BIOENERGETICS

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Definition

- Bioenergetics or biochemical thermodynamics is the study of energy changes accompanying biochemical reactions or in biological system.

Laws of thermodynamics

- First law
- The Total energy of a system is constant , including its surroundings.

Second law

Total entropy of a system must increase for a spontaneous reaction to occur.

Eg: no energy is required to drop the things scattered

But energy is required for arranging the things from a scattered status.

Free energy change (Useful energy)

- Gibbs change in free energy (ΔG)is that portion of the total energy change in a system available for doing work. It is also known as the chemical potential .
- $\Delta G = \Delta H - T \Delta S$.
- Useful energy = change in Enthalpy – change in entropy
- Enthalpy – energy content
- Entropy - Randomness of the system

Types of reactions

- Exergonic is a spontaneous reaction that releases energy. If the free energy change is negative ,this reaction is due to loss of energy from reactants, so it is called exergonic.

  E.g. catabolic reactions.
- Endergonic is an anabolic reaction that consumes energy. If the free energy change is positive, the reaction is called endergonic. E.g. synthetic reactions,
- But at equilibrium, it is zero
- The energy coupling occurs by coupling of Exergonic and endergonic reactions and liberation of heat.

Energy currency of the cell

- ATP is the primary and universal carrier of chemical energy in the cell .

  Terminal (alpha) phosphate group of ATP on hydrolysis yields   - 7.3 kcl/mol
- ATP $\rightarrow$ ADP + Pi
- -7.3 kcal/mol

High energy Phosphates P

- The phosphate compounds whose ΔG values higher than that of ATP, they are called high energy Phosphates
- Eg. Phosphoenol pyruvate,creatine phosphate

- The phosphates whose ΔG values lower than that of ATP are low energy Compounds
- Eg. ADP ,Glucose 1-phosphate

Phosphagens

- They are storage forms of high energy phosphates.
- Eg: Creatine phosphate in vertebrate muscle
- Arginine phosphate in invertebrate muscle

- ATP + Creatine $\leftrightarrow$ ADP + Creatine phosphate

Adenylyl kinase(Myokinase)

- 2 ADP ⟷ AMP + ATP
- When ATP is depleted ,

  AMP acts a metabolic signal (Allosteric)

  to increase catabolic pathways

ADP can be formed from AMP by this reaction

Nucleoside diphosphate kinase

- ATP + UDP $\leftrightarrow$ ADP + UTP

- By this reaction nucleoside diphosphates can form corresponding triphosphates.

- Oxidation : it is defined as the removal of electrons
- Reduction : it is defined as the addition of electrons
- Eg. Fe^{++} is oxidized to Fe^{+++} **e^- removed**
- Fe^{+++} is reduced to Fe^{++} **e^- added**
- The affinity of an oxidation reduction system for electrons is referred to as oxidation – reduction potential (or) redox potential

Redox couple

- A biological system which has a strong tendency to donate electrons has a negative redox potential
- The redox potential of a system is usually compared against the potential of hydrogen electrode at pH 7. 0 with -0.42 volt in biological system.
- Eg. Redox potential   redox system (redox pair)
- -0.32   NADH/NAD+
- + 0.82 H_2 / ½ O2
- The electrons flow from electro negative redox couple to more electro positive system

Oxidoreductases

Oxidation that occurs in biological system is called biological oxidation

- Enzymes involved in oxidation and reduction reactions are called oxido reductases. There are four groups of oxidoreductases
- 1.Oxidases 2.Dehydrogenases 3.Hydroperoxidases 4.Oxygenases

Oxidases

- They use oxygen as hydrogen acceptor
- e.g. cytochrome oxidase (cyt aa3) (copper containing) -Water forming
- H_2O_2 **forming**
- D amino acid oxidase (FAD linked)
- L amino acid oxidase (FMN linked)
- Xanthine oxidase (molybdenum containing)
- Aldehyde dehydrogenase (FAD-linked)

Dehydrogeneases

- Involved in transfer of hydrogen from one substrate to other in a coupled oxidation reduction reactions
- e.g. Nicotinamide coenzymes. NAD is involved in oxidation reactions
- NADP is involved in reductive synthesis. Riboflavin coenzymes : FMN & FAD
- Cytochromes except cytochrome oxidase

