METABOLISM

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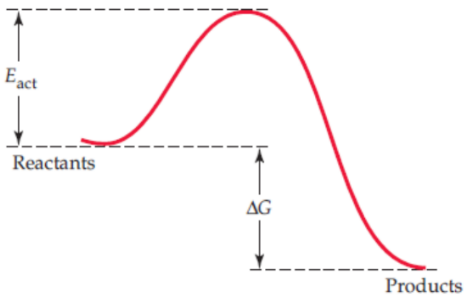
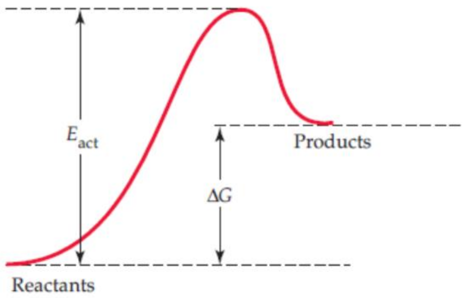
❖ Bioenergetics

- Energy: It is the capacity to perform a work (active transport, biosynthesis, heat)
- Types of energy:
  - Kinetic: Energy in the process of doing work or Energy of <u>motion</u>
  - Potential: Energy content <u>stored</u> in a matter
- Metabolism: Sum of all biochemical reactions in living organisms, which include:
  - Mainly energy generation (degradation of biomolecules, Catabolism)
  - Synthesis of building blocks (Anabolism)
  - Synthesis of macromolecules (Anabolism)
- Bioenergetics: Energy <u>transformations</u> in the cell
- **ΔG :** The <u>free energy difference</u> of a system at any condition
  - If ***ΔG < 0***, reaction is *spontaneous (Favorable)*
  - If ***ΔG > 0***, reaction is *not spontaneous (Unfavorable)*
  - if ***ΔG = 0***, reaction is at *equilibrium*

Equilibrium: It is the state when there is **<u>no net</u>** production of reactants or products (Forward = Backward)
- It is not affected by the enzymes
- It is determined by **ΔG**





- ΔG = ΔH - TΔS
  - ΔH: Heat of the reaction
  - ΔS: Difference in the entropy (***randomness*** of the reaction)
- **ΔGº** = The free energy difference of a system at standard conditions
  - **25Cº**, **1** atmospheric pressure, **1M** concentration of reactants and products and pH = **7**
  - ΔGº is **constant** for the same reaction
- $\mathbf{\Delta G = \Delta G^o + RT \ \ln \frac{[Products]}{[Reactants]}}$
  - ln = 2.3 log
- At equilibrium:

  $\mathbf{\Delta G^o = -RT \ln Keq}$

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

- ΔG depends on the ΔGº, equilibrium and the concentration of reactants and products
  - If more reactants are added, ΔG is more negative (More spontaneous)
  - If more products are added, ΔG is more positive (Less spontaneous)
  - ΔG is not affected by the presence of enzymes or not

- Metabolism is divided into:
  - Catabolism: Degradation or oxidation of biological molecules in order to release energy
  - Anabolism: Synthesis of biological molecules, which requires an input of energy

- The endergonic reactions get their energy by "***energy coupling***"
  - Energy coupling: It is the process of **utilizing** the energy released by an exergonic (favorable) reaction to drive an endergonic (non-favorable) reaction
  - The exergonic reaction can be either an essential step of the pathway or by hydrolyzing an activated intermediate (such as ATP) to release energy
    - ✓ The exergonic reaction is mostly ATP hydrolysis (ATP → AMP + PP_i), where PP_i (Pyrophosphate) is broken down into 2 inorganic phosphates (2 P_i) to release more energy

- Endergonic reaction can be driven by changing the ***concentration of reaction reactants and products***

- **ATP:** A high-energy **intermediate**, utilized to couple exergonic and endergonic reactions
  - It is the major ***energy coupling*** molecule
  - Stores an intermediate amount of energy (ΔG = -7.3)
  - It can't be used for long-term storage of energy

Energy coupling intermediates:
- ATP
- **UTP**, in **sugar** metabolism
- **CTP**, in **lipid** metabolism
- **GTP**, in **protein** metabolism

- *Creatine phosphate* (ΔG = -10.3) *phosphoenolpyruvate* (ΔG = -14.8) represents energy sources that reproduce (replenish) ATP when it is deficient

- Example of energy coupling:
  - Glucose phosphorylation (Glucose + Pi → Glucose–P) [ΔG = +3.3], which is coupled to ATP hydrolysis [ΔG = -7.5]
  - The net coupled reaction [ΔG = (+3.3) + (-7.3) = -4]
  - This reaction traps glucose inside the cells

- Net ΔG for the coupled reaction = $\Delta G_{\text{Exergonic}} + \Delta G_{\text{Endergonic}}$

❖ Biochemical (Metabolic) Pathways

- Biochemical pathways are interdependent
  - Are subjected to thermodynamics laws
  - Allosteric enzymes are the predominant **regulators**
  - Biosynthetic & degradative pathways are almost always **distinct** (regulation)
  - Metabolic pathways are linear, cyclic or spiral

