no.6

Biochemistry 2

Doctor 2018 | Medicine | JU

carbohydrates isomers ketone starch lipid protein amine

◉ Sheet ○ Slides

Done By

Lujain&Lujain

Contributed in the Scientific Correction

Lujain Alaqtash

Contributed in the Grammatical Correction

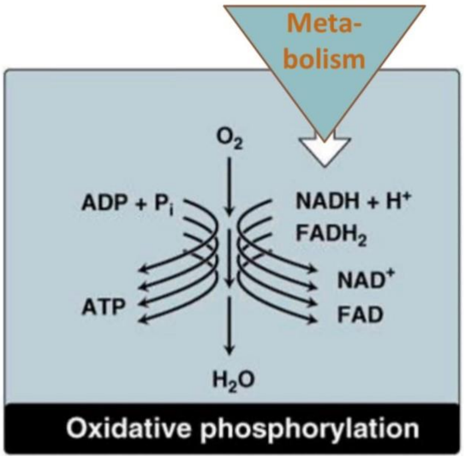
Lujain Akram

Doctor

Faisal Alkhateeb

Last time we introduced you to the process of phosphorylation

Oxidative Phosphorylation



Lippincott Ch 6 or Harpers Ch. 13

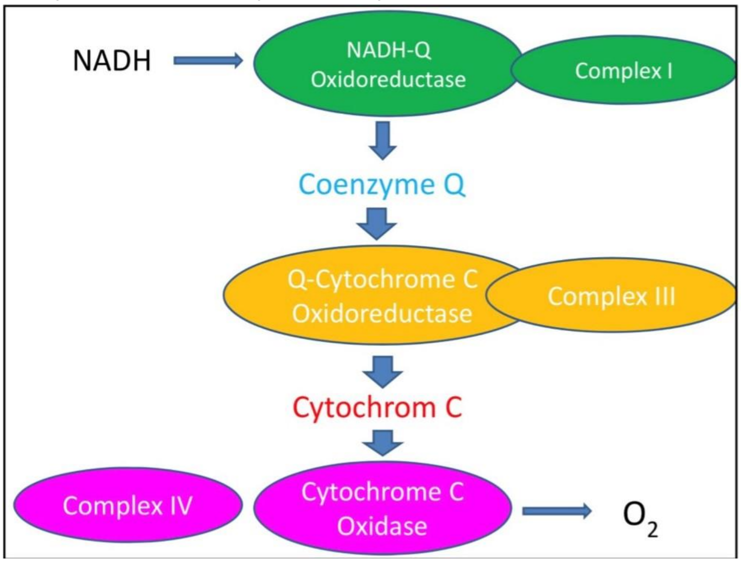
In oxidative phosphorylation metabolism usually there is oxidation-reduction reactions where electrons are transported to the dinucleotide (NAD/FAD) SO the oxidation of NADH and FADH2 by o2 gives a huge amount of energy that is used for syntheses of ATP (this explains the oxidation part of oxidation phosphorylation) , and it's named phosphorylation because of the addition of phosphate to ADP , and these two mechanisms are coupled to each other , meaning : no oxidation happens without phosphorylation and vice versa because they are endergonic reaction coupled to exergonic) .

$$NADH + O_2 \longrightarrow NAD^+ + H_2O \quad \Delta G^{o} = -52.6\ Kcal/mole$$

Last time we calculated how much energy would be produced by oxidation of NADH based on reduction potential which is -52.6kcal/mol and it's a large amount that can synthesize about 7 ATP molecules BUT It was found that this is not the actual amount synthesized , only 3 ATP molecule (due to loss of some energy in other stuff)

*note: the negative ΔG doesn't mean that the reaction is fast , it doesn't predict the speed of the reaction , there should be enzymes or catalysts to speed the reaction

What are these enzymes ?!!