Hydroperoxidases

- They use hydrogen peroxide or an organic peroxide as substrate
- e.g. catalase and peroxidases (glutathione peroxidase containing selenium)
- Peroxisomes are rich in these enzymes
- $H_2O_2 + H_2O_2 \xleftrightarrow{\text{catalase}} 2\ H_2O$

Oxygenases

They catalyze the direct transfer and incorporation of oxygen into a substrate molecule

- ***Dioxygenases***

  incorporate both atoms of oxygen molecule into the substrate

  e.g. homogentisate dioxygenase (oxidase) $A+O2 \rightarrow AO_2$ tryptophan dioxygenase (pyrrolase)

- ***Monooxygenases*** or mixed function oxidases

  incorporate only one atom of molecular oxygen into the substrate

  e.g. cytochrome P450 – hydroxylation of steroids

  cytochrome b5 helps to increase the solubility of compounds

  and so promoting excretion

SOD

- Superoxide dismutase protects aerobic organisms against oxygen toxicity due to superoxide anion free radical ($O^{-2.}$)
- $O_2^{\cdot -} + O_2^{\cdot -} + 2H^+ \longrightarrow H_2O_2 + O_2$
- Catalase removes H_2O_2

Oxidative phosphorylation

- It is the process by which free energy liberated when protons are pumped by respiratory chain is trapped in the form of ATP *by **phosphorylation** of ADP with phosphate.*
- The process of oxidation coupled with phosphorylation is called oxidative phosphorylation and it occurs in the mitochondria.

- Most of the energy liberated during the oxidation of carbohydrate, fatty acids and amino acids is made available within mitochondria as reducing equivalents (-H or electrons)
- Reducing equivalents (Hydrogen or Electrons) thus obtained is oxidized by oxygen forming water and the energy liberated is used for ATP synthesis.
- Mitochondrial inner membrane contains the respiratory or electron transport chain that collects and transports reducing equivalents.

