بسم الله الرحمٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Metabolism | Lecture 4

# Bioenergetics Pt.4


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# PRINCIPLES OF BIOENERGETICS

3- Biological Oxidation-Reduction Reactions

(Redox)

# OXIDATION-REDUCTION REACTIONS (REDOX)

- **Enzymes** are divided into **7 classes**, the first class is **Oxidoreductases**, we are going to study this class and the **oxidation-reduction reaction** rather than others, why ?

- ✓ Because it is highly associated and relevant to the topic of **Bioenergetics**.

- ✓ **Energy production** is all about the **transfer of electrons** from **one molecule to another** (for example, Krebs cycles main goal is to produce an electron carrier molecules (NADH & FADH2) which is an oxidation-Reduction reaction. Also, these electrons carrier molecules goes to the electron transport chain and give their electrons to complex I and complex III (this is also an oxidation reduction reaction). Also, these electrons will be transferred from one complex to another (which is also oxidation-reduction reaction).

- ***The Energy production is about the transmission of electrons from one molecule to another.***

# OXIDATION-REDUCTION REACTIONS (REDOX)

## Let's talk about electricity :

- When you are charging your phone, what is happening? The electricity (electron current) is moving from the energy source to your phone, why is this happening? This because there is a **difference in potential energy** between your phone battery and the energy source, and depending on that, the potential difference between the source and your phone battery is what drives the movement of electrons from the higher potential (source) to the lower potential (battery).

- Can we reverse the direction of electrons?

- Yes, if we reverse the potential, the direction of electron movement will be reversed since electrons are always moving from higher potential to lower potential.

- But, does this concept that apply to electricity apply to our body?

- Yes, the physical concepts that applies to electrons in the electricity applies to the electrons in our body molecules. The InBody test works by measuring the speed at which electrical signals travel through different components of your body, such as fat, protein, and water.

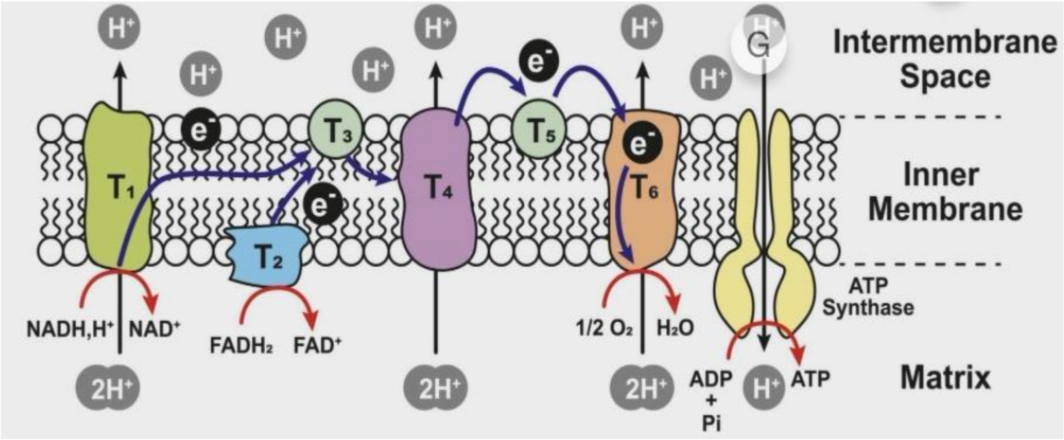
# OXIDATION-REDUCTION REACTIONS (REDOX)

- If there is a potential difference between 2 molecules there will be a transfer of electrons from the higher potential to the lower one.

- What is potential energy?

- **Potential energy** (الطاقة الكامنة) is the energy stored in the electron and it depends on the environment around the electron (the same electron in different molecules stores different energy). The energy content of an electron in orbit around the nucleus varies depending on its distance from the nucleus.

- In Electron transport chain, the electrons are moving from one Heme group to another, but the presence of this heme group in different enzymes gives them and their electrons different potentials and this makes a **potential differences** between these enzymes and drives the transfer of electrons.