In such sequential reaction , the product of each step will be the reactant of the next step ,

1)NADH(oxidized) coenzymeQ (reduced)

2)coenzyme Q (oxidized)   cytochrome C (reduced)

These sequential oxidation-reduction reactions each has an enzyme specialized for it

** the enzymes are named according to the substrate and product + the type of reaction

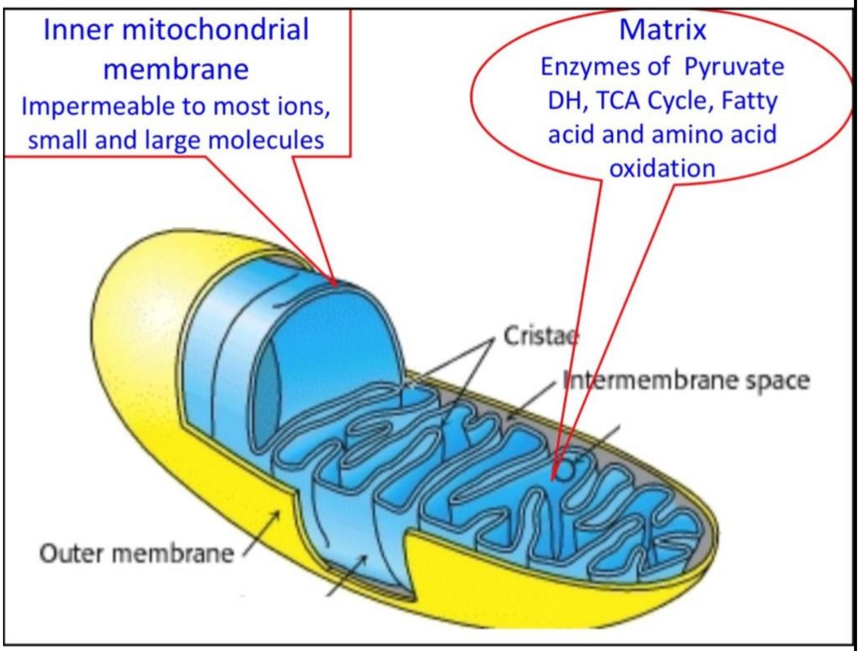
Note: the enzyme catalyzing the oxidation of cytochrome c and reduction of o2 is not called oxidoreductase , that's because it is known that if the acceptor of electrons (the reduced molecule) is o2 we call the enzyme OXIDAZE .

Also these enzymes were named before as complex1,complex3 and complex4 (and they are found in the inner membrane of mitochondria)

THIS chain of reaction is called electron transport chain , because of the transport of electrons from NADH to O2 through this chain of reactions in an ordered manner from one carrier to the other .

-Enzymes usually are proteins and proteins are unable to conduct electricity or transfer of electrons by themselves , meaning that there is no protein that can reversibly act as an electron acceptor and donor . so there need to be something within this protein that is capable of donating and accepting electrons (these are coenzymes)

The electron transport chain is found in the mitochondrial inner membrane



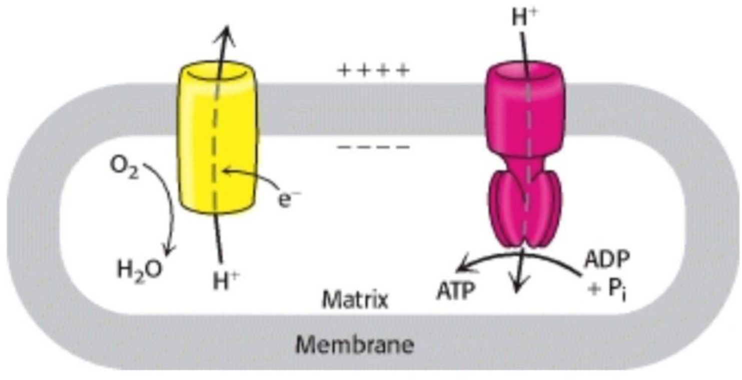
*The outer membrane is permeable for ions and molecules .

*The inner membrane is strictly impermeable even to the smallest proton , it is formed from phospholipids and proteins

** the protein content in the mitochondrial inner membrane is among the largest of biological membranes (because of the synthesis of the electron transport chain components)

-its also highly convoluted to increase its surface area to accommodate all the proteins .

