لجان الدُّفعات

BIOCHEMISTRY

MORPHINE ACADEMY

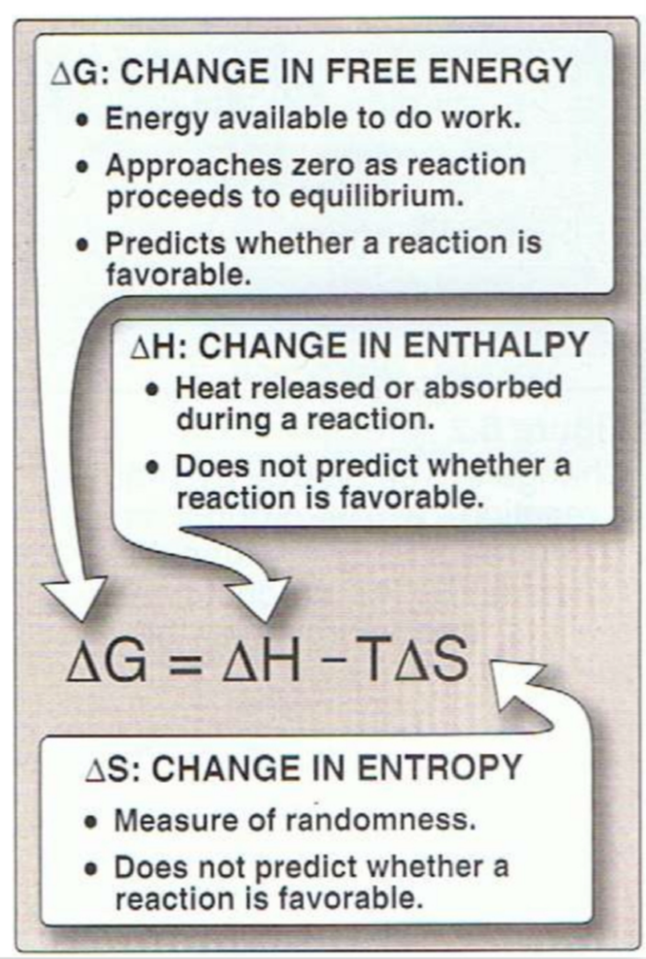
By Maryam Alhasan

MORPHINE ACADEMY

Bioenergetic and oxidative phosphorylation

Bioenergetics

- Is the study of energy changes accompanying biochemical reaction which explains why some reactions occur while others not
- Biological systems conform to the general laws of thermodynamics
  - The free energy (G) predicts the direction in which the reaction will spontaneously proceed



ΔG

- هو اللي بحدد اذا الreaction بمشي او ما بمشي وبتحكم بالتفاعل
- وهو additive

Free energy change

- The sign of ΔG predicts the direction of the reaction
  - -ΔG: there is a net loss of energy, the reaction goes spontaneously (Exergonic)
  - + ΔG: there is a net gain of energy, reaction needs energy to preceed (energonic)
  - ΔG is zero: reactants are in equilibrium
- The ΔG of the forward reaction is equal in magnitude but opposite in sign to that of the back reaction
- ΔG depends on the concentration of the reactants and products at constant temperature and pressure