# OXIDATION-REDUCTION REACTIONS (REDOX)

- Any material that can switch between two states **(Oxidized & Reduced)** we call these two states → **(A Redox Couple)**, For Example :

- **NAD+ + H+ + 2e- ⟶ NADH (NAD+ / NADH)**
- **FAD + 2H + 2e- ⟶ FADH2 (FAD / FADH2)**
- **Cytochrome C + e- ⟶ Cytochrome C (oxidized)**

- **Reduction Potential :** The **ability** of the molecule to be **reduced**.
- **Oxidation Potential :** The **ability** of the molecule to be **oxidized**.
- <u>**By knowing the reduction or oxidation potential of two molecules, we can know the potential difference and predict the direction of electrons transfer and the direction of the reaction.**</u>

# OXIDATION-REDUCTION REACTIONS (REDOX)

➢ **How we can know the oxidation and reduction potential for all the molecules in the universe?**

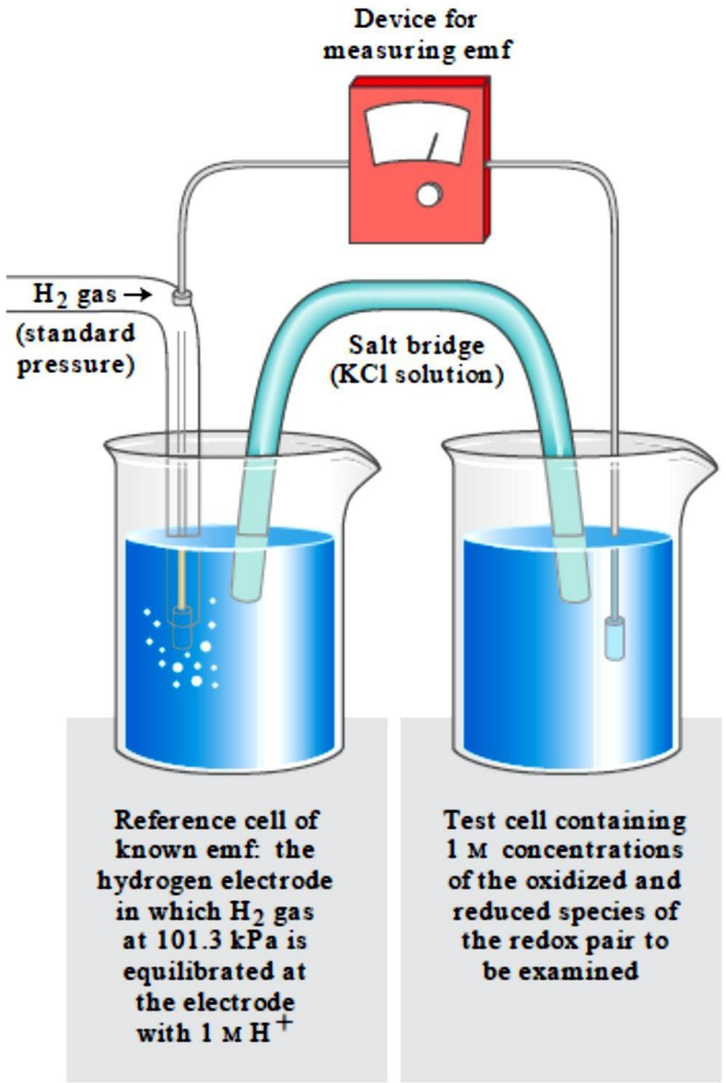
1) We standardise a molecule (or an element) as a standard electrode.

$$H^+ + e^- \longrightarrow H \qquad E = 0.00\ V \text{ zero point}$$

2) We put the molecule (or element) that we want to know its reduction (or oxidation) potential as the other electrode.

3) We write down the voltmeter readings and know the direction in which the electrons move, and we repeat that with every molecule (or element) in the universe.