In the matrix : most of the enzymes of catabolism are found in it (fatty acid oxidation, amino acid oxidation, citric acid cycle , pyruvate dehydrogenase and other enzymes)



This figure represents the oxidative phosphorylation

The yellow represents the electron transport chain by all its components (here they are representing it by only one object)

It includes the transport of electrons from NADH to 02 , and it also includes pumping of protons from the matrix to outside of the inner mitochondrial membrane

(these two are coupled together and non can happen without the other)

** note: the pumping of protons happen against the concentration gradient , thus it requires energy (from the exergonic reaction , oxidation of NADH TO NAD)

*since the protons are positively charged , when they are pumped outside , the outside becomes more positive than the inside = electrical potential across the membrane (higher concentration of H+ outside)

However the protons can get back inside through a protein complex called ATP synthase (the pink one) , IT synthesizes ATP from ADP (which requires energy) , this energy is brought from the flow of protons with the concentration gradient (from high conc outside to low conc inside)

And also here phosphorylation of ADP and the flow of H+ are coupled and one cant happen without the other

-note that if all the ADP is converted to ATP , this means no need for energy production thus no longer oxidation will occur thus no longer proton pumping or proton flow will occur thus no more phosphorylation .

All processes in oxidative phosphorylation are tightly coupled to each other

**Because of the difference in chemical concentration , the difference in osmotic pressure in oxidative phosphorylation , they call it the chemo osmotic theory

Electron carrying groups

As we said before no protein could reversibly act as electron acceptor and donor so :

There are multiple electron carrying groups (which are organic or inorganic groups):

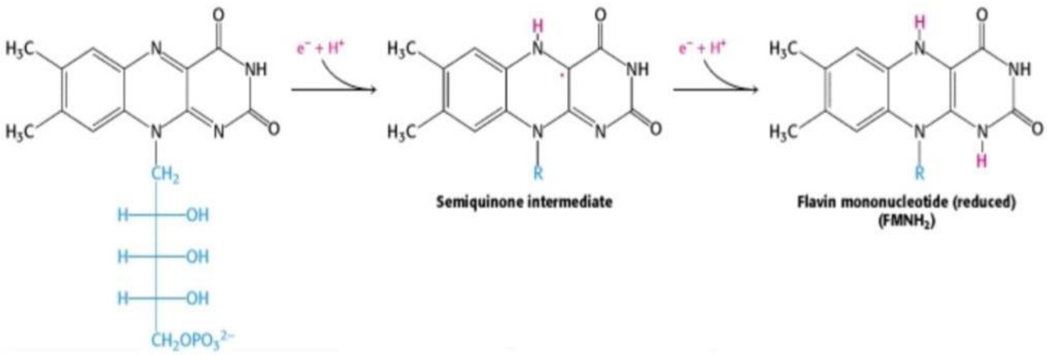
-Flavin mononucleotide

-iron sulfur centers

-coenzyme Q

-cytochromes

-cupper



Flavin mono nucleotide (FMN)

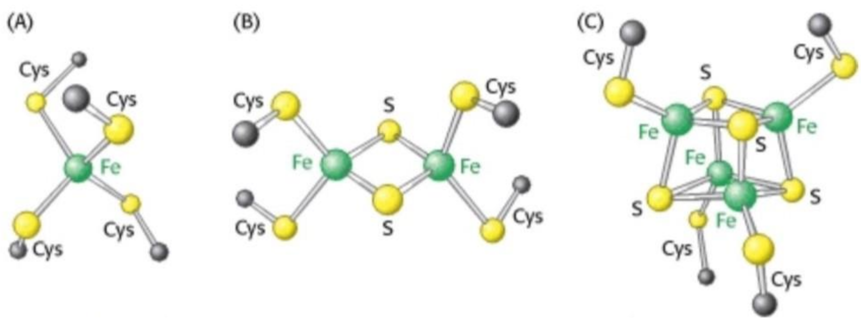
-Can accept one or two electrons

-tightly bound to protein (which could be an enzyme)

-reduction potential is what determines its ability to lose or accept electrons , and its affected by the interaction with protein because it is affected by different environments ex: presence of charges/water …

So the presence of amino acids around the FMN can affect its reduction potential .

