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# BIOLOGICAL OXIDATION

**Bioenergetics**: It describes the transfer and utilization of energy in biological system.

All the catabolic products of the food components → (CHO, fats and proteins) are **metabolized** into principle sources of **reducing equivalents** (such as **NAD** & **FAD**). These NAD and FAD have a high **transfer** [redox] potentials.

$$RH_2 + NAD^+ \rightarrow NADH + H^+ + R$$

**Electron Transport:** Electrons carried by reduced coenzymes (**NADH** & **FADH**) are passed through a chain of proteins and coenzymes to drive the generation of an **electrochemical or proton gradient across** the inner mitochondrial membrane.

Redox potential →Electron affinity

**Oxygen** has the **highest** electron affinity (↑↑↑ highest- redox-potential), **electrophilic**. Hydrogen has the **lowest** electron affinity (↓↓↓ lowest redox potential), **nucleophilic**.

**Oxidative phosphorylation** is the process of converting this high redox potential into energy-rich ATP molecules.

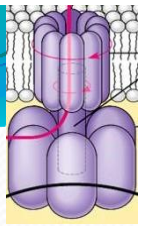
$RH_2$→NADH & FADH→ETC Proteins

(electron transport + H+ pumping → Electrochemical Gradient) →$O_2$ → $H_2O$ + ATP

Components of ETC are **arranged** in order of **increasing** redox potential.

Electron passes on from **electronegative NADH** to **electropositive $O_2$**.

- Electron transfer to $O_2$ is **highly exergonic**.
- Called **respiratory** chain because of the reduction of **$O_2$** from respiration into **$H_2O$**.
- **95%** of oxygen consumed by humans is reduced to $H_2O$ by cytochrome oxidase (**300** ml $H_2O$/day) and called **metabolic water**.




Amino acids
Fatty acids
Glucose
Stage 1
Acetyl-CoA production
Glycolysis
Pyruvate
pyruvate dehydrogenase complex
$e^-$
$CO_2$
Acetyl-CoA
Stage 2
Acetyl-CoA oxidation
Citrate
Oxaloacetate
Citric acid cycle
$CO_2$
$CO_2$
NADH, $FADH_2$
(reduced $e^-$ carriers)
Stage 3
Electron transfer and oxidative phosphorylation
$2H^+ + \frac{1}{2}O_2$
$H_2O$
Respiratory (electron transfer) chain
ADP + $P_i$
ATP

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# Correlation between Electron Transport system & oxidative phosphorylation

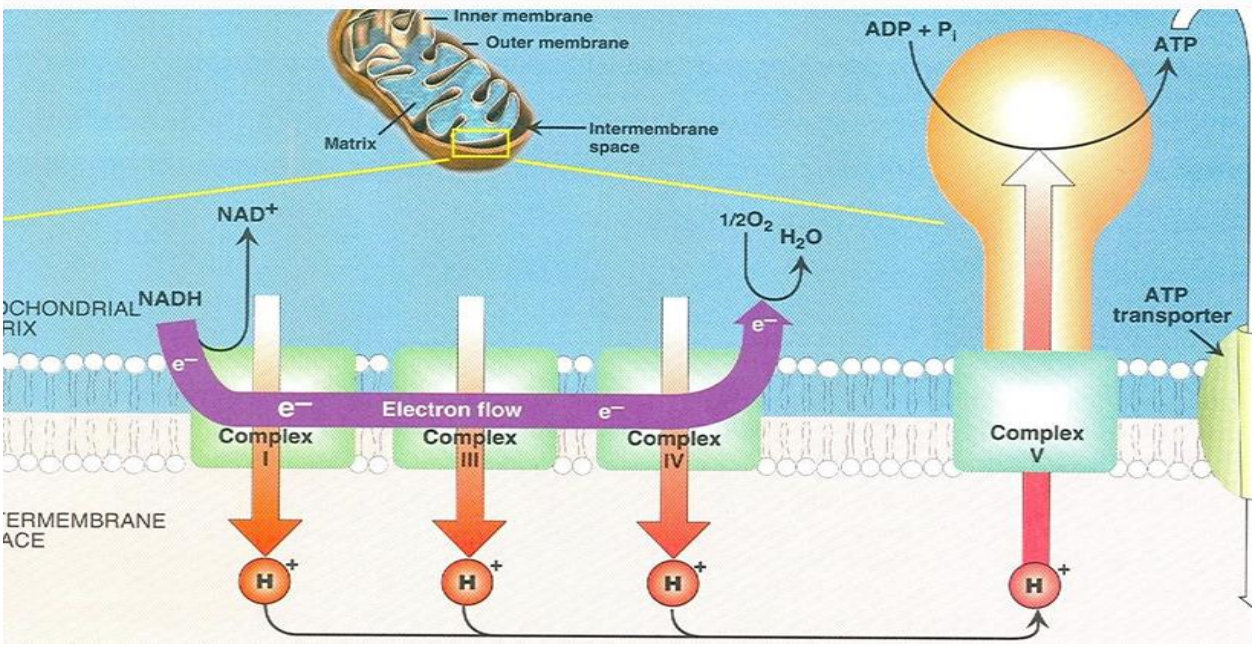
**Electron Transport:** Electrons carried by reduced coenzymes are passed through a chain of proteins and coenzymes (in ETC) to drive the generation of a **proton gradient** across the **inner** mitochondrial membrane.