***By doing this over and over we have the table shown in the next slide.***



# OXIDATION-REDUCTION REACTIONS (REDOX)

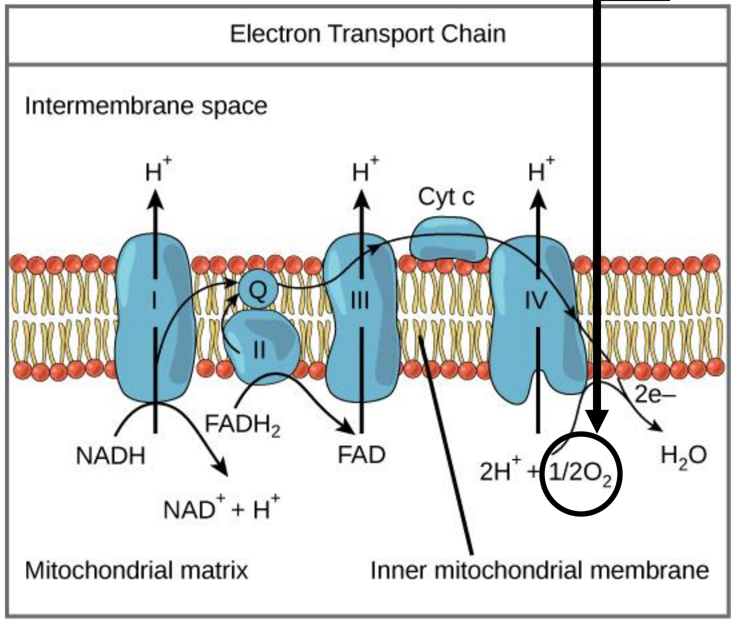
- **Why we Breath ?**

We breath to pick up oxygen, why we need oxygen? To supply our tissue and cells, why we need to supply our cells with oxygen?

Because the **oxygen** plays a vital role in the production of energy since it is the **<u>final electrons acceptor</u>** at the **electron transport chain** in the mitochondrion.

- And as you can see, **the oxygen get reduced into O-2** and **accompanies with protons (H+)** which are highly abundant in the mitochondria resulting in the **formation of Water (H2O).** That's why the oxygen has the highest reduction potential ( highest ability to accept electrons).

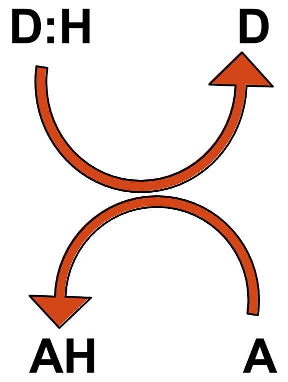
- **This explains how we keep homeostasis of water inside our body.**




# OXIDATION-REDUCTION REACTIONS (REDOX)

- **Oxidation:** Can happen through :
    - Gain of Oxygen
    - Loss of Hydrogen
    - Loss of electrons
- **Reduction**: Can happen through :
    - Gain of Hydrogen
    - Gain of electron
    - Loss of Oxygen

- E (redox Potential): it is a POTENTIAL ENERGY that measures the tendency of oxidant/reductant to gain/lose electrons, to become reduced/oxidized
- <u>Electrons move from compounds with lower reduction potential (more negative) to compounds with higher reduction potential (more positive)</u>
- Oxidation and reduction must occur simultaneously



# REDUCTION POTENTIAL

- $A\text{-}P + B \longrightarrow A + B\text{-}P$

**Type of reaction?** Group transfer reaction (if you calculate the oxidation number, you will find that it is an oxidation reduction reaction.

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

$\Delta G^o$ and $\Delta E^o$; and we are going to learn what is $\Delta E^o$ as we are moving through the slides.