Iron sulfur centers



It has different forms :

The first : 1 iron coordinated with 4 cystine which has SH group

We know that Fe could be present as Fe +2 / Fe+3 therefore : when its Fe+3 it can accept an electron to be converted to Fe+2 and reversibly Fe+2 can donate an electron to be Fe+3

That's why it can act as electron transfer substance (carrier)

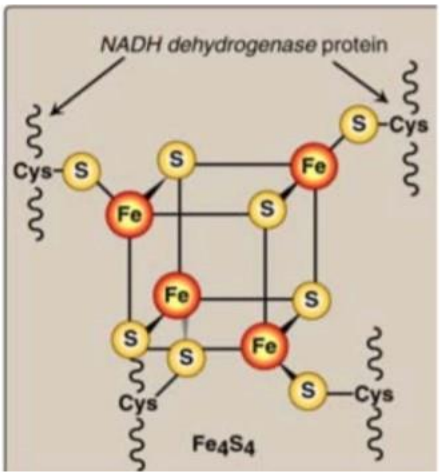
The second form : 2 Fe / 2 S

The last one : 4 Fe / 4S

In all of these the iron can alternate between

Fe+3 and Fe+2 .

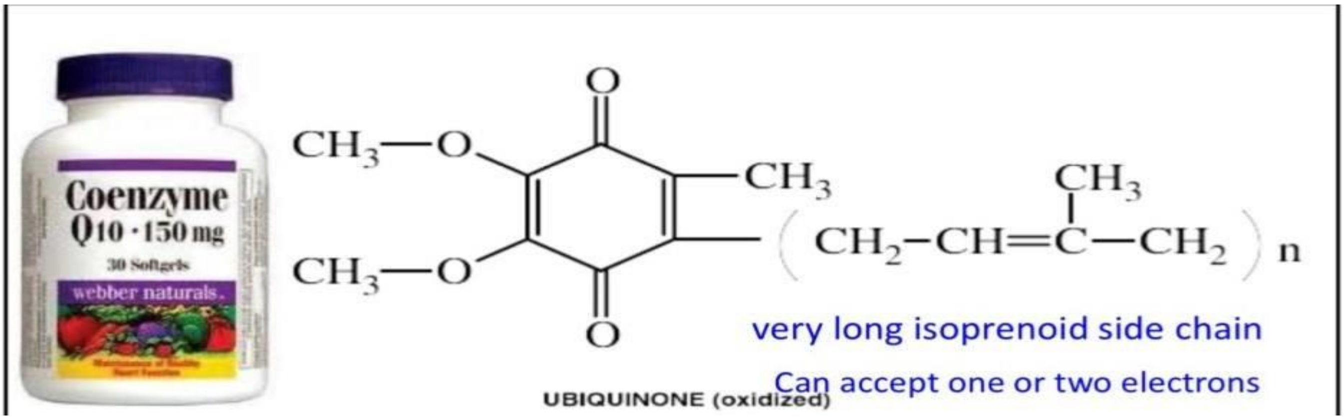
Imp: iron sulphur centres are found as parts of the protein in complex1 and complex 3