Negative يعني spontaneous
التفاعل هون رح يمشي

Positive يعني مش spontaneous
بده طاقة واشي يمشيه
رح يمشي irreversible

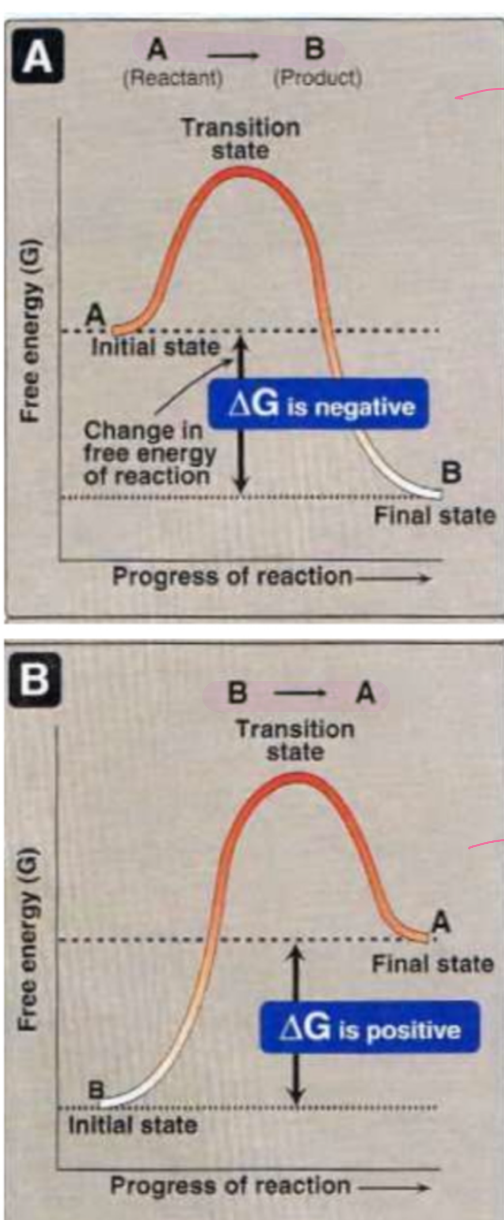
الforward reaction و reverses reaction
بساووا بعض بس الاشارة معكوسة

$$\Delta G = \Delta G^o + RT \ln \frac{[B]}{[A]}$$

[B] Products, [A] reactants

بتعتمد على

where
ΔG^o is the standard free enrgy
T is the absolute temperature (K°)
R the gas constant (1.987cal/mol.degree)
[A] and [B] are actual conc. of reactants and products



هون عم بتطلع طاقة
فهي negative و
spontaneous

Positive
معكوس
بحتاج طاقة

Negative
Spontaneous
من A الى B
(شوفو الthickness
للسهم اللي باتجاه B)

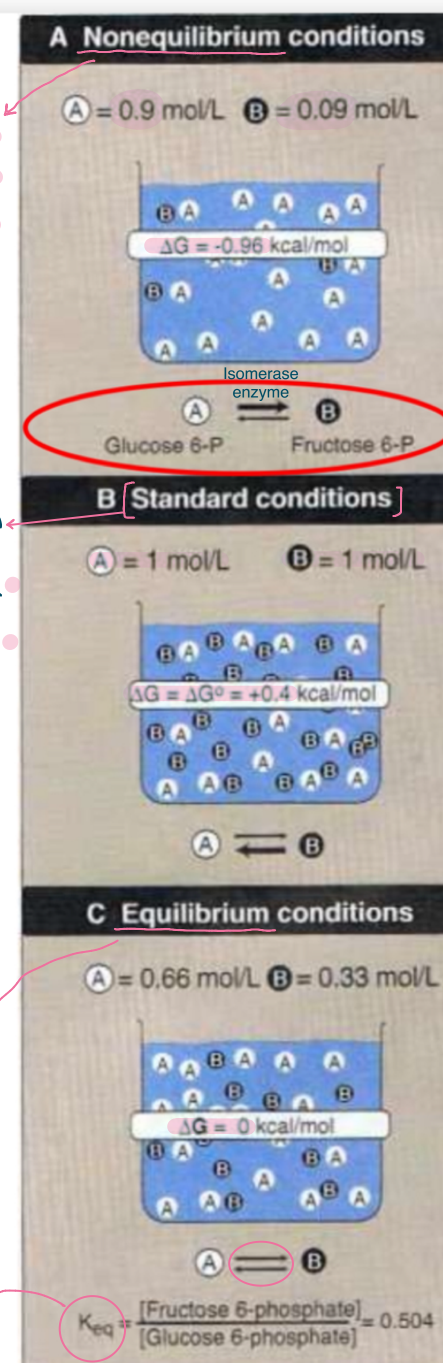
بتصير بالمختبر

الـ concentration A بساوي concentration B
التفاعل من B الى A

$\Delta G = \Delta G^o + RT \ln \frac{[B]}{[A]}$
$= \Delta G^o + RT \ln \frac{1}{1}$
$= \Delta G^o + RT \ln 1$ (zero)
$\Delta G = \Delta G^o$