**Oxidative Phosphorylation**: The proton gradient runs downhill to drive the synthesis of ATP.

In biologic systems:

Cells use electron transport chain to transfer electrons **stepwise** from substrates to oxygen thus producing energy **gradually**. This process is **stepwise**, **efficient** and**controlled**. During hydrogen (H+ and electron) transfer through different components of the redox chain, energy is released **gradually** in **small** utilizable amounts instead of a **massive** energy production in the form of **heat,** which if happens may **destroy** the living cells.

## ETC Complexes



**Four** protein complexes (**I to IV**) in the **in** mitochondrial membrane and **one ATP synthase complex**.

A **lipid** soluble coenzyme (**UQ, CoQ**) and a **water** soluble protein (**cytc**) shuttle between protein complexes.

Electrons generally **fall or flow** in energy through the chain - from complexes I and II to complex III→ IV (**$RH_2 \rightarrow H^+ e^- \rightarrow O_2$**).

**Complex I = NADH-CoQ10 oxidoreductase (**Electron transfer from NADH to CoQ10) = **4H+ pumped**

This complex accept $H^+$ and Hydride ion from reduced NAD.

**Complex II = succinate dehydrogenase (succinate CoQ10 oxidoreductase)**

This complex accept $H^+$ and Hydride ion from reduced FAD and **no H+ pumped.**

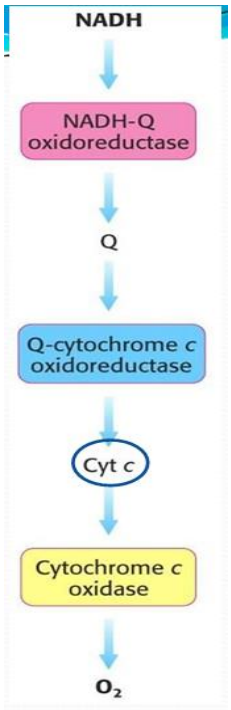
**CoQ: Lipid** soluble Ubiquinone called Coenzyme Q that accept H atoms from complex I and II to **transfer** it into complex III.

**Complex III= CoQ10-Cytochrome c oxidoreductase** CoQ10 (contains cytochromes, **b and c**) passes electrons to Cyt c (and pumps $H^+$) in a unique redox cycle known as the Q cycle. **4H+ pumped.**

Cytochrome c: **is a water-soluble electron carrier, transfer electrons from complex III to complex IV.**

Complex IV = Cytochrome oxidases

($a+a_3$ and copper center). Electrons from cytochrome c are used in a four-electron reduction of $O_2$ to produce $2H_2O$. $O_2$ is the final electron acceptor. 2H+ pumped.



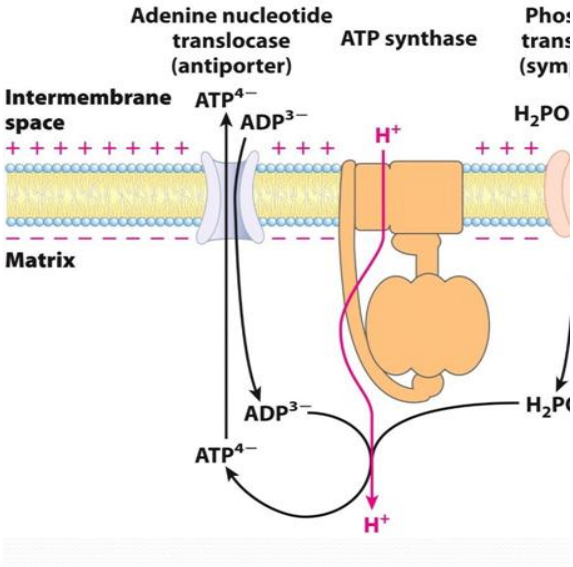

## Mobile Electron Carriers

| CoQ (Ubiquinone) | Cyt C |
|---|---|
| Lipid soluble mobile electron carrier | Water soluble mobile electron carrier |
| Organic molecule (not a protein). | Metallo-protein. |
| Carry electron from Complex I or II to complex III | Carry electron from Complex III to complex IV |

## Complex V = ATP Synthase

It is H+ channel responsible for the Coupling of the energy from **e⁻** Transport and H+ flow with **oxidative phosphorylation** to produce energy as **ATP**.