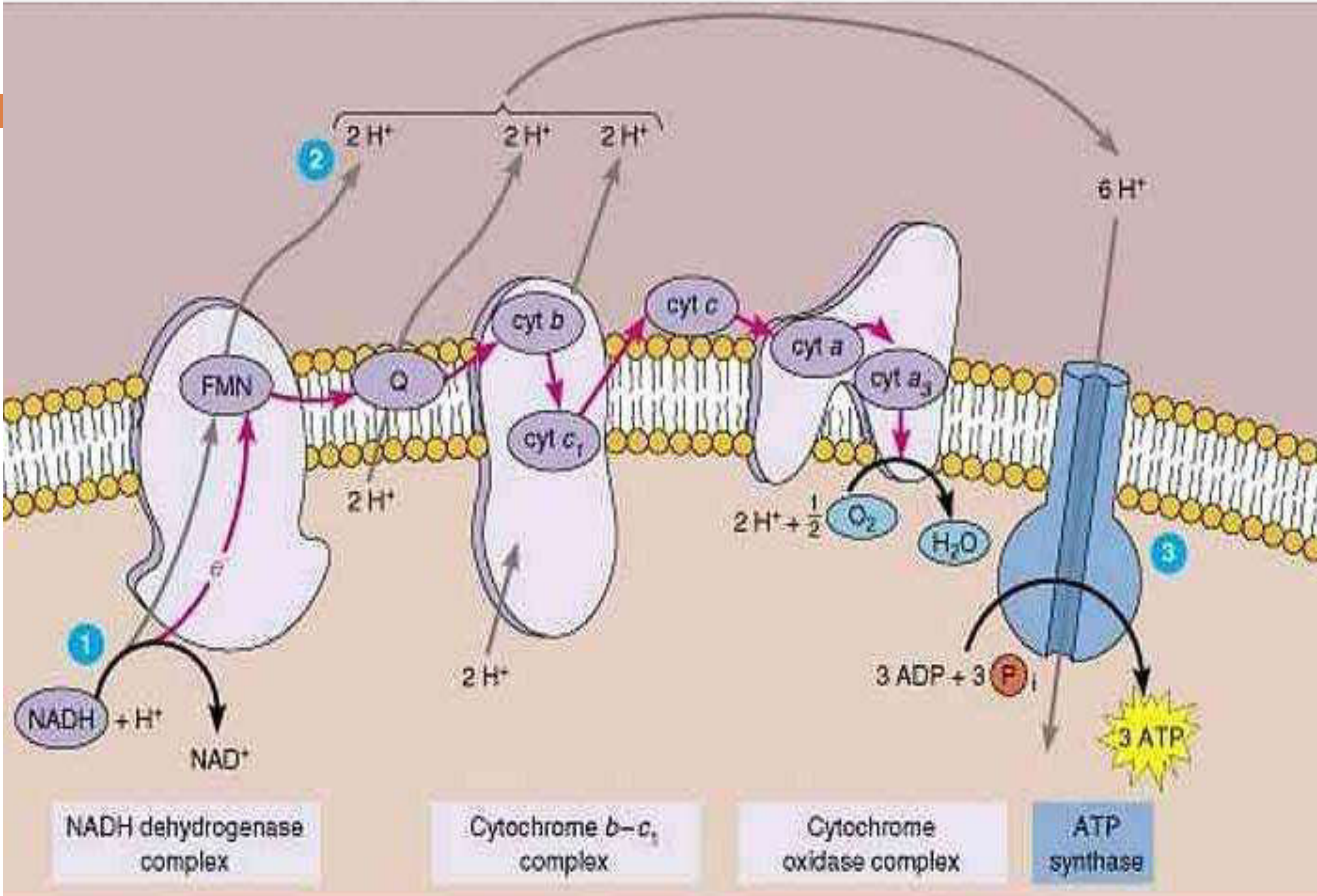
Respiratory chain

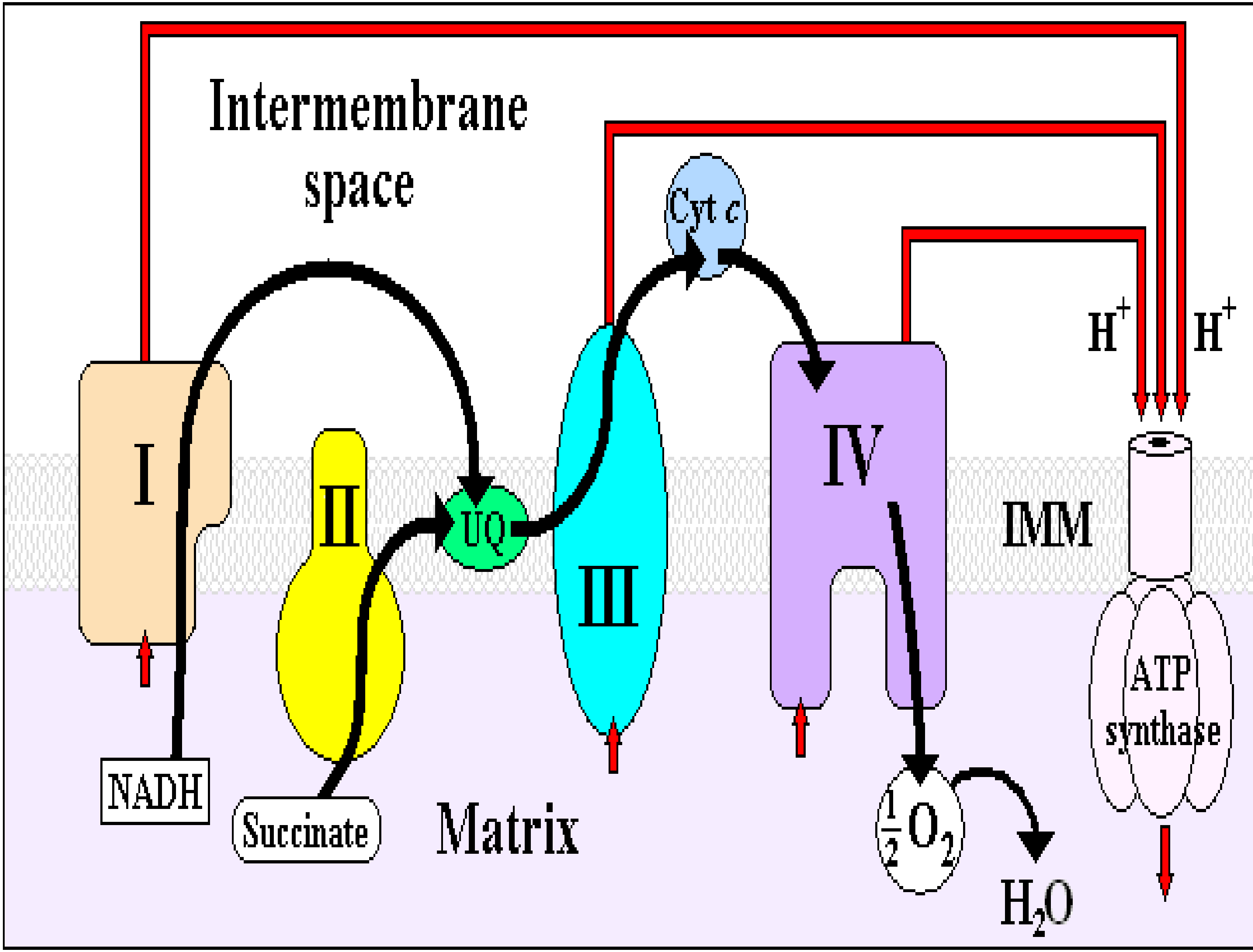
- The components of respiratory chain are arranged in order of increasing redox potential.
- ie . from NAD+ / NADH to O_2/H_2O redox couples