$\Delta G = 0$
معناه
$\Delta G^o = -RT \ln \frac{[B]}{[A]}$

At equilibrium
$K_{eq} = \frac{[B]}{[A]}$



Standard free energy change, ΔG°

- The energy change when the reactants and products are at concentration of 1 mol/L
- ΔG° can predict the direction of the reaction only under standard conditions (ΔG = ΔG°) but not under physiological conditions
- At equilibrium Keq = [B]/[A] and ΔG = 0 so:

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

This equation allows some simple predictions:

ln1=0

If $K_{eq} = 1$, then $\Delta G^o = 0$	$A \rightleftarrows B$
If $K_{eq} > 1$, then $\Delta G^o < 0$	$A \rightarrow B$
If $K_{eq} < 1$, then $\Delta G^o > 0$	$A \leftarrow B$

- ΔG° of consecutive reactions are additive
- ΔGs of a pathway are additive

$$A \longrightarrow B \longrightarrow C \longrightarrow D$$

- As far as the sum of ΔGs of the pathway reaction is negative, reaction proceeds even if the ΔG of the individual reaction is positive

- حتى لو كان في وحدة positive ، المجموع الكلي لازم يكون بالnegative

ATP as energy carrier

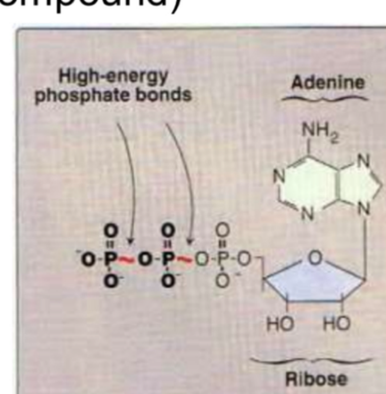
- If the reaction or process has +ΔG (as movement of ions against concentration gradient across cell membrane), it can be coupled with the spontaneous hydrolysis of ATP to ADP and Pi

1. Reactions are coupled through common intermediate
2. A + B ⟶ C + D
3. Energy carried by ATP (high energy phosphate compound)

ATP ⟶ ADP + Pi ⟶ AMP + Pi

ΔG° for each hydrolysis = -7300 cal/mol

تكسير ATP بطلع



- اي reaction حتى لو كان بالpositive بتدخل معه الATP وبتحول لspontaneous
- يعني عادي الreaction اللي صعب يمشي we couple it with ATP

Electron transport chain

- In the metabolism of glucose to CO_2 and water, many metabolic intermediates donate electrons to specific coenzymes (NAD^+ and FAD) to form energy rich reduced coenzymes NADH and $FADH_2$