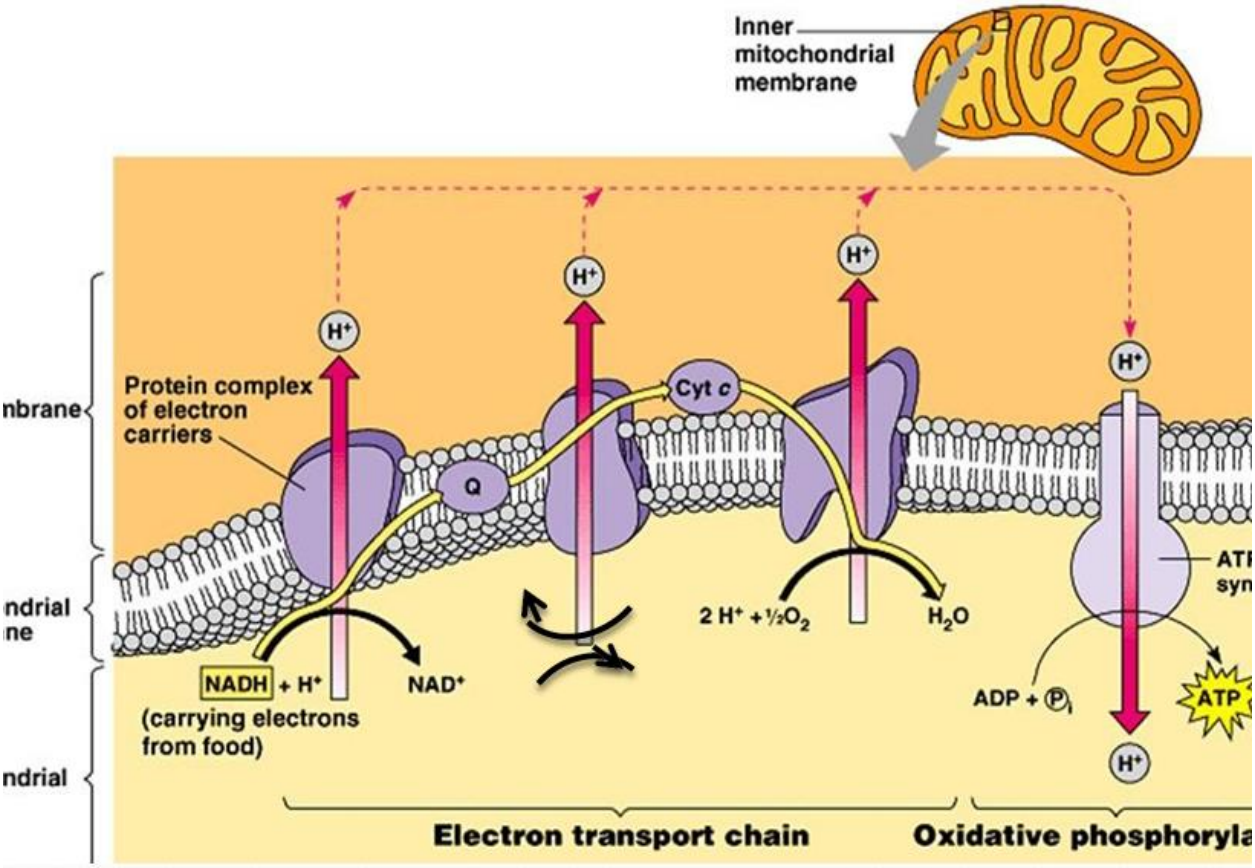
The **enzyme** use the **proton gradient** across the inner membrane to drive the synthesis of ATP




## Mitchell's hypothesis (chemiosmosis model)

Complex I, III and IV act as **proton pumps**.

The translocation of protons $H^+$ from the mitochondrial matrix into the inter-mitochondrial space is called (**proton pumping)** H+ pumping & electron transport results in an **electrochemical gradient**




**Summary of ETC and oxidative phosphorylation**

- ✓ **If substrate enter ETC through NADH+$H^+$ → 3ATP**
- ✓ **If substrate enter ETC through FADH2 (flavoprotein) → 2ATP**

## Chemiosmotic Hypothesis

**Proton motive force**: energy released by flow of $H^+$ down its gradient is used for ATP synthesis.

The energy obtained from **electron transport** is coupled to the **proton motive force** in what's called **Chemiosmosis**.

Mitchell proposed that a proton gradient across the inner membrane could be used to drive ATP synthesis.

**Electrochemical gradient**.

Energy generated by **Electrochemical gradient** is sufficient to drive ATP synthesis i.e. **couples oxidation to phosphorylation.**

Findings to support chemiosmosis model

Addition of protons (acid) to the external medium of the mitochondria stimulates ATP production. Oxidative phosphorylation does **not** occur in case of solubilising mitochondrial membranes.