Reminder: complex1 and 3 are the enzymes in the electron transport chain

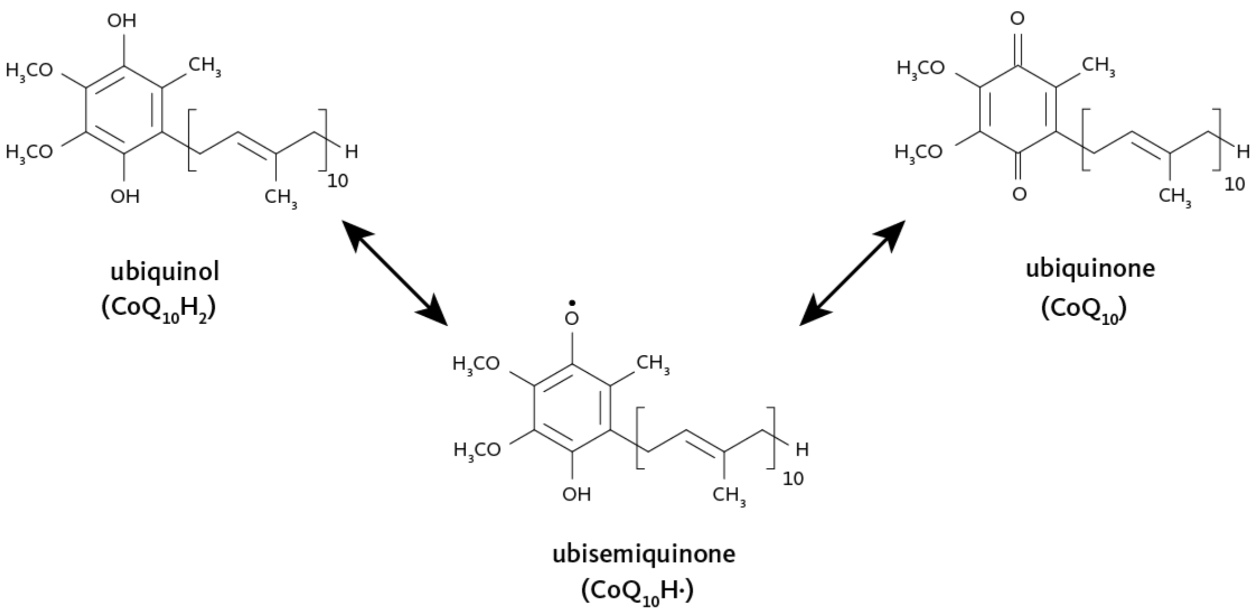
NADH → coenzyme Q → cytochrome C → O2

Coenzyme Q (Ubiquinone)



- Ubiquitous means that it is universally present in all kinds of cells.
- It has very long isoprenoid side chain , isoprenoid is repeated n times (n in humans equal 10)
- It is found in the inner mitochondrial membrane
- It can accept one or two electrons