Components of respiratory chain

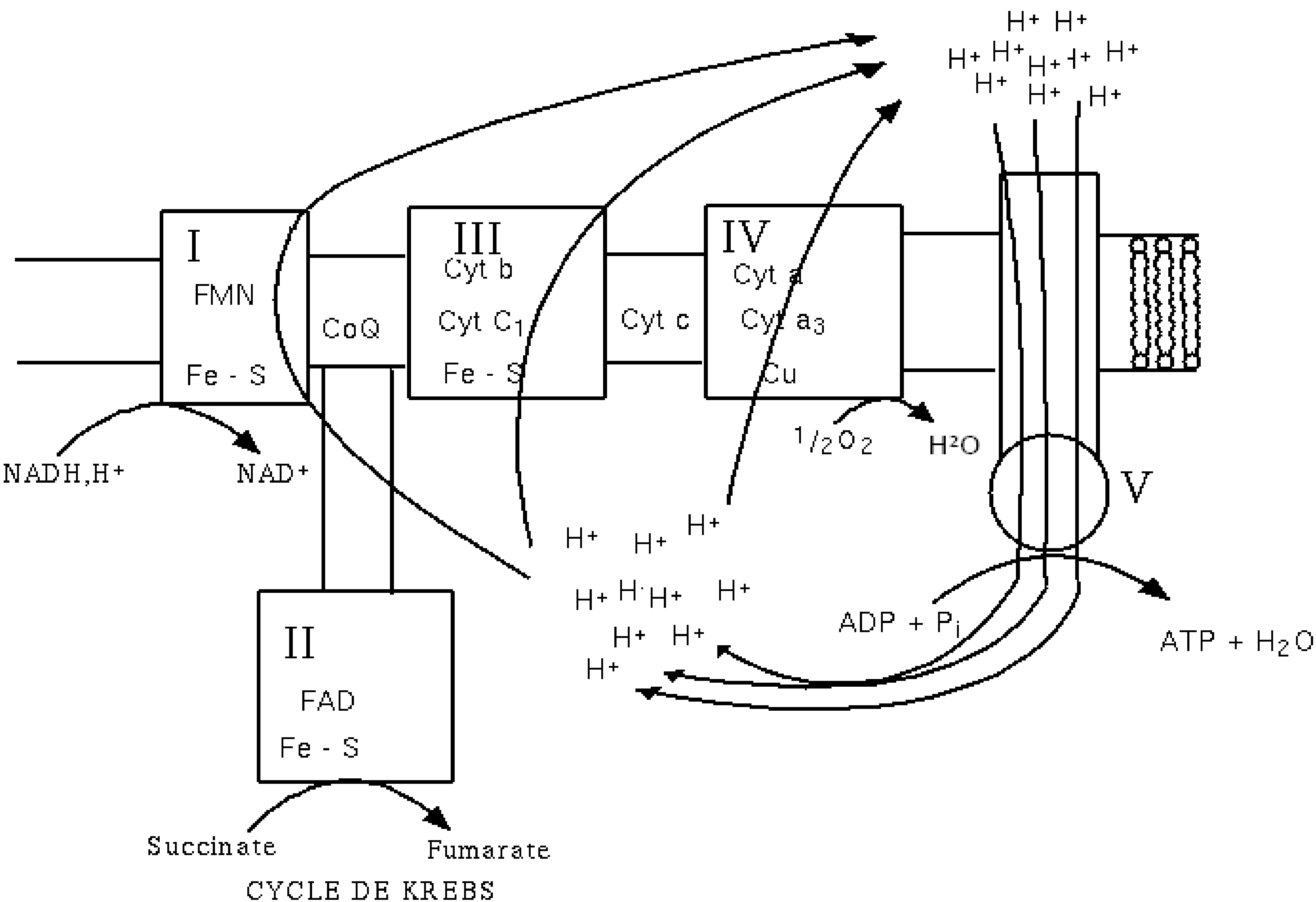
- Complex I : NADH : ubiquinone oxidoreductase
- Complex II : succinate : ubiquinone oxidoreductase
- Complex III : Ubiquinol : cytochrome C oxidoreductase
- Complex IV : cytochrome aa3: oxygen oxidoreductase

ELECTRON TRANSPORT CHAIN





Intermembrane space
Cyt c
H+
H+
I
II
UQ
III
IV
IMM
ATP synthase
NADH
Succinate
Matrix
1/2 O2
H2O



H+ H+
H+ H+ H+ H+ H+
H+ H+ H+
I
FMN
Fe - S
CoQ
III
Cyt b
Cyt C1
Fe - S
Cyt c
IV
Cyt a
Cyt a3
Cu
1/2 O2
H²O
V
NADH,H+
NAD+
H+ H+ H+
H+ H H+ H+
H+ H+
H+
ADP + Pi
ATP + H2O
II
FAD
Fe - S
Succinate
Fumarate
CYCLE DE KREBS

- Iron sulphur centers (Fe-S) form prosthetic groups of iron sulphur proteins
- Non heme proteins also function in the transfer of electrons eg from $FMNH_2$ to Coenzyme Q and cytochrome b to cytochrome c_1.
- Coenzyme Q_{10} is a fat soluble quinone compound
- Cytochromes b,c,c_1, aa_3 contain haem
- Cytochromes aa3 also contains copper
- ATP synthetase is involved in the formation of ATP

Mitchell's chemiosomotic hypothesis

- Electron transport chain pumps protons into inter membrane space across the inner membrane which is normally not permeable to protons. This creates an electro chemical potential gradient. Now the protons (H+) flow back across inner membrane through ATP synthetase resulting in trapping of free energy as ATP

P:O ratio

- It is the number of high energy phosphates produced per atom of oxygen used.
- ie : for $NADH+H^+$ - 2.5 ATP
- for $FADH_2$ – 1.5 ATP
- ***Respiratory control:***
- In the presence of adequate O_2 and substrate, ADP becomes rate limiting.

Inhibitors of electron transport chain:

- Complex I is inhibited by rotenone, amobarbital & piercidin A
- Complex III is inhibited by antimycin A, dimercaprol
- Complex IV is inhibited by cyanide, hydrogen sulphide, carbon monoxide, sodium azide

Uncouplers of oxidative phosphorylation

- Uncouplers are the substances that allow electron transport chain to function without phosphorylation and so ATP is not synthesized but oxidation proceeds. They are lipophilic and allow transport of H^+ across the inner membrane but not through ATP synthetase and so the proton gradient is cancelled without ATP formation and the free energy is liberated as heat.

  e.g 2.4 dinitrophenol

  thermogenin (natural) – uncoupling protein

  Thyroxine

1.The adenine nucleotide transporter.

ADP and ATP

2. The phosphate transporter.

- Exchange of $H_2PO_4^-$ for OH^-, or cotransport of $H_2PO_4^-$ with H^+. Transport of reducing equivalents across the mitochondrial membrane from cytosol is mediated by two important shuttles
- 1.Malate - Aspartate shuttle - 2.5 ATP
- 2.Flavoprotein dehydrogenase -Glycerol 3 P shuttle- electrons to E.T.chain – 1.5 ATP

Substrate level phosphorylation

- The formation of ATP within certain steps of metabolic pathway i.e susbstrate level without passing through ETC is called as substrate level phosphorylation
- e.g. pyruvate kinase, phosphoglycerate kinase , succinate thiokinase

Mitochondrial diseases

1.MELAS(Mitochondrial encephalopathy,lactic acidosis ,stroke due to Complex I deficiency

2.Fatal infantile mitochondrial myopathy and renal dysfunction

3.Leber’s hereditary optic neuropathy

4. Alzheimer’s disease

5. Parkinsons’ disease

6.Diabetes mellitus

Thank You