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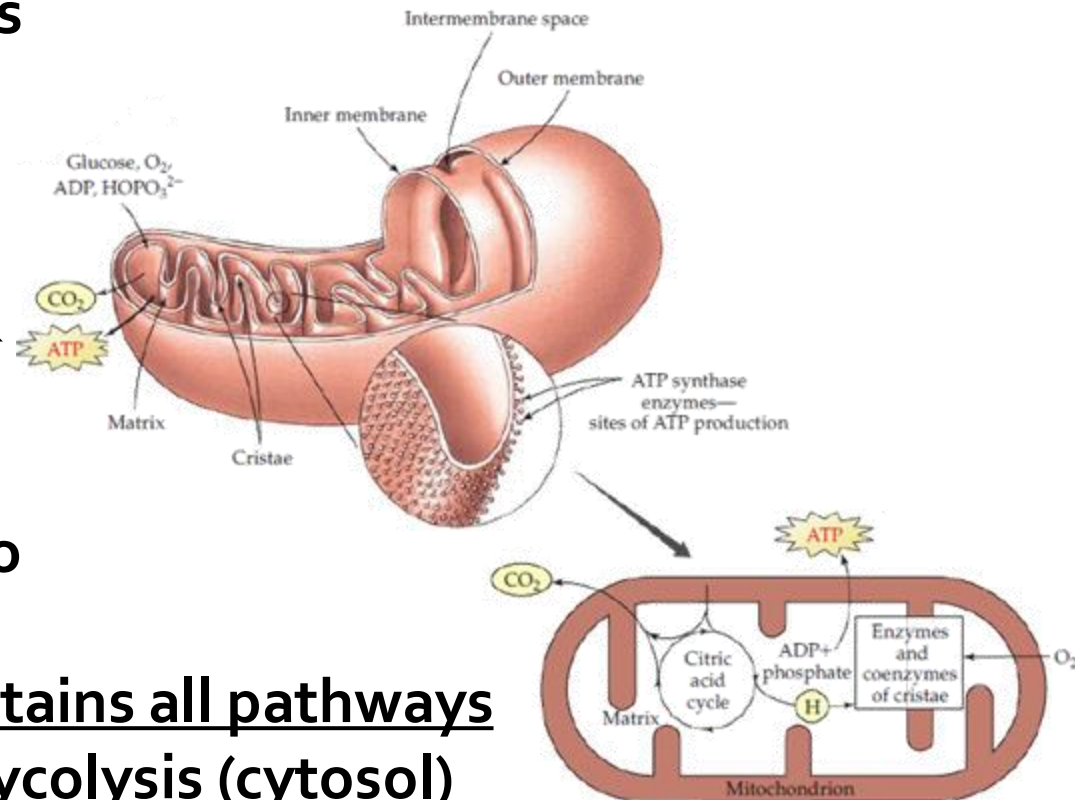
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Oxidative Phosphorylation

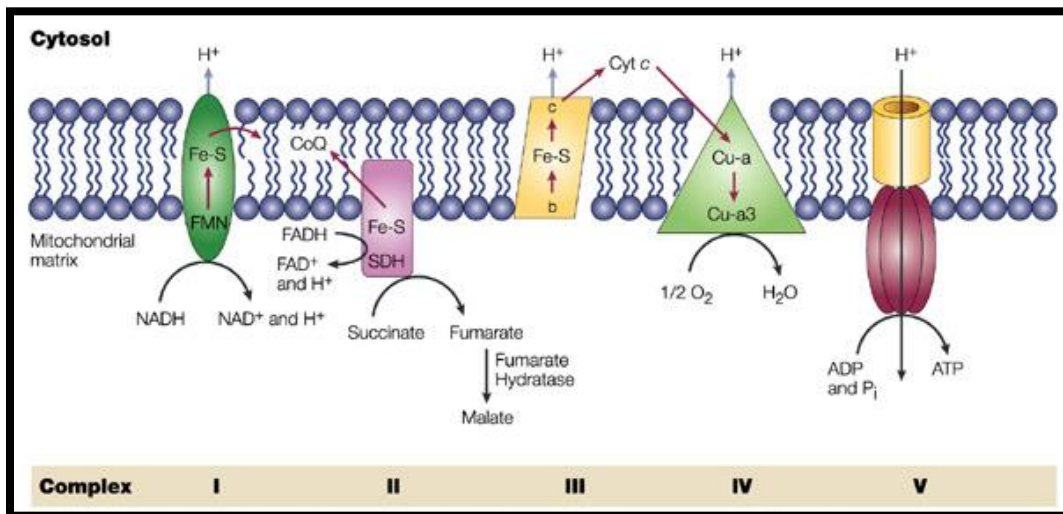
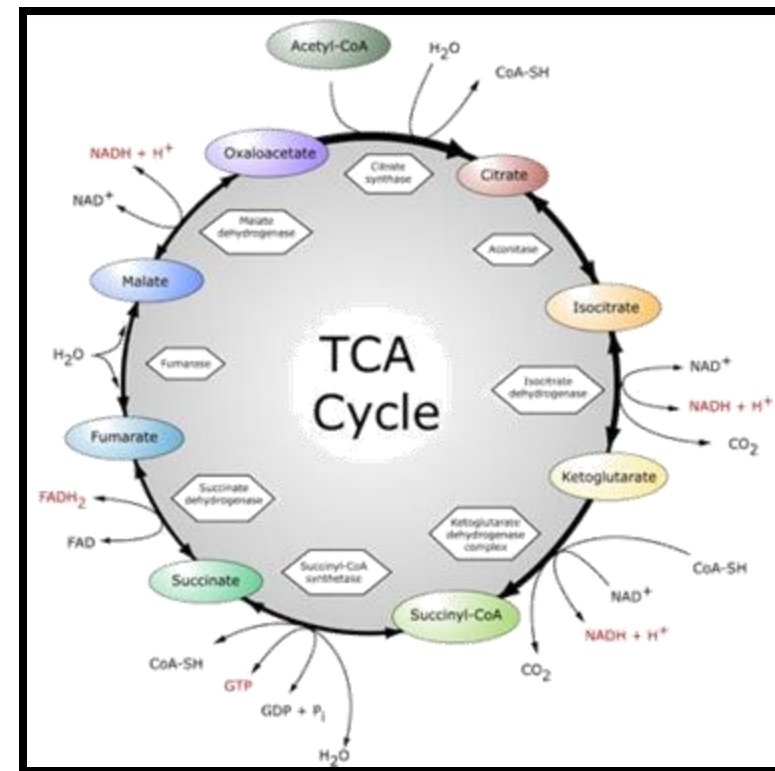
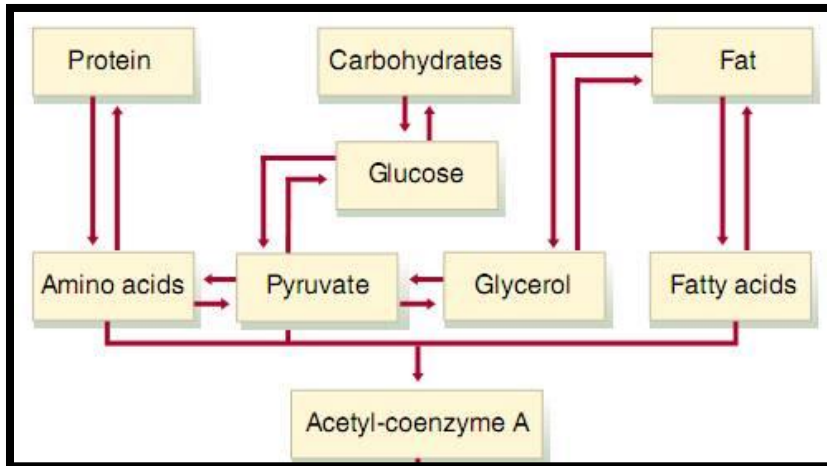
The Mitochondria

- OMM: permeable to small molecules (**MW<5,000**) & ions, porins (transmembrane channels)
- IMM: impermeable even to H^+ ; specific transporters
- IMM bears the components of the respiratory chain and the ATP synthase
- Matrix: contains pyruvate dehydrogenase complex & TCA cycle enzymes, fatty acid β -oxidation pathway, and the pathways of amino acid oxidation
- In other words: matrix contains all pathways of fuel oxidation except glycolysis (cytosol)



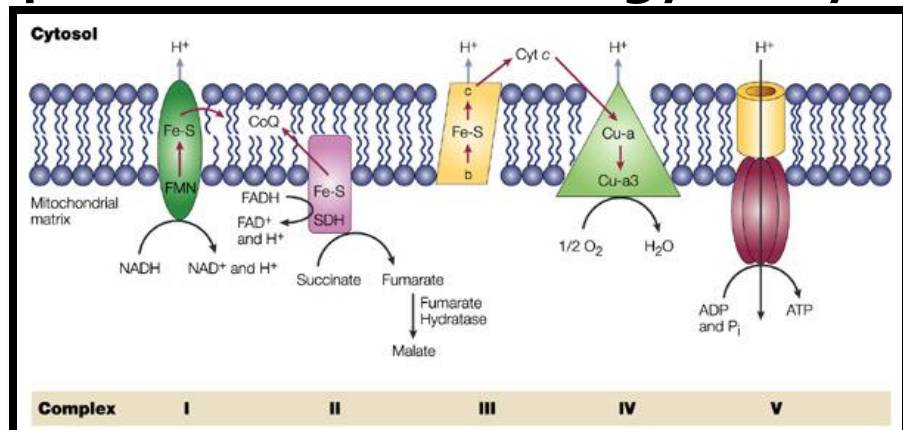
The oxidative phosphorylation, Where are we?

➤ Stages: Digestion; Acetyl-CoA, TCA, OxPhos

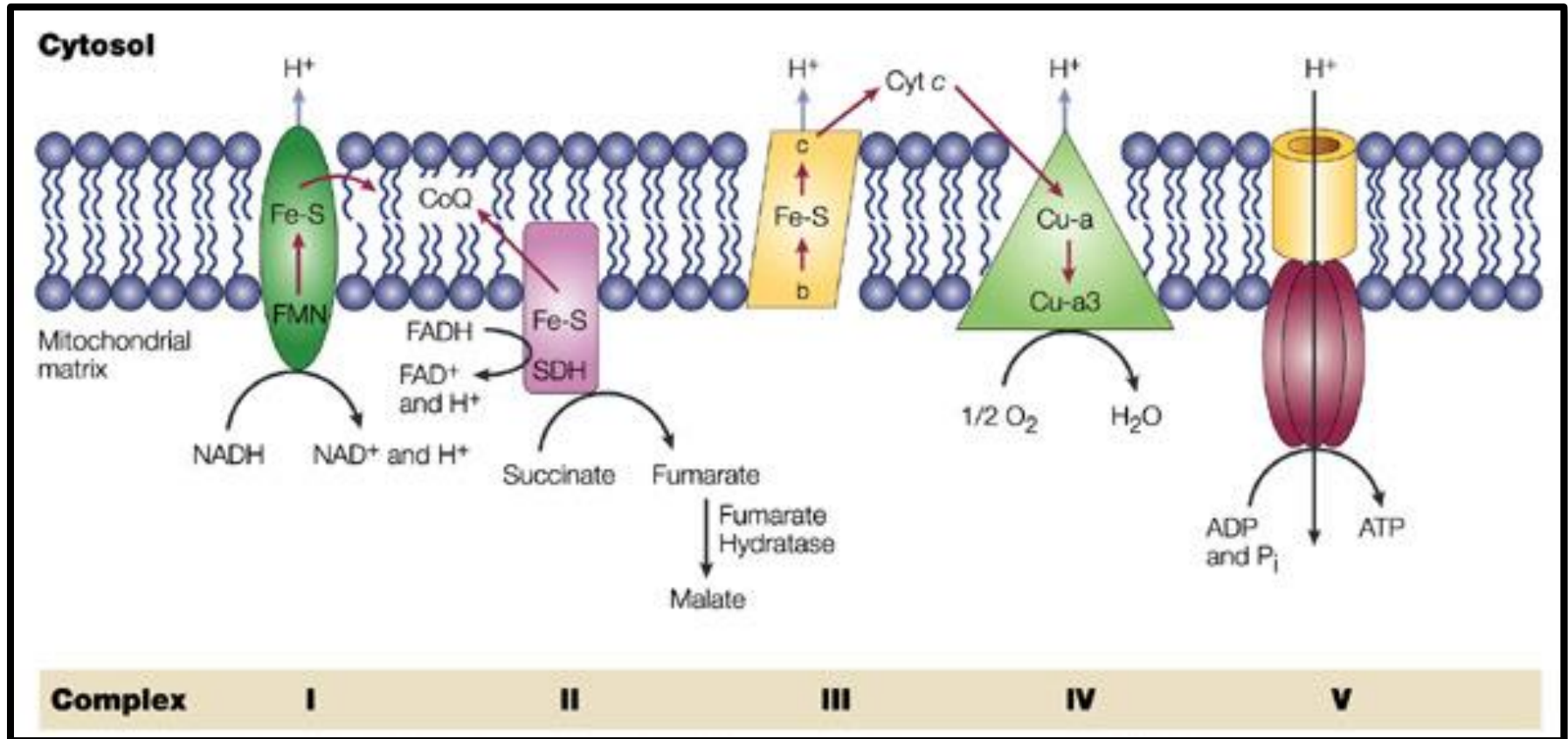


Oxidative phosphorylation (OxPhos)

- Generation of ATP aided by the reduction of O_2
- Peter Mitchell (1961): the chemiosmotic theory
- Oxidative phosphorylation have 3 major aspects:
 - ✓ (1) It involves flow of electrons through a chain of membrane-bound carriers (prosthetic groups)
 - ✓ (2) The free energy available (exergonic) is coupled to transport protons across a proton-impermeable membrane
 - ✓ (3) The transmembrane flow of protons down their concentration gradient provides the free energy for synthesis of ATP (ATP synthase)

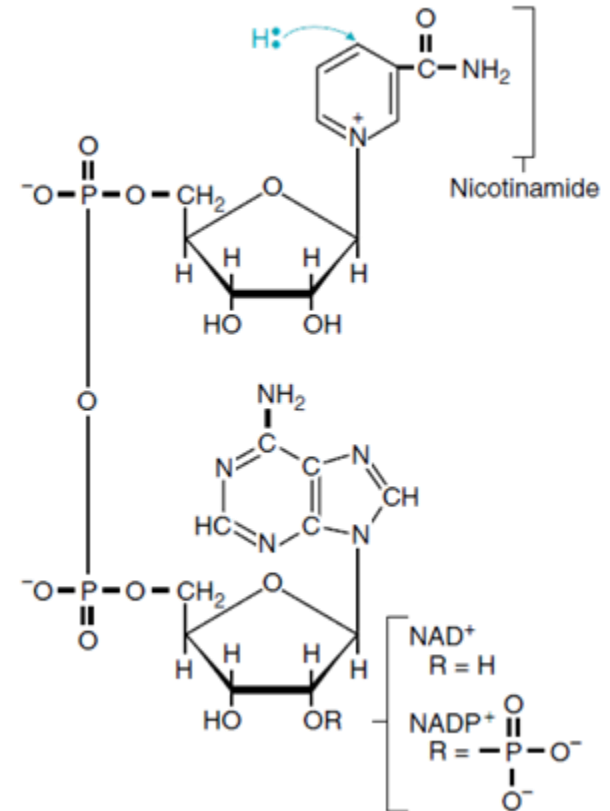
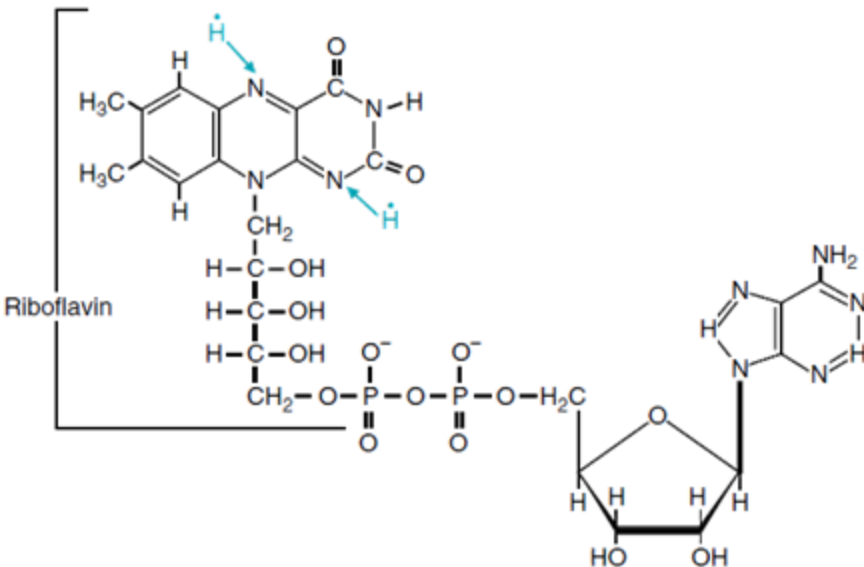
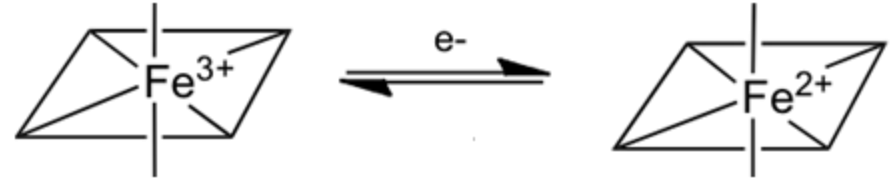


Oxidative phosphorylation (OxPhos)



Types of electron transfer (ET) through the electron transport chain (ETC)

- 3 types of ET occur in OxPhos:
 - ✓ Direct ET, as in the reduction of Fe^{+3} to Fe^{+2}
 - ✓ Transfer as a hydrogen atom $\{(\text{H}^+) + (\text{e}^-)\}$
 - ✓ Transfer as a hydride ion $(:\text{H}^-)$



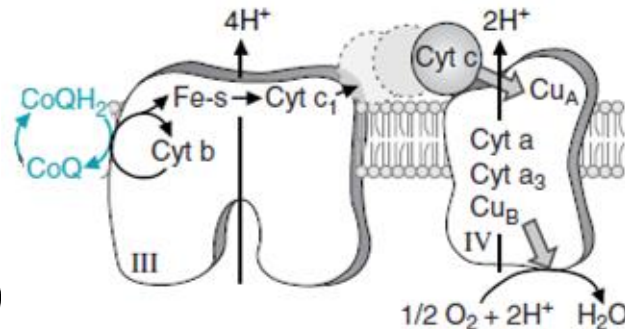
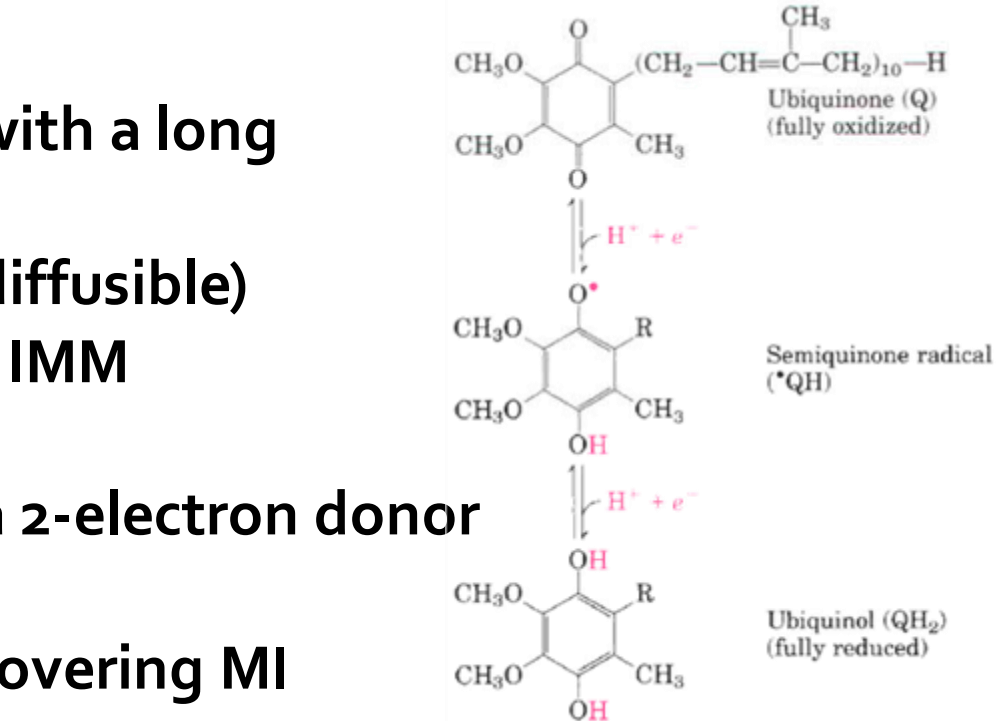
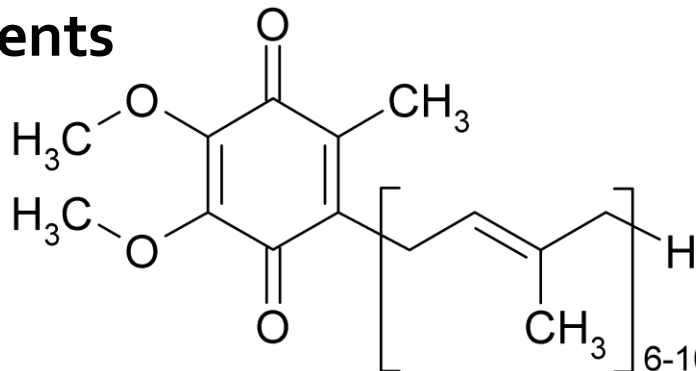
Electrons are funneled to a universal electron acceptors

COENZYME	AS OXIDIZING AGENT	AS REDUCING AGENT
Nicotinamide adenine dinucleotide	NAD^+	NADH/H^+
Nicotinamide adenine dinucleotide phosphate	NADP^+	NADPH/H^+
Flavin adenine dinucleotide	FAD	FADH_2
Flavin mononucleotide	FMN	FMNH_2

Other electron-carrying molecules

“Ubiquinone”

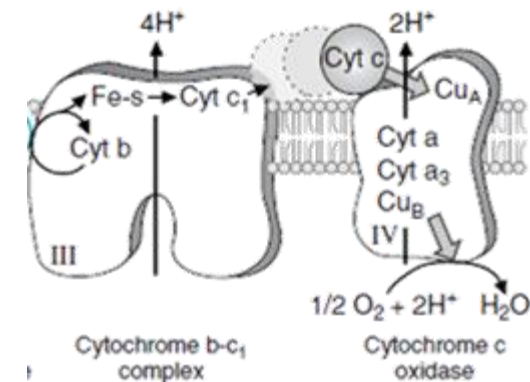
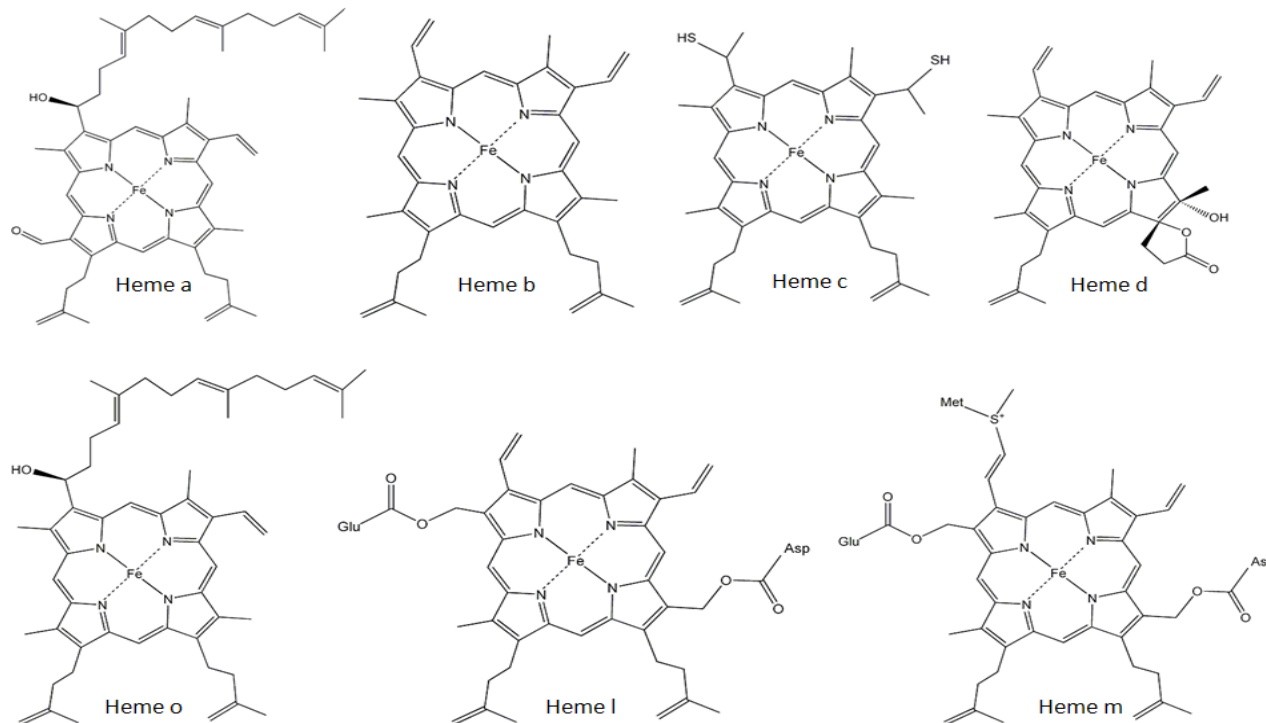
- Also called coenzyme Q, or Q
- Lipid-soluble benzoquinone with a long isoprenoid side chain
- Small & hydrophobic (freely diffusible)
- Carries electrons through the IMM
- Can accept either 1 e⁻ or 2 e⁻
- Act at the junction between a 2-electron donor and a 1-electron acceptor
- Sometimes prescribed for recovering MI patients



Other electron-carrying molecules

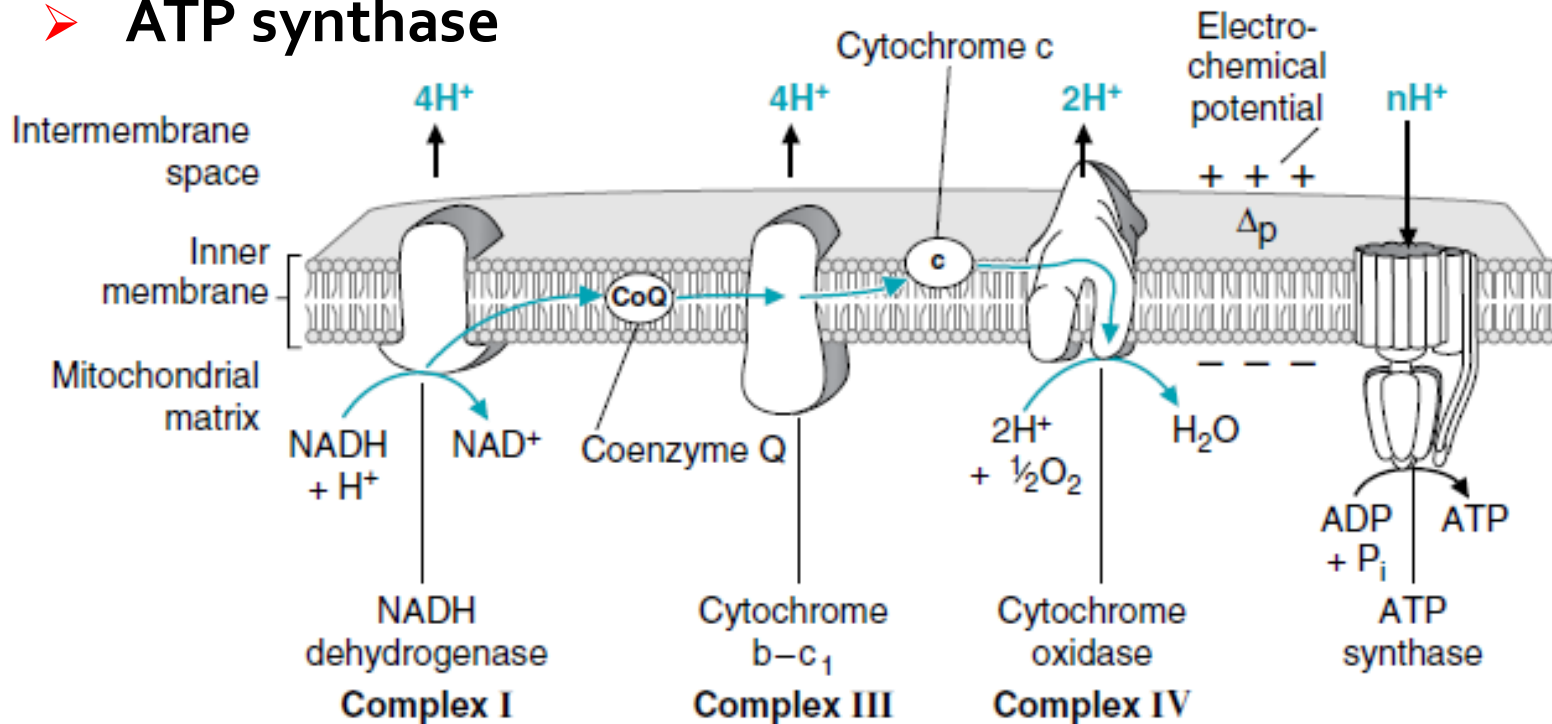
"Cytochromes"

- Proteins with characteristic strong absorption of visible light (Fe-containing heme prosthetic groups)
- Classification based on light absorption
- Mode of binding (a, b, c)
- Mitochondria contain three classes of cytochromes (a, b, & c)



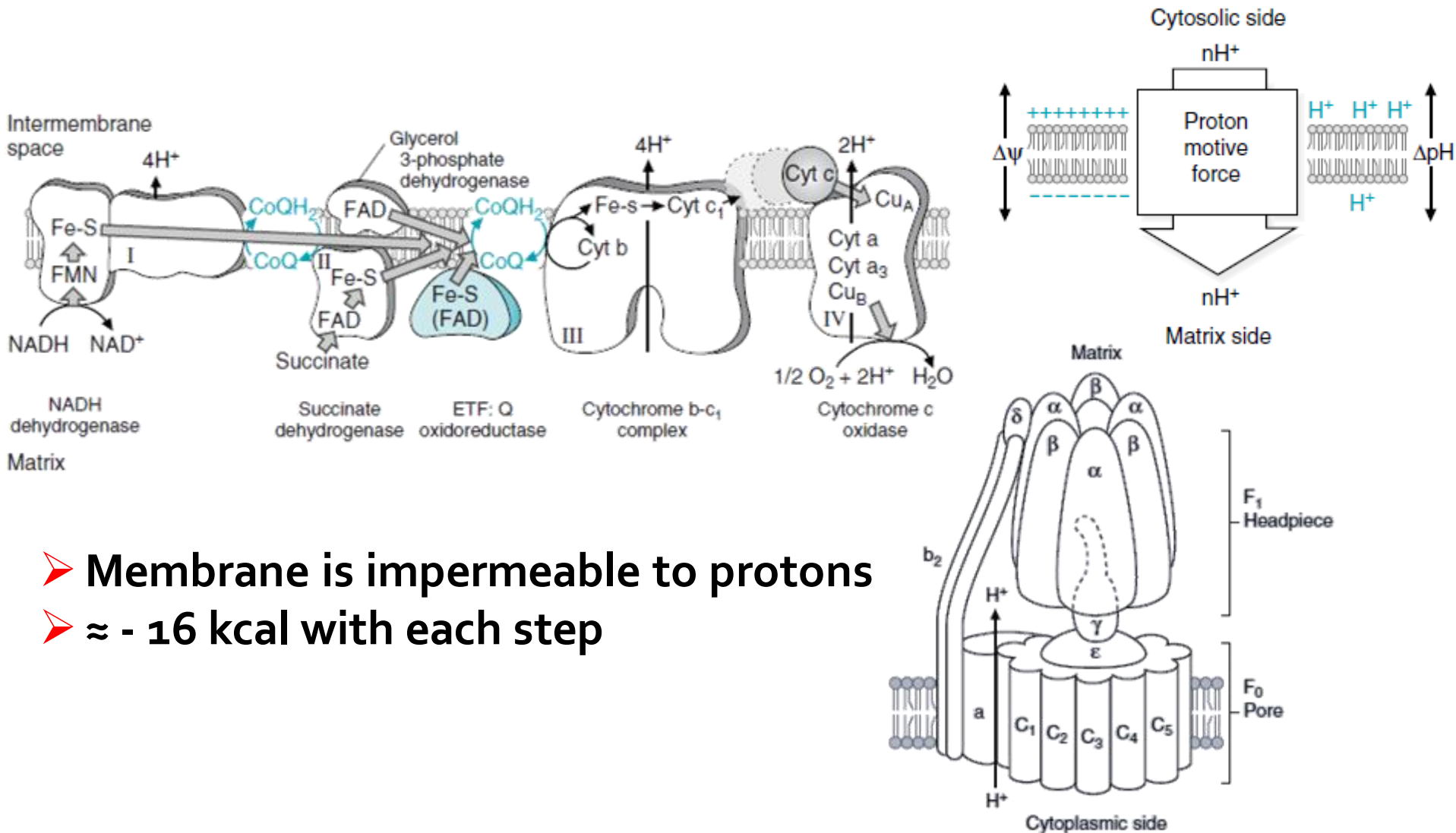
Requirements of OxPhos

- Redox reaction: electron donor (NADH or FADH₂) & electron acceptor (O₂)
- An intact IMM
- ETC of proteins
- ATP synthase



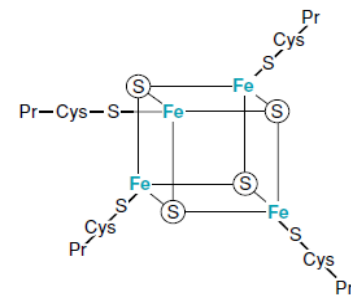
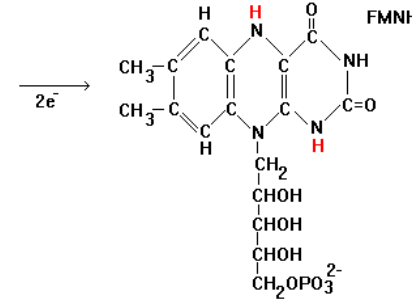
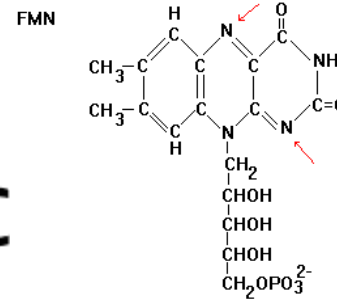
ET to O₂, how does the process occurs?

“The chemi-osmotic theory”



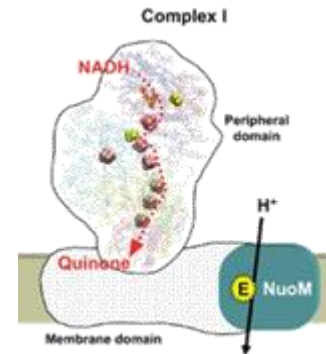
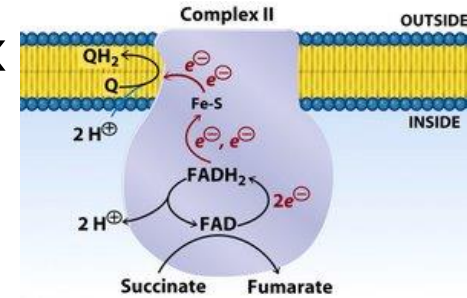
- Membrane is impermeable to protons
- ≈ - 16 kcal with each step

Oxi-Red Components of ETC



➤ "NADH Dehydrogenase" – Complex

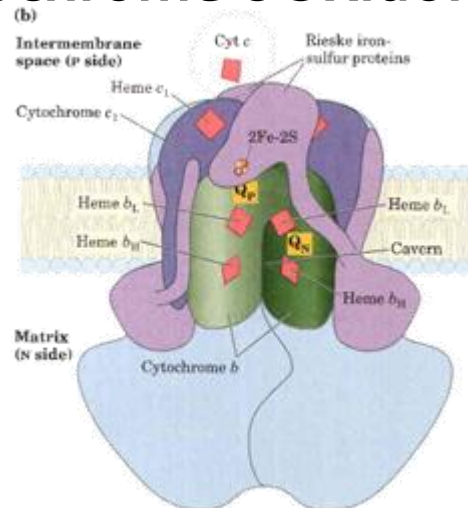
➤ NADH-Q oxidoreductase



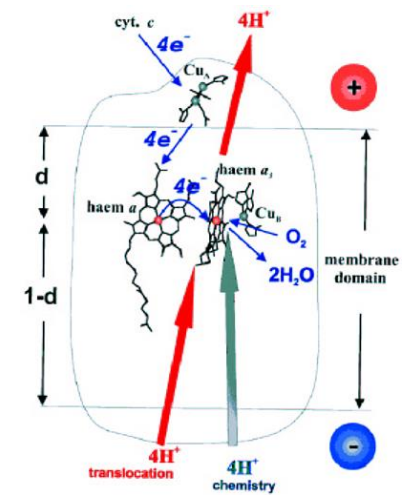
➤ "Succinate Dehydrogenase" – Complex II

➤ ≈ 0 kcal, H+?

➤ "Cytochrome bc₁" – Complex III
Q-cytochrome c Oxidoreductase

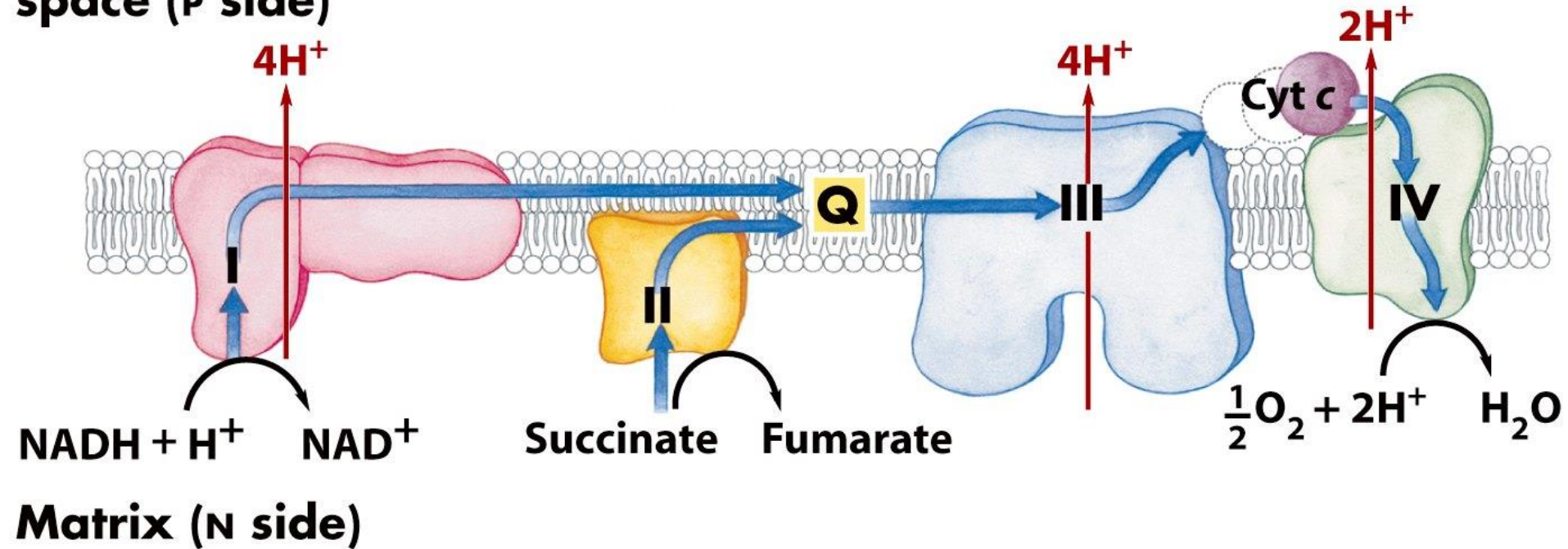


"Cytochrome c oxidase" – Complex IV



Pumping of Protons

Intermembrane
space (P side)

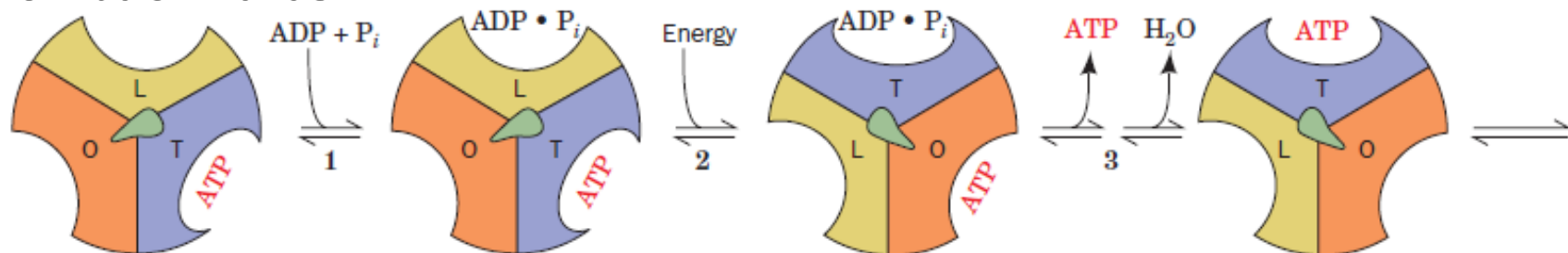