NAD: Nicotinamide adenine dinucleotide

FAD: Flavin adenine dinucleotide

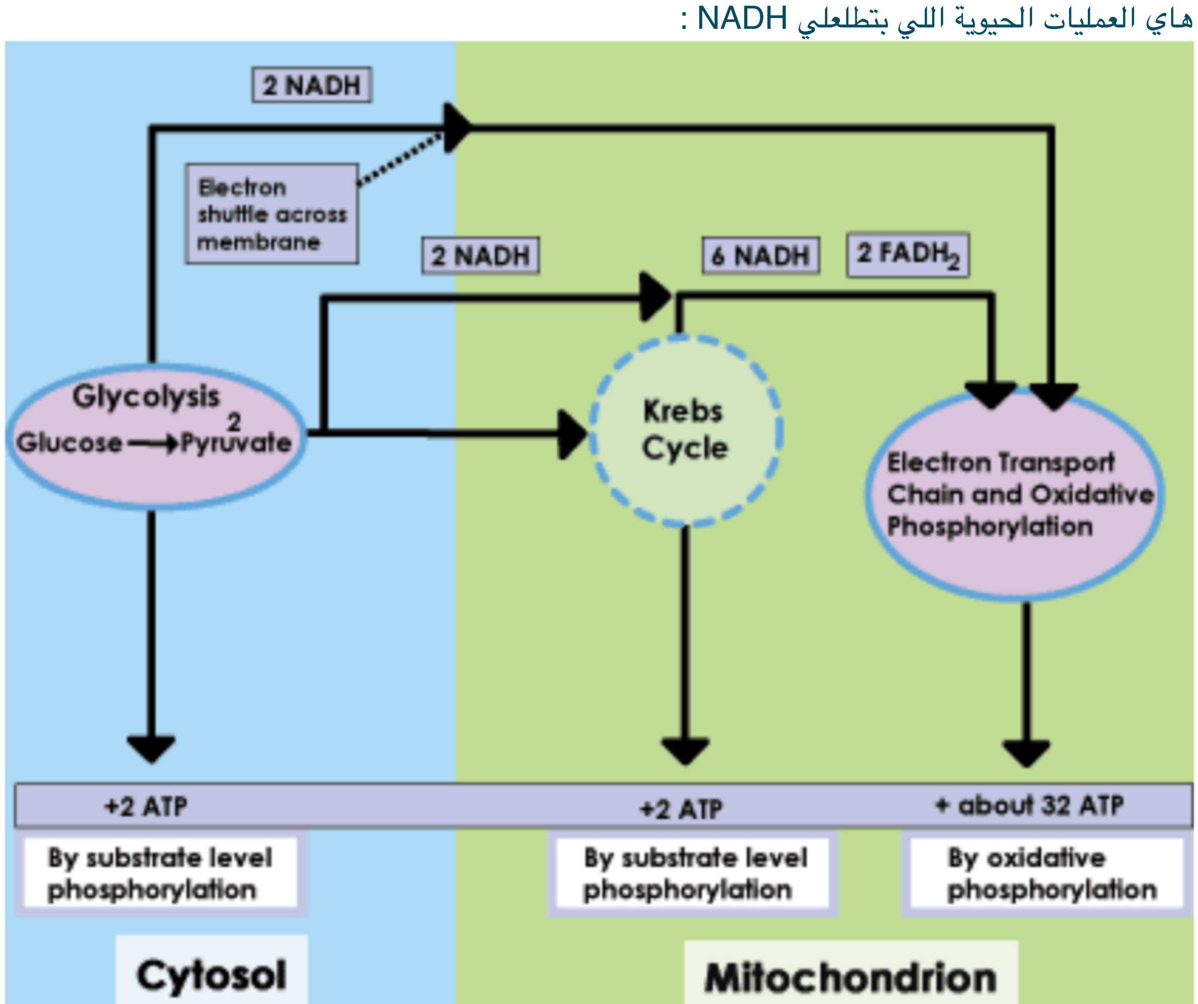
- The reduced form (NADH and $FADH_2$) donate a pair of electrons to special set of electron carriers (Electron transfer chain)

- The flow of electrons leads to the loss of of free energy which can be captured and stored by the production of ATP from ADP and Pi (oxidative phosphorylation)

- مثلا NADH عشان احوله لطاقة لازم يروح على electron transport chain اللي عنا بالinner membrane للميتوكندريا

- اللي موجود بالinner membrane عبارة عن oxidative phosphorylation
جزء oxidative و جزء phosphorylation وهدول التنين should be coupled with each other شغالين مع بعض

هاي العمليات الحيوية اللي بتطلعي NADH :