- $A^{++} + B^{++} \longrightarrow A^{+} + B^{+++}$

**Type of reaction** Oxidation & Reduction Reaction

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

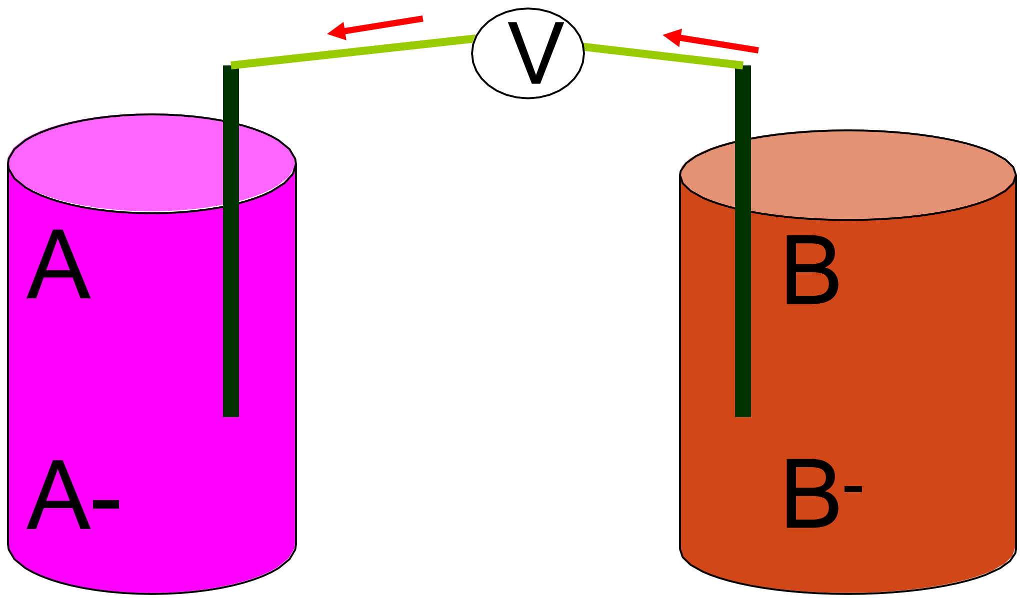
# REDUCTION POTENTIAL AND DIRECTION OF THE REACTION

$$A \quad + \quad B^- \longrightarrow A^- \quad + \quad B \qquad \Delta G^{o} = -ve$$

**B oxidized form**

**B- reduced form**

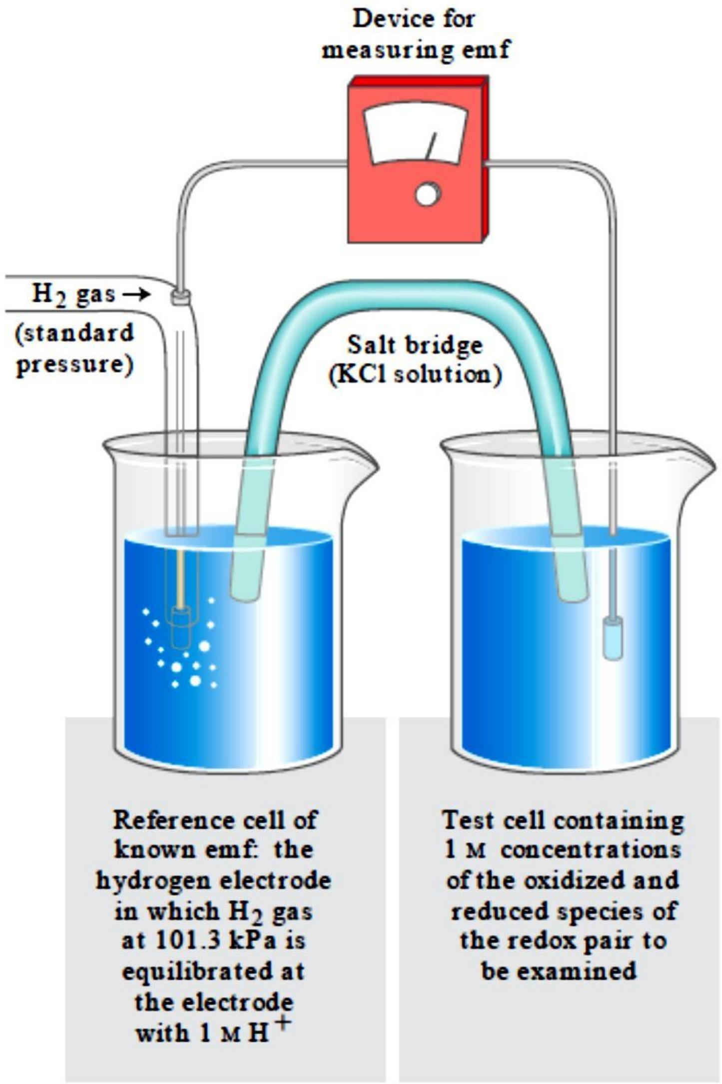
**Redox couple**



# WHAT IS THE STANDARD?

- Hydrogen electrode
- $H_2$ Gas sensor

$$H^+ + e^- \longrightarrow \tfrac{1}{2}H_2$$



# REDUCTION POTENTIAL AND DIRECTION OF THE REACTION

$$H^+ + X^- \longrightarrow H_2 + X \qquad \Delta G^o = -ve$$

$X$ **oxidized form**

$X^-$ **reduced form**

**Redox couple**

**X- has higher tendency to lose electrons than H2 does**

**➔**

**Negative reduction potential**

# STANDARD REDUCTION POTENTIAL ($E^0$)

$$E = E^\circ + \frac{RT}{n\mathcal{F}} \ln \frac{[\text{electron acceptor}]}{[\text{electron donor}]}$$