Figure 1. The Different Redox Forms of Coenzyme Q_{10}

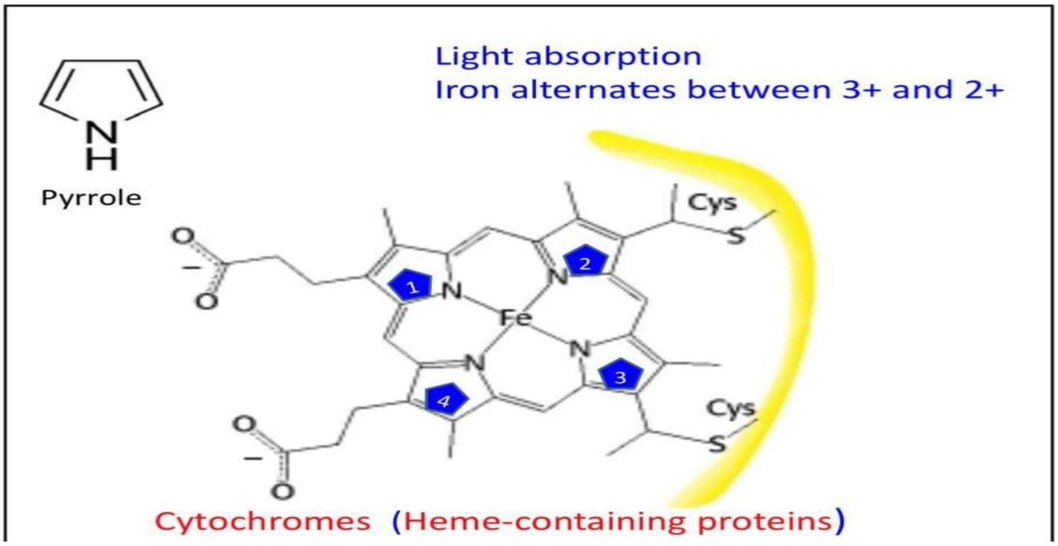


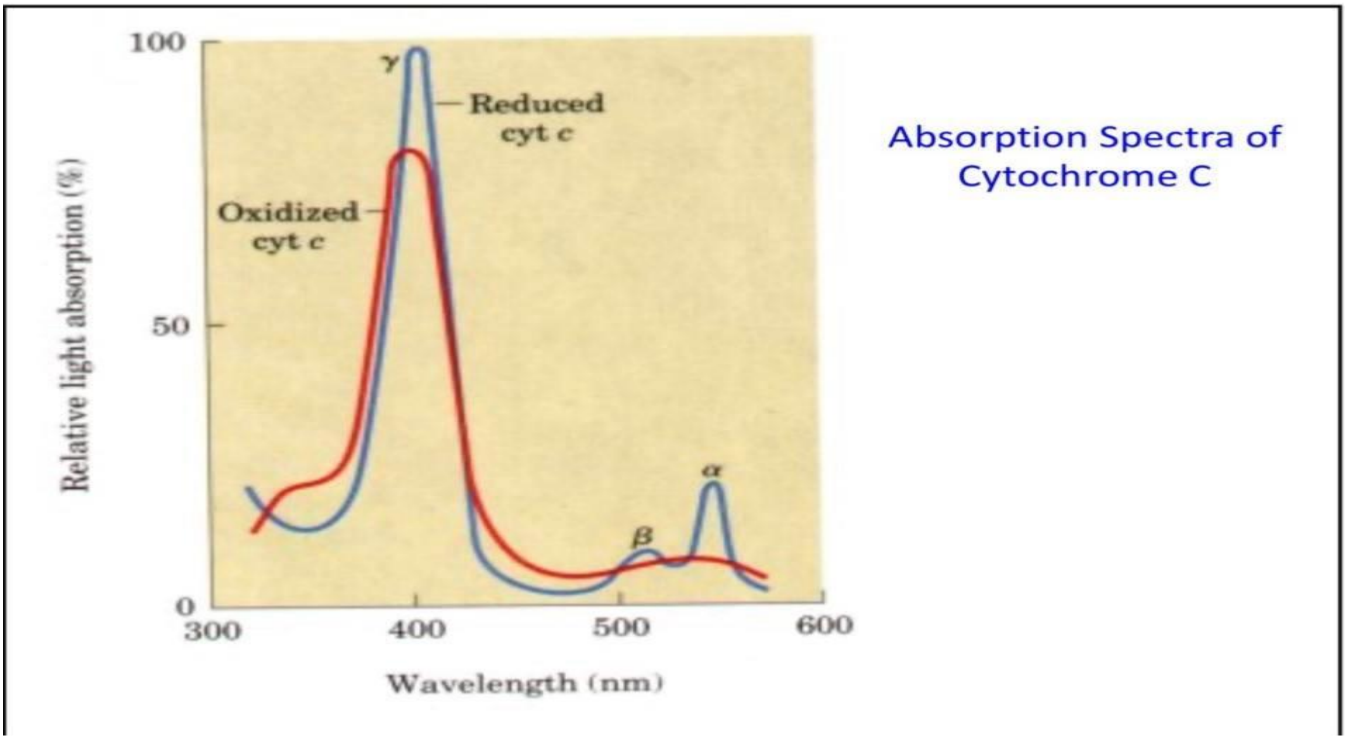
Coenzyme Q_{10} exists in three oxidation states: the fully reduced ubiquinol form ($CoQ_{10}H_2$), the radical semiquinone intermediate ($CoQ_{10}H\cdot$), and the fully oxidized ubiquinone form (CoQ_{10}).