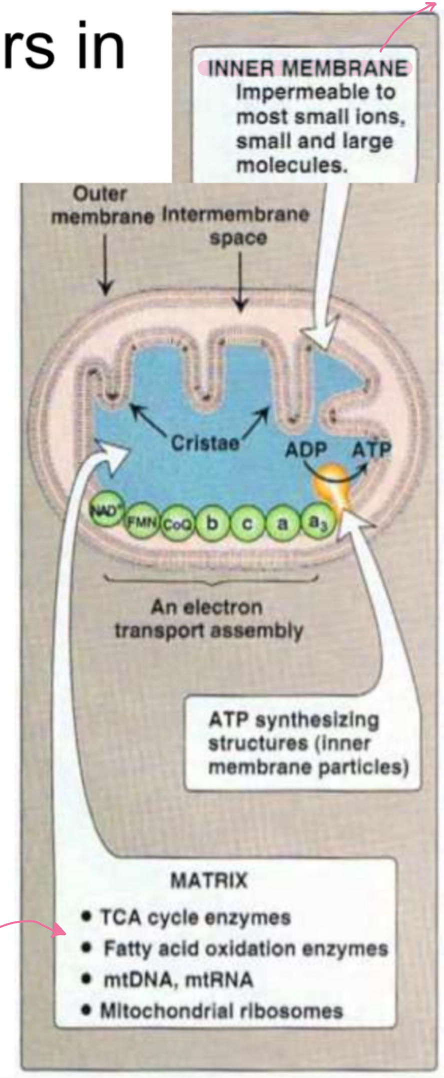
ما يمرق ولاشي
الـphospholipid اللي موجود بس فيه
اسمه Cardiolipin

Oxidative phosphorylation occurs in mitochondrion

يمرق كلشي

- The outer membrane is permeable for most of substances
- Oxidative phosphorylation occurs in the inner membrane of mitochondrion
- ATP synthesizing structures are present at the end of the e⁻ transport assembly
- Different enzymes for TCA cycle, fatty acid oxidation, mtDNA (mitochondrial), mtRNA and ribosomes are present in the matrix.

