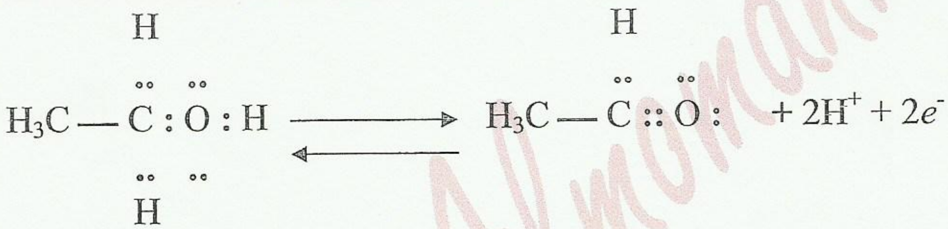
$$\text{Oxidation: } Zn \rightarrow Zn^{+2} + 2e^-$$
$$\text{Reduction: } Cu^{+2} + 2e^- \rightarrow Cu$$

- In the human body redox reactions are more complex, but the same principles apply. We can see molecules containing carbon atoms ranging from their most reduced form (an alkane) that becomes oxidized to an alcohol, then to an aldehyde, and then to a carboxylic acid before ultimately reach their final end product the most oxidized carbon atom, ***Carbon Dioxide CO_2***.



☒ Coenzymes in Biologically Important Oxidation-Reduction Reactions:

Before discussing the role of coenzymes lets take an example of a biochemical redox reaction, this example would be the oxidation half reaction for the conversion of ethanol to acetaldehyde.



Ethanol (12 electrons) Acetaldehyde (10 electrons)

- In the figure above, you can notice according to Lewis dot presentation that the number of dots in the ethanol part responsible for the reaction is 12, which means that there are 12 electrons in that part, whereas in the acetaldehyde part responsible for the reaction the number of dots is 10, meaning that there are 10 electrons, and this illustrates the loss of 2 electrons; hence this is an oxidation reaction.

- Note: [Sometimes it is difficult to use this method to determine the type of reaction, so for most biochemical reactions but not all of them;

  – ***The gain of oxygen (O) or the loss of hydrogen (H) or the gain of + sign indicates oxidation.***

  – ***The loss of oxygen (O) or the gain of hydrogen (H) or the loss of + indicates reduction.***

- As we said earlier oxidation-reduction reactions always occur together, there is no such a thing as the release of free electron to the surrounding, that is, there has to be an acceptor to the electrons.

- In the human body the ultimate electron acceptor in catabolic reactions is oxygen, as we said earlier, the transfer of electrons to either oxygen in catabolic reactions or to other molecules in anabolic reaction does not occur directly.

- Electrons are transferred to what we call *Coenzymes* first and then to either destination.

The most important coenzymes involved in redox reactions in the human body are:

1. **Nicotinamide adenine dinucleotide**, of which we have 2 forms, **NADH** (the reduced form, will be oxidized during the reaction; so it is a reducing agent) and **NAD^+** (the oxidized form, will be reduced during the reaction; so it's an oxidizing agent).

2. **Nicotinamide adenine dinucleotide phosphate**, of which we have 2 forms, NADPH (the reduced form, will be oxidized during the reaction; so it is a reducing agent) and $NADP^+$ (the oxidized form, will be reduced during the reaction; so it is an oxidizing agent).

3. **Flavin adenine dinucleotide**, of which we also have 2 forms, $FADH_2$ (the reduced form, will be oxidized during the reaction; so it is a reducing agent) and FAD (the oxidized form, will be reduced during the reaction so it is an oxidizing agent).

So from the previous discussion we can write the equation of acetaldehyde conversion into ethanol in the following manner:

$$NADH \rightarrow NAD^+ + H^+ + 2e^- \quad \text{half reaction of oxidation}$$
$$CH_3CHO + 2\,H^+ + 2e^- \rightarrow CH_3CH_2OH \quad \text{half reaction of reduction}$$

$$CH_3CHO + NADH + H^+ \rightarrow CH_3CH_2OH + NAD^+$$

- In here we can see that acetaldehyde is reduced to ethanol, whereas NADH is oxidized to NAD^+. This actually what happens in the human body, if the first reaction is to be carried out, NAD^+ will change to NADH which will hold the electrons and carry them where a reduction reaction needs them and vice versa.

Coupling of Production and Use of Energy:

- Human body gain energy from the breakdown of large molecules (oxidation of nutrients), this energy cannot be used directly; it must be shunted into another form of chemical energy that is more easily accessible.