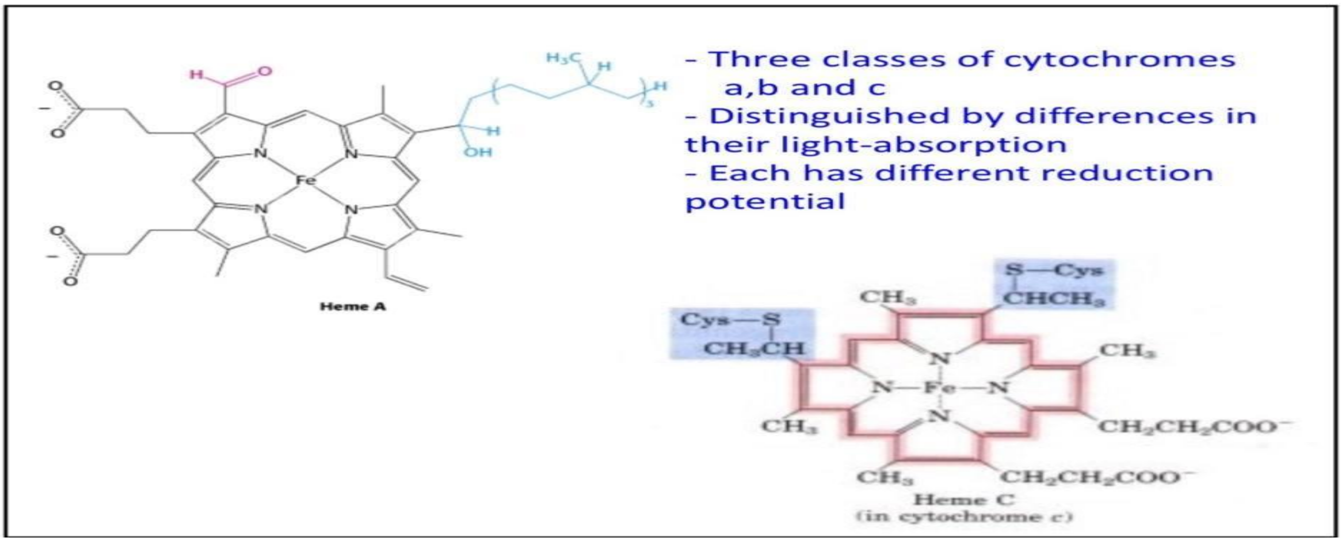
Cytochromes (heme containing proteins)

- It absorbs light ,absorption of light makes it colored
- It contains 4 pyrrole rings connected by CH, and they are all connected to iron which alternates between 3+ and 2+

- Absorption of light is a characteristic of substrates, each substrate absorbs always one light color at a certain wavelength
- Substances differ in their absorption spectra
- By looking at the absorption spectra we can know whether the substance is oxidized or reduced and how much it is oxidized/reduced
- There are 3 classes of cytochromes A,B and C ,each one of them has different reduction potential ,we can distinguish them by the difference in their light absorption .







Enzymes have:

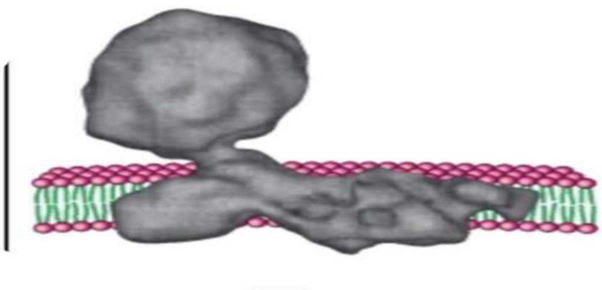
1-long name ,according to the name of the two substrates and the type of the overall reaction

2-short name, according to the name of one substrate and its reaction

Oxidation phosphorylation complexes

Complex 1 (NADH dehydrogenase or NADH-Q oxidoreductase)