عمليات حيوية تتم في
matrix of mitochondria

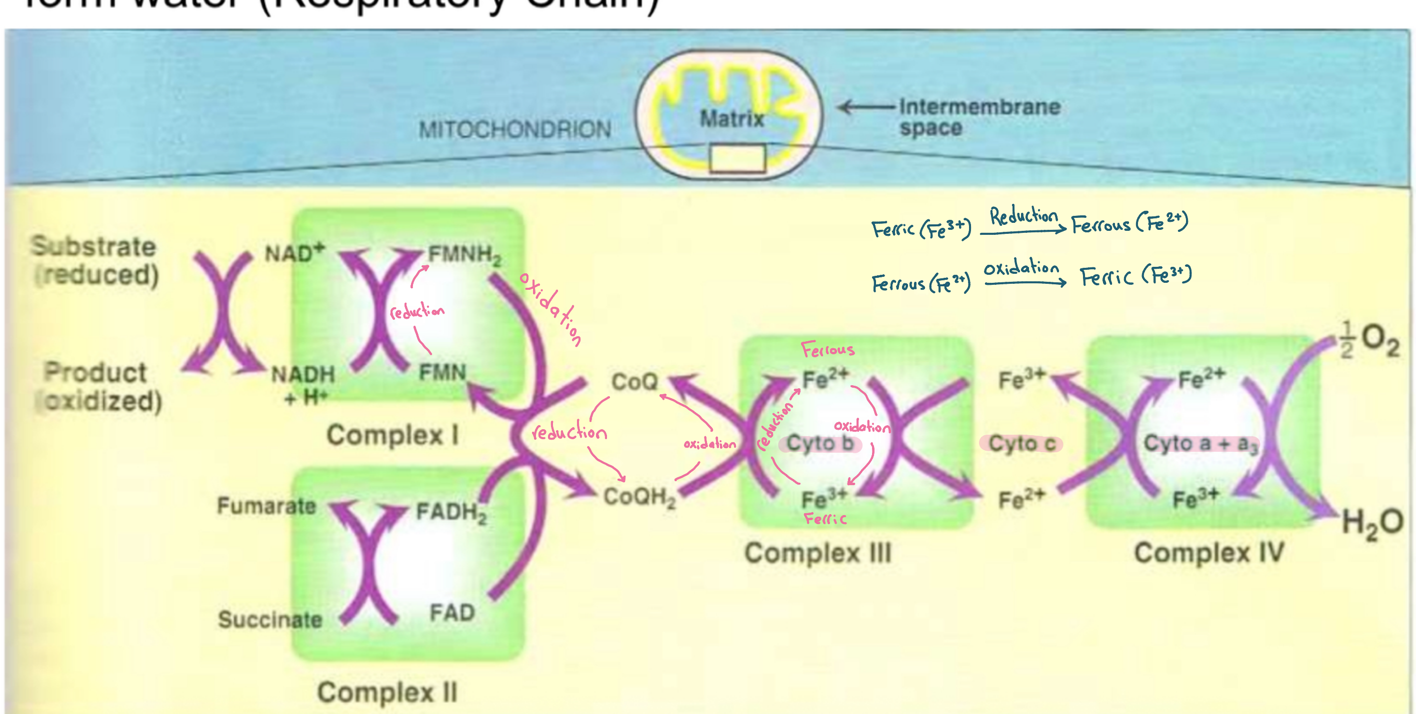


- عنا مجموعة من enzymes
- عمليات oxidation و reduction شغالة
- واخر اشي عنا عملية phosphorylation في ATP synthase enzyme

Organization of the chain

نبدا بعملية الـoxidative phosphorylation في

- Present in the inner mitochondrial membrane
- Consist of 5 separate enzyme complexes until e⁻ combine with O_2 to form water (Respiratory Chain)



- اول شي oxidation reduction بتحول NAD+ الى NADH
- الNADH بروح للinner membrane of mitochondria وبتفعل مع FMN
- اللي بلش الreaction هو NADH dehydrogenase enzyme
- عندي مجموعة من الenzymes وcytochromes كلهم proteins ما عدا الCoenzyme Q
- كلها عمليات oxidation و reduction
- عندي انتقال الكترونات لما يكون عندي flow of electrons يعني عندي تيار current معناها بترتفع حرارة الجسم اذا ما قدرت اخزنه كATP
- فآخر اشي بالعملية بروحو الالكترونات للoxygen وبحوله لwater
- خلال عمليات الانتقال للالكترونات رح يرافقها خروج H+ من الmatrix للintermembrane space
- اخر اشي هاي العملية كلها بتروح للATP synthase وبضل داخل لجوا ، عملية دخوله بتعطي طاقة كافية لتربط ADP زائد inorganic phosphate وبصنع ATP (وهاي الطاقة عشان اربطهم بجيبها من عملية دخل H+)
الoxidation is coupled with phosphorylation

Reactions of the electron transport chain

- All components of this chain are proteins except coenzyme Q
- Some of them contain metals (iron and copper) to function

1. Formation of NADH: needs dehydrogenase which transfers $2e^-$ and one proton to form $NADH + H^+$
2. NADH dehydrogenase: $NADH + H^+$ is complexed with NADH dehydrogenase which has tightly bound flavin mononucleotide (FMN) which accept $2e^-$ and $2 H^+$ to become $FMNH_2$
NADH dehydrogenase has iron-sulfur center necessary for the transfer of H^+ to coenzyme Q
3. Coenzyme Q: is quinone derivative which can accept hydrogen atoms from FMNH2 and from FADH2.

Reactions of the electron transport chain

4. Cytochromes: the rest of electron transfer chain are cytochromes with heme group (iron)

اغلبهم iron وفي عندي ممكن يكون copper

5. Cytochrome a + a3 (cytochrome oxidase) → اللي بنقل للاكسجين الكترونات
   - is electron carrier in which the heme iron has a free ligand that can react directly with molecular O_2 to produce water
   - contain bound Cu atoms required for complex reaction to occur

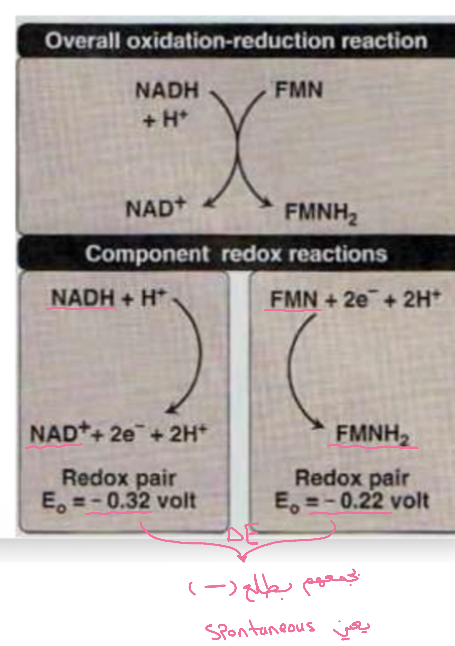
6. Site specific inhibitor:

Some compounds prevent passage of e^- by binding one of the components of the chain which blocks oxidation/reduction and inhibit ATP synthesis

Release of free energy

- Free energy is released as electrons are transferred along the electron transport chain from an electron donor (reducing agent or reductant) to an electron acceptor (oxidizing agent or oxidant)
- The electrons can be transferred in different forms, for example, as hydride ions, as hydrogen atoms, or as electrons
- Oxidation of one compound is always accompanied by reduction of a second substance.
- Redox pairs differ in their tendency to lose electrons, which is a characteristic of a particular redox pair, quantitatively specified by a constant, E_0 (the standard reduction potential) in volts

Redox pair	E_o
$NAD^+/NADH$	-0.32
$FMN/FMNH_2$	-0.22
Pyruvate/lactate	-0.19
Cytochrome c Fe^{3+}/Fe^{2+}	+0.07
$1/2\ O_2/H_2O$	+0.82



- التفاعلات لما يكون عندي oxidation لازم يكون عندي بالمقابل reduction
- ΔE بحددلي الreaction رح يمشي ولا لا

Standard reduction potential (E_0)

- The standard reduction potentials of various redox pairs can be listed to range from the most negative E_o to the most positive.
- The more negative the standard reduction potential of a redox pair, the greater the tendency of the reductant member of that pair to lose electrons.
- The more positive the E_o, the greater the tendency of the oxidant member of that pair to accept electrons.
- So electrons flow from the pair with the more negative E_o to that with the more positive E_o.

NADH ⟶ 2,5 ATP

$FADH_2$ ⟶ 1.5 ATP

NADH and FADH2

- Oxidation of one mole of NADH results in free energy sufficient to produce 3 ATP
- Oxidation of one mole of FADH2 and FMN results in free energy sufficient to synthesize 2 ATP

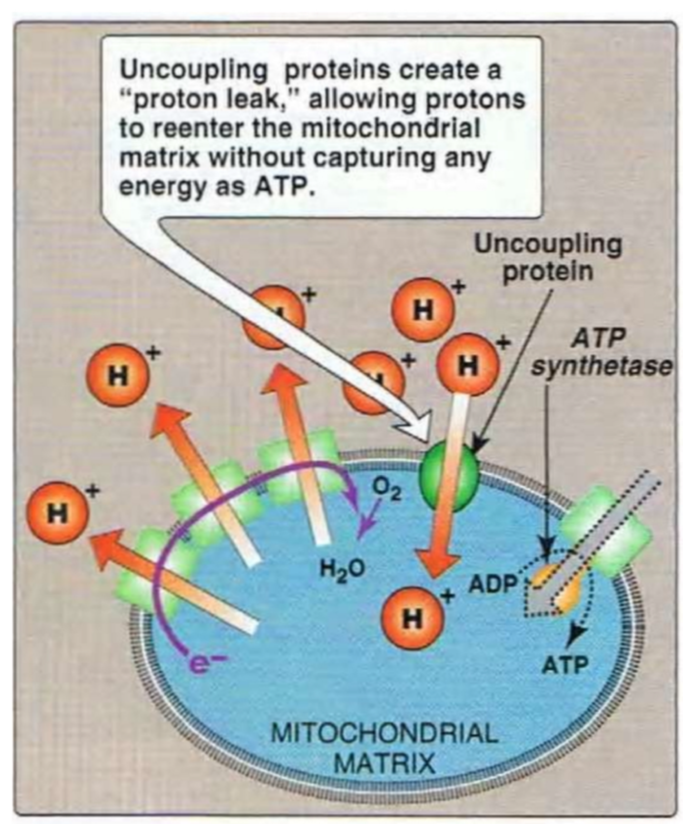
ATP synthase (ATPase)

- The enzyme complex ATP synthase synthesizes ATP, using the energy of the proton gradient generated by the electron transport chain.
- The chemiosmotic hypothesis proposes that after protons have been transferred to the cytosolic side of the inner mitochondrial membrane. they reenter the mitochondrial matrix by passing through a channel in the ATP synthase complex, resulting in the synthesis of ATP from ADP + Pi and, at the same time, dissipating the pH and electrical gradients.
- Oligomycin binds to the stalk of ATP synthase, closing the H channel, and preventing reentry of protons into the mitochondrial matrix leading to stop in electron transport
- Electron transport and phosphorylation are tightly coupled processes and inhibition of phosphorylation inhibits oxidation.