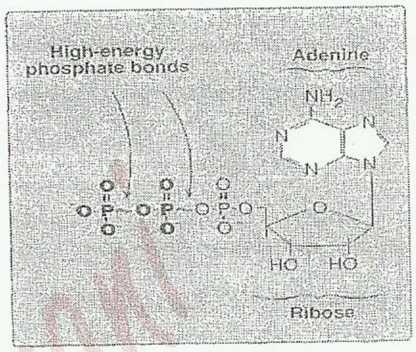
- In the same way that oxidation-reduction reactions are coupled by the use of coenzymes (NADH, NADPH and $FADH_2$), energy production reactions and energy requiring reactions are coupled by different other substances, the most important one of those is the high energy one ATP (adenosine triphosphate) and its correspondent low energy ADP (adenosine diphosphate).

- When a reaction releases energy the body uses this energy to transform ADP to ATP which has a higher energy. Then the ATP molecule goes to site where a reaction needs energy and is transformed into ADP releasing energy by the following equation:

$$ATP + H_2O \longrightarrow ADP + P_i + H^+$$

The $\Delta G^{o'}$ for this reaction is -30.5 kJ/mol which means that this reaction generates energy.

- From figure below you can see that the ATP molecule contains 4 negative charges which exert electrostatic repulsion and makes ATP less stable than ADP which has 3 negative charges. Hence breaking these bonds releases energy and making them requires energy.



- In fact the energy released not only comes from the breakdown of an unstable bond, but also from the generation of inorganic phosphate which assumes a resonance structure making it more stable and hence decreases its energy which should have been released with the reaction.

- Other energy transporters are also present in the human body among those PEP (Phosphoenolpyruvate) is the most important.

- In the human body, ATP is not produced and stored, it is produced as needed, chemical energy is only stored in the form of fats and carbohydrates. The process of using the energy from exergonic reactions to transform ADP to ATP (an endergonic reaction) is termed ***Coupling.***

- This can be illustrated in the following equation which denotes the use of glucose as a source of energy to generate ATP under **anaerobic conditions**:

$$\text{Glucose} + 2\,ADP + 2P_i \longrightarrow 2\text{ Lactate ions} + 2\,ATP$$

- The previous reaction occurs under anaerobic conditions, the $\Delta G^{o'}$ for the conversion of glucose to lactate ions is equal to -184.5 kJ/mol (exergonic), and that needed for 2 ADP molecules to be phosphorylated into ATP, for each mole of glucose, is + 61 kJ/mol (endergonic).

- So, we can see that the remaining energy -184.5 + 61= -123.5 kJ/mol which will be generated as heat, and so the efficiency of energy use in anaerobic metabolism is (61/184.5) × 100 % is about 33%.

Under **aerobic conditions** the following equation stands:

$$\text{Glucose} + 6O_2 + 32ADP + 32P_i \longrightarrow 6CO_2 + 6H_2O + 32ATP$$

- $\Delta G^{o'}$ for glucose breakage is -2867 kJ/mol, $\Delta G^{o'}$ for the formation of 32 ATP molecules is 32 × 30.5 = 976 kJ/mol. Net $\Delta G^{o'}$ = -2867 + 976 = -1891 kJ/mol which will be generated as heat, the efficiency is (976/2867) ×100 % = 34 %, so we can see that aerobic metabolism of 1 glucose molecules produces 32 ATP molecules compared to only 2 ATP molecules through anaerobic metabolism.

Coenzyme A in Activation of Metabolic Pathways:

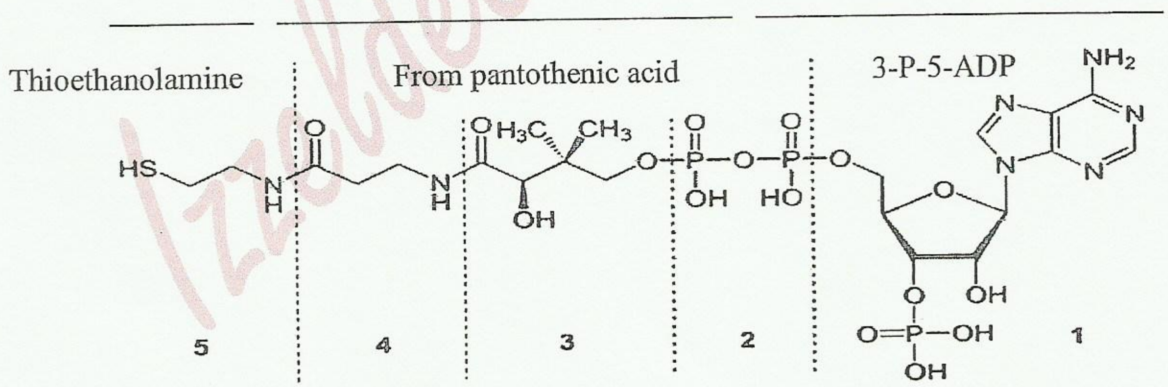
As we said previously if $\Delta G^{o'}$ is negative then the reaction is spontaneous or exergonic, this feature is used by the body to drive reactions that need energy in a process called activation.