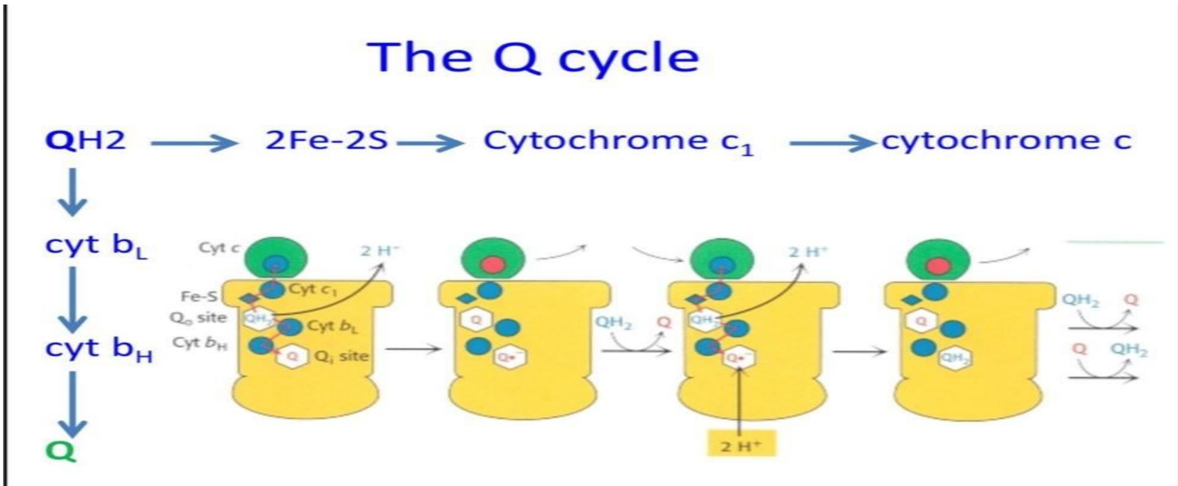
- it is a huge flavoprotein complex ,tightly bound FMN group
- it is a membrane spanning protein,made of more than 25 polypeptide chain
- it has seven **Fe-S** centers of at least two different types
- drop in energy ≈-13 to -14 kcal

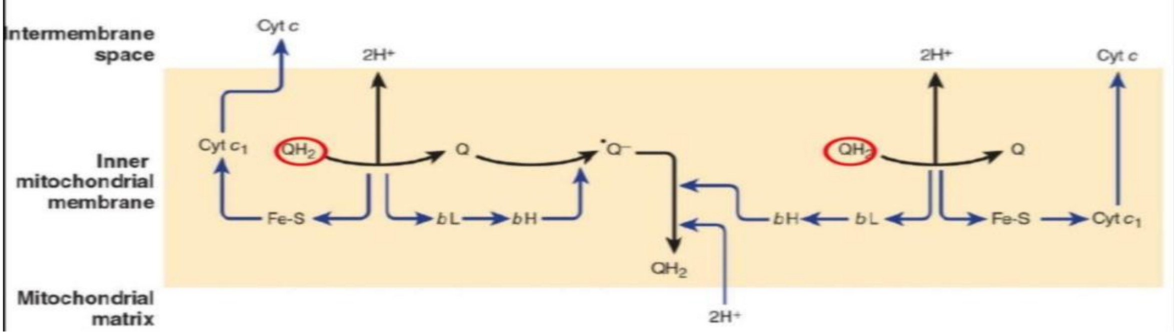


complex 3 (cytochrome reductase or cytochrome bc1 or Q-cytochrome c oxidoreductase)

- catalysis the transfer of electrons from QH1 to cytochrome c
- 11 subunits including two cytochrome subunits
- Contain iron sulfur center
- Contain three heme groups in two cytochrome subunits
  -B_L and B_H in cytochrome b
  -c type in cytochrome c1
- Contain two CoQ binding sites

The Q cycle :QH2 is a donor of 2 electrons in the form of 2 hydrogen, the first electron passes to the iron sulfur center then to cytochrome c 1 and finally to cytochrome c (it becomes partially reduced)
The second electron Cannot follow the same route because the reduction potential of the two electrons differ, so the second electron transfers to cytochrome B_H then to cytochrome B_H Then to another Q





Test yourself :

Question from Lippincott textbook : which one of the following has the strongest tendency to gain electrons ?

a)coenzyme Q

b)Cytochrome c

c)Flavin adenine dinucleotide

d) Nicotinamide dinucleotide

e)oxygen

The answer is : e : oxygen is the terminal acceptor of electrons in the electron transport chain (ETC) , electrons flow down the ETC to oxygen because it has the highest (most positive)reduction potential , the other choices precede oxygen in the ETC and have lower reduction potential values