Farady constant, equals 23.06 Kcal/mol

E : Reduction Potential
E° : Reduction Potential at standard condition
R : Gaz constant, equals 8.314 J/(K.mol)
n : Number of transferred electrons
T : Temperature in calvin

$$E = E^\circ + \frac{0.026\ \text{V}}{n} \ln \frac{[\text{electron acceptor}]}{[\text{electron donor}]}$$

$$\frac{RT}{F} = 0.026\ \text{Volt}$$

# REDUCTION POTENTIAL

| Oxidized + e- | → Reduced | ΔEº (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 |

**TABLE 13–7** Standard Reduction Potentials of Some Biologically Important Half-Reactions, at pH 7.0 and 25 °C (298 K)

| *Half-reaction* | $E'°$ (V) |
|---|---|
| $\frac{1}{2}O_2 + 2H^+ + 2e^- \longrightarrow H_2O$ | 0.816 |
| $Fe^{3+} + e^- \longrightarrow Fe^{2+}$ | 0.771 |
| $NO_3^- + 2H^+ + 2e^- \longrightarrow NO_2^- + H_2O$ | 0.421 |
| Cytochrome $f$ ($Fe^{3+}$) + $e^-$ $\longrightarrow$ cytochrome $f$ ($Fe^{2+}$) | 0.365 |
| $Fe(CN)_6^{3-}$ (ferricyanide) + $e^-$ $\longrightarrow$ $Fe(CN)_6^{4-}$ | 0.36 |
| Cytochrome $a_3$ ($Fe^{3+}$) + $e^-$ $\longrightarrow$ cytochrome $a_3$ ($Fe^{2+}$) | 0.35 |
| $O_2 + 2H^+ + 2e^- \longrightarrow H_2O_2$ | 0.295 |
| Cytochrome $a$ ($Fe^{3+}$) + $e^-$ $\longrightarrow$ cytochrome $a$ ($Fe^{2+}$) | 0.29 |
| Cytochrome $c$ ($Fe^{3+}$) + $e^-$ $\longrightarrow$ cytochrome $c$ ($Fe^{2+}$) | 0.254 |
| Cytochrome $c_1$ ($Fe^{3+}$) + $e^-$ $\longrightarrow$ cytochrome $c_1$ ($Fe^{2+}$) | 0.22 |
| Cytochrome $b$ ($Fe^{3+}$) + $e^-$ $\longrightarrow$ cytochrome $b$ ($Fe^{2+}$) | 0.077 |
| Ubiquinone + $2H^+$ + $2e^-$ $\longrightarrow$ ubiquinol + $H_2$ | 0.045 |
| Fumarate$^{2-}$ + $2H^+$ + $2e^-$ $\longrightarrow$ succinate$^{2-}$ | 0.031 |
| $2H^+ + 2e^- \longrightarrow H_2$ (at standard conditions, pH 0) | 0.000 |
| Crotonyl-CoA + $2H^+$ + $2e^-$ $\longrightarrow$ butyryl-CoA | −0.015 |
| Oxaloacetate$^{2-}$ + $2H^+$ + $2e^-$ $\longrightarrow$ malate$^{2-}$ | −0.166 |
| Pyruvate$^-$ + $2H^+$ + $2e^-$ $\longrightarrow$ lactate$^-$ | −0.185 |
| Acetaldehyde + $2H^+$ + $2e^-$ $\longrightarrow$ ethanol | −0.197 |
| FAD + $2H^+$ + $2e^-$ $\longrightarrow$ $FADH_2$ | −0.219* |
| Glutathione + $2H^+$ + $2e^-$ $\longrightarrow$ 2 reduced glutathione | −0.23 |
| $S + 2H^+ + 2e^- \longrightarrow H_2S$ | −0.243 |
| Lipoic acid + $2H^+$ + $2e^-$ $\longrightarrow$ dihydrolipoic acid | −0.29 |
| $NAD^+ + H^+ + 2e^- \longrightarrow NADH$ | −0.320 |
| $NADP^+ + H^+ + 2e^- \longrightarrow NADPH$ | −0.324 |
| Acetoacetate + $2H^+$ + $2e^-$ $\longrightarrow$ β-hydroxybutyrate | −0.346 |
| α-Ketoglutarate + $CO_2$ + $2H^+$ + $2e^-$ $\longrightarrow$ isocitrate | −0.38 |
| $2H^+ + 2e^- \longrightarrow H_2$ (at pH 7) | −0.414 |
| Ferredoxin ($Fe^{3+}$) + $e^-$ $\longrightarrow$ ferredoxin ($Fe^{2+}$) | −0.432 |

NAD+ reduction potential and all molecules (or elements) reduction potential is constant in all reactions.