Uncouplers of oxidative phosphorylation

- Are substance that inhibit the oxidative phosphorylation by ETC.
- They dissociate oxidation from phosphorylation
- The oxidation of hydrogen with O_2 to form water proceed while there is no conversion of ADP to ATP
- The free energy librated during reaction is librated as heat leading to increase in body temperature.
- Billirubin, high Ca level, hyperthyroidism, toxins from bacteria, some drugs (warfarin, aspirin) and 2,4-dinitrophenol.

حرارتهم مرتفعة
لانه ما بحول ADP الى ATP

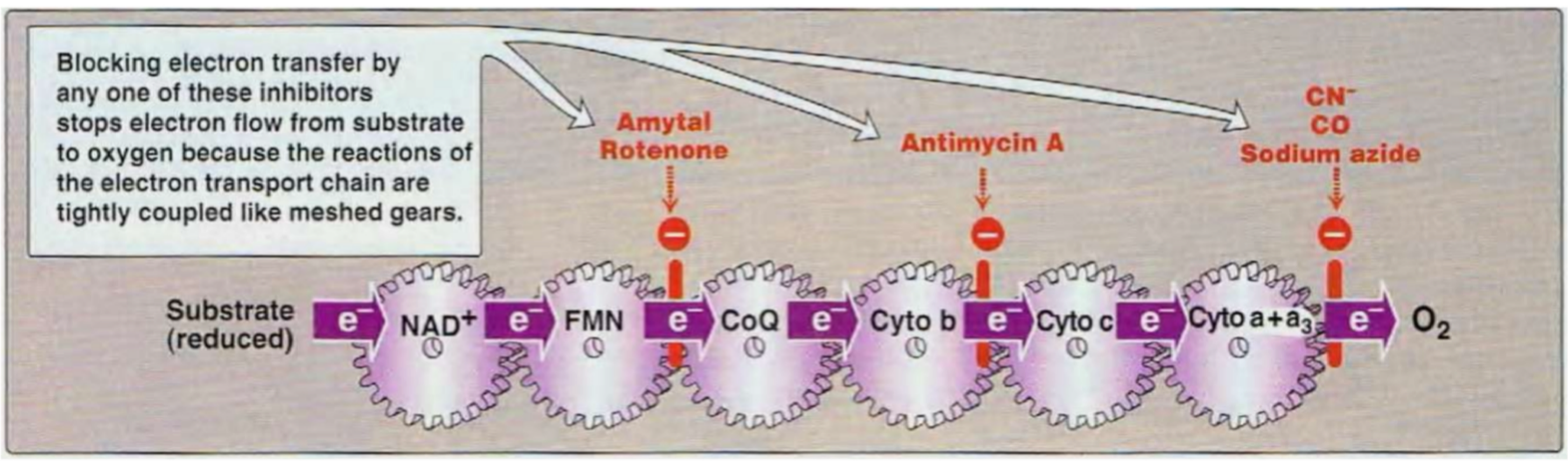


ادوية بتعمل للETC inhibition

Drugs that inhibit ETC

- CO, CN-, sodium azide inhibit the cytochrome oxidase which is fatal
- Rotenone used insecticide
- Amytal as hypnotic
- Antimycin A as antibiotic

- بشتغلوا عالcytochrome oxidase enzyme اللي بنقل الالكترونات للoxygen
- فبعملو inhibition للcytochrome oxidase وما بنقل الكترونات ، ما في استهلاك للاكسجين فما في تنفس للخلية وما في انتاج ATP فالنتيجة موت هاي الخلايا ويؤدي وفاة



Summary