- Energy-producing metabolism involves many stages, including:
  - Stage 1: digestion where food is digested into its polymers, then Polymers are broken down into monomers
  - Stage 2: Monomers are oxidized reaching Acetyl-Coenzyme A (Acetyl CoA)
  - Stage 3: Citric acid cycle
  - Stage 4: Electron Transport chain and oxidative phosphorylation

❖ Thermogenesis

- Heat production is a natural consequence of burning fuels
- Thermogenesis refers to energy expended for generating heat (37ºC) in addition to that expended for ATP production

- There are 2 types of thermogenesis:
  - *Non-shivering thermogenesis* (ATP **production** efficiency)
  - *Shivering thermogenesis* (ATP **utilization**): Responding to *sudden cold* with asynchronous muscle contractions

- Oxidation-Reduction reactions (Redox)
  - Oxidation: **Gain** of oxygen, **loss** of hydrogen and electrons
  - Reduction: **Gain** of hydrogen and electron, **loss** of oxygen

Redox reactions involve the transfer of electrons and the release of energy

- **Redox potential ΔEº**
  - The energy (work) of the transferred electrons under standard biological conditions
  - More negative redox potential means that a substance has a higher ability to be oxidized (loss electrons) with a less affinity for electrons so it is considered as a strong reducing agent
  - More positive redox potential means that a substance has a higher ability to be reduced (accept electrons) with a higher affinity for electrons, so it is considered as a strong oxidizing agent

- **$\Delta G^o = nF (\Delta E^o)$**
  - **n** = number of electrons
  - **F** = Faraday's number

- Example: Calculate ΔGº for the following reaction consisting of 1 & 2 half reactions (F = 2306 cal/ Volt)
  1) OAA + $2H^+$ + 2e → malate (ΔEº = - 0.17 v)
  2) NAD + $2H^+$ +2e → NADH + H^+ (ΔEº = - 0.32 v)
  - Answer:

    OAA + NADH + H^+ → malate + NAD (ΔEº = + 0.15 v)

    $\Delta G^o = -2 \times 23060 \times 0.15 =$ **- 6918** cal/mol

- Calculate ΔGº of the following reaction

  NAD + H^+ + 2e ⟶ NADH (Eº = - 0.32)

  ½ O_2 + $2H^+$ + 2e ⟶ H_2O (Eº = + 0.82)
  - Answer:

    ΔGº = **- 52.6** kcal/mol

- **NAD^+ and NADH:** Electron Transfer-Coenzymes, involved in oxidation reduction reactions
  - Consist of 2 nucleotides, Adenine and nicotinamide
  - Involves the transfer of a pair of electrons in the form of a Hydride ion (H^-)
  - Usually gets electron from the same source (***alcohols***) transferring them to ketones
  - It is the most common used electron transfer coenzyme in most metabolic pathways
  - NADPH is similar to NADH but it is used in the ***Fatty acids synthesis*** and ***detoxification*** reactions

- **FAD and $FADH_2$:** similar to NADH but it releases a single electron in the form of H atom
  - It must be ***tightly*** (covalently) bound to an enzyme
  - Can get electrons from ***different sources***
  - It is used in some reactions including:
    - ✓ Succinate to Fumarate
    - ✓ Lipoate to lipoate disulfide

Past Papers

1. All of the following regarding thermodynamics are incorrect, except:
   - A. If ΔG < 0, reaction is spontaneous and releases energy
   - B. If ΔG< 0, reaction is spontaneous and consumes energy
   - C. If ΔG>0, reaction is spontaneous and consumes energy
   - D. If ΔG>0, reaction is non-spontaneous and releases energy

2. In the second stage of metabolism, most molecules are oxidized into:
   - A. Pyruvate
   - B. Acetyl CoA
   - C. Acetylcholine

3. In an experimental reaction at equilibrium, the free energy change (ΔG) is -7282.4 J at 25°C. Given that the gas constant (R) is 1.987 J/(K·mol), calculate the equilibrium constant (Keq):
   - A. 146.6
   - B. 0
   - C. 2.2×10^5
   - D. 9521.6
   - E. 3.48×10^6

4. Calculate standard ΔG for the ethanol metabolism reaction that is catalyzed by alcohol Dehydrogenase: (F = 23 kcal/volt)
   - A. 5.5 Kcal
   - B. – 5.5 Kcal
   - C. 11 Kcal
   - D. 2.25 Kcal
   - E. – 2.25 Kcal

Reaction	ΔE°
Acetaldehyde → Ethanol	- 0.2
NAD+ → NADH	- 0.32

5. A reaction has a positive delta G note, one statement is correct:
   - A. This reaction will not happen in a cell.
   - B. It could happen if coupled with an endergonic reaction.
   - C. It can happen when changing the concentration of the reactants and the product.

6. Which one of the following cannot be a mechanism used in the body to overcome an endergonic reaction?

   A. Reaction coupling
   B. Increased substrate concentration
   C. Low intermediate concentration
   D. Decreased product concentration

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