FAD differ from NAD+, since it produces a free radical, so it is always accompanied with an enzyme, so its reduction potential differs depending on that enzyme, (reduction potential of FAD at Succinate dehydrogenase differ from reduction potential of FAD at other enzymes).

That's why FAD has a star.

# CALCULATION OF ΔGº FROM ΔEº

- There is a direct relationship between **the standard Gibbs free energy change (ΔGº)** and the **standard difference in the reduction potential (ΔEº)** because both describe the thermodynamic **favorability** of a reaction, just in different units.

- The equation that connects them is:

$$\Delta G^{\circ} = -nF\Delta E^{\circ}$$

Where:

**ΔGº** = standard **Gibbs free energy change** (in joules).
**n** = number of **electrons transferred** in the redox reaction.
**F** = **Faraday's constant** (23.06 Kcal/mol).
**ΔEº** = standard difference in **reduction potential** (in volts)
**ΔEº=** ( Eº of the electron acceptor – Eº of the electron donor ).


- **ΔGº** represent **the amount of energy difference** that is stored in the **same electron** but in different molecules (**the electron donor** and **acceptor**).

# CALCULATION OF ΔGº FROM ΔEº

$\Delta G^{o} = -\, nf\Delta E^{o}$ $\quad \Delta G = -n\mathcal{F}\,\Delta E$ or $\Delta G'^{\circ} = -n\mathcal{F}\,\Delta E'^{\circ}$

F = Farady constant = 23.06 kcal/Volt

Calculate ΔGº of the following reaction

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

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

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

$\Delta G^{o} = -\, 52.6$ kcal/mol

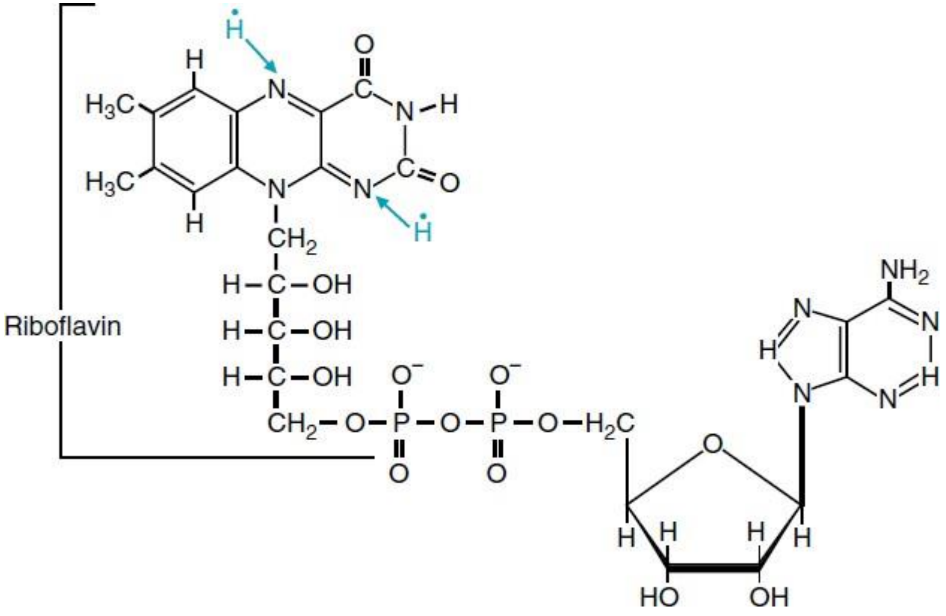
# OXIDATION-REDUCTION REACTIONS (REDOX)

- $\Delta E = E_A - E_D$
- $\Delta E^o =$ **at standard condition**
- **<u>Does $\Delta E$ determine the feasibility of a reaction?</u>** Yes, Already explained