For example, if substance A is to react with substance B to produce AB then A can be linked to a co-enzyme to produce A—co-enzyme which when broken generates energy that can be used to join A and B to form AB, this is illustrated by the following equation:

A + Co-enzyme → A—Co-enzyme (Activation step)

A—Co-enzyme + B → AB + Co-enzyme $\Delta G^{o'} < 0$ (Exergonic reaction)

- The formation of a more reactive substance in this fashion is called **activation.**
- The most important coenzyme in the body is **coenzyme A**



- The figure above shows the **structure of coenzyme A** which is complex and consists of several smaller components covalently linked together. It is composed of a 3'-P-5'-ADP derived from adenosine with phosphate groups esterified to the sugar. Another part is derived from the vitamin pantothenic acid, and the active part involved in the different chemical reactions done by the coenzyme A is the thiol group. In fact it is sometimes written as Co-A-SH because the SH (sulfhydryl group) is the one responsible for its actions.

- One of the most important examples on the function of Co-A is the release of acetate from the molecule Acetyl-Co-A, and since the thioester bond in it has a high energy content this release is spontaneous and generates energy. This is also stressed by the resonance structure acetate assumes when released, which increases entropy and stabilizes the molecule. This is illustrated by the following reaction.

Acetyl group ↓

$$\text{Co-A—S—COCH}_3 + \text{H2O} \longrightarrow \text{Co-A—SH} + \text{CH}_3\text{COOH}$$

↓ Thioester bond

$$\Delta G^{o'} = -31.4 \text{ kJ/mol}$$

Important Notes:

1- The coenzymes NAD^+, $NADP^+$, FAD and coenzyme A share an important structural feature: all contain ADP.

2- The coenzymes NAD^+, $NADP^+$ and FAD are needed in catabolism in their oxidized form to act as the intermediate oxidizing agents.

3- The coenzymes NADH, NADPH and $FADH_2$ are needed in anabolism in their reduced form to act as the intermediate reducing agents.

4- Metabolic pathways proceed in many stages, allowing for efficient use of energy.

Questions:

1. Which of the following <u>does not correctly</u> define an oxidation reaction?

A. The removal of electrons from amolecule
B. The reaction of any molecule with carbon
C. The reaction of any molecule with O2
D. The removal of hydrogen atoms from a molecule

2. Energy from the metabolism of energy nutrients is released as:
A. Heat B. ATP C. Water D. CO2 E. Both A & B

3. For two coupled reactions, the overall process will be exergonic if
A. at least one reaction is spontaneous
B. both reactions have delta $G° > 0$
C. at least one reaction generates no heat
D. $\Delta G°1 + \Delta G°2 < 0$

4. The active part involved in the different chemical reactions done by coenzyme A:
A. pantothenic acid
B. 3'-P-5'-ADP
C. Thioethanolamine
D. None of the above

5. For the oxidation-reduction reactions, which of the following statements is CORRECT?
A. Oxidation of biomolecules involves electron transfer.
B. Conversion of FADH2 to FAD is a reduction process.
C. Conversion of lactate to pyruvate is a reduction process.
D. Anabolism is the reverse of catabolism.

6. The value of the free energy change (ΔG) of a reaction
A. equals zero at equilibrium
B. is negative at equilibrium
C. is positive at equilibrium
D. does not depend on the concentration of reactants and products

Answers:

Questions #	Answers
1	B. The reaction of any molecule with carbon
2	E. Both A & B
3	D. $\Delta G°1 + \Delta G°2 < 0$
4	C. Thioethanolamine
5	A. Oxidation of biomolecules involves electron transfer
6	A. equals zero at equilibrium