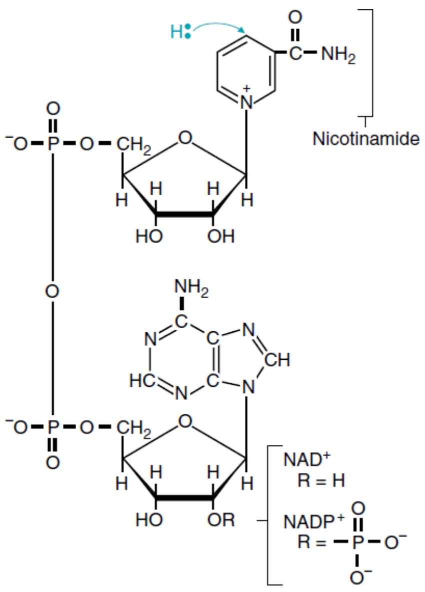
- $\Delta G^o = -nf\Delta E^o$
- **In other words; energy (work) can be derived from the transfer of electrons.**

- **Or Oxidation of food can be used to synthesize ATP**

## FAD

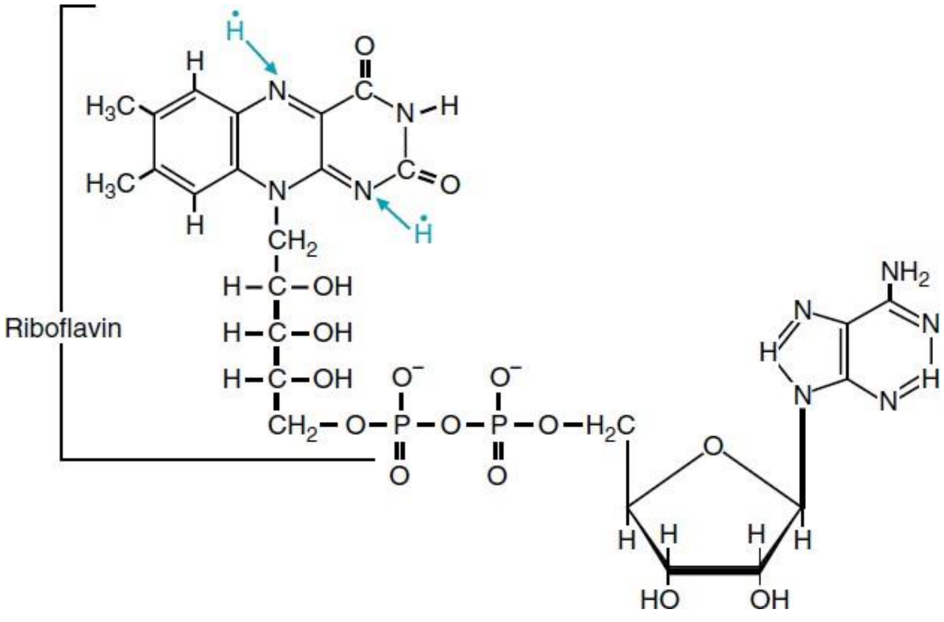



## NAD+




# OXIDATION-REDUCTION REACTIONS (REDOX)

- Always involve a pair of chemicals: an electron donor and an electron acceptor (Food vs. NAD+)
- NAD+ vs. FAD
- NAD+ vs. NADP+ (fatty acid synthesis and detoxification reactions)




# FAD

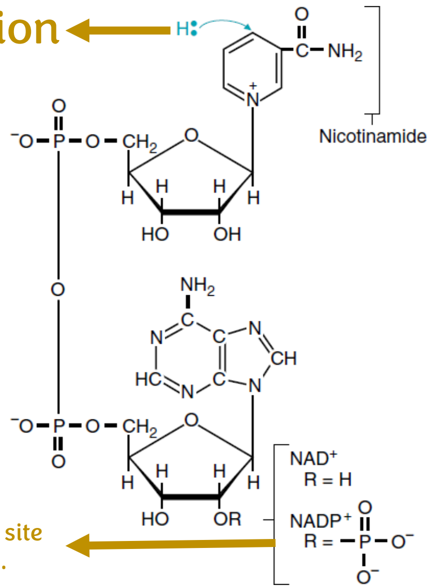
- Accept 2 electrons at 2 different places.

$$FAD + 2H^{+} + 2e^{-} \rightleftarrows FADH_2$$

- You can't find it alone, it produce a free radical which is harmful for the cell after binding to the first H and then forms FADH2 by binding to the other H subsequently.
- There is another molecule called FMN (reduced to FMNH2), these 2 molecules with the same function, are present for **organisational purposes.**

# NAD+

Site of Action



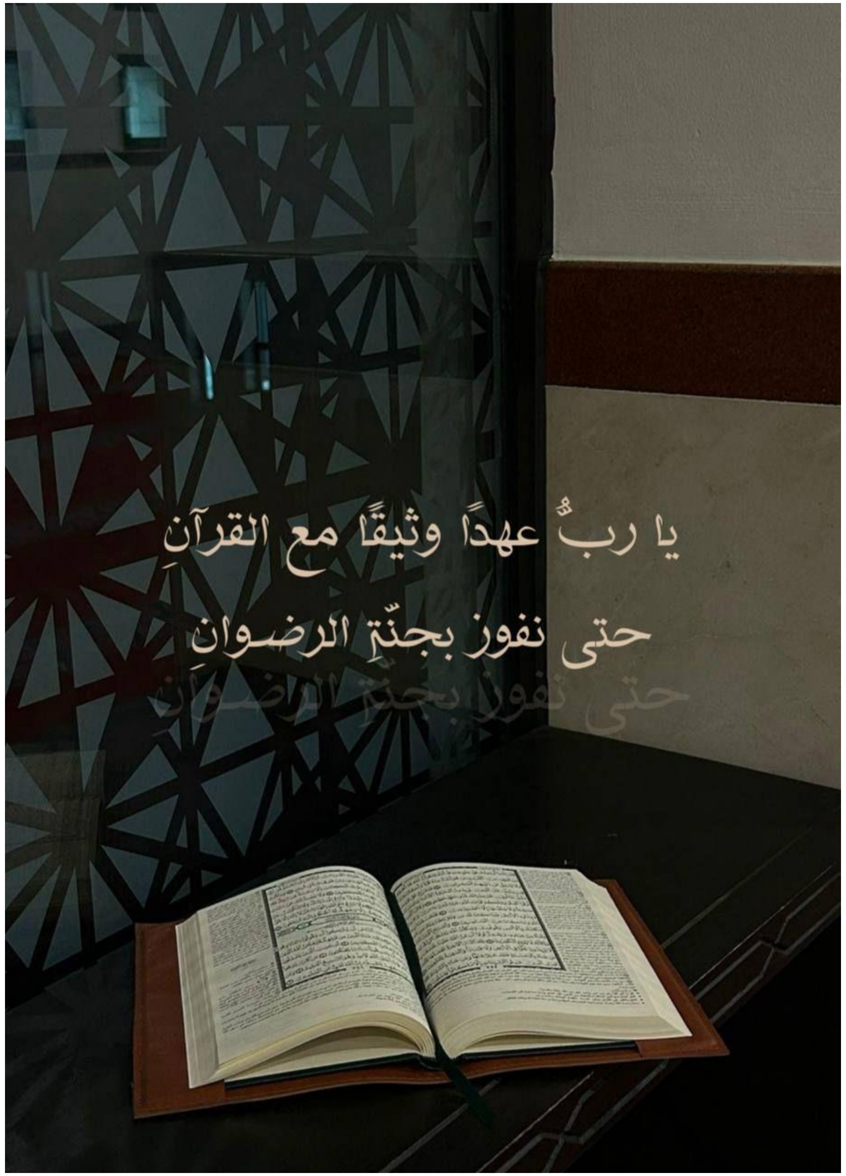

In NADP+ this is the site of phosphate group.

- Reduced by getting two electrons as a hydride ion.

$$NAD^{+} + H^{+} + 2e^{-} \rightleftharpoons NADH$$

- You can find it alone, it doesn't produce a free radical.
- There is other form of it that is phosphorylated called NADP+ and the phosphate is away from the site of action, they perform the same function, the benefit of having two molecules (NAD+/NADP+) performing the same function is **for organisations purposes.**

# رسالة من الفريق العلمي:



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Corrections from previous versions:

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| V0 → V1 | | | |
| V1 → V2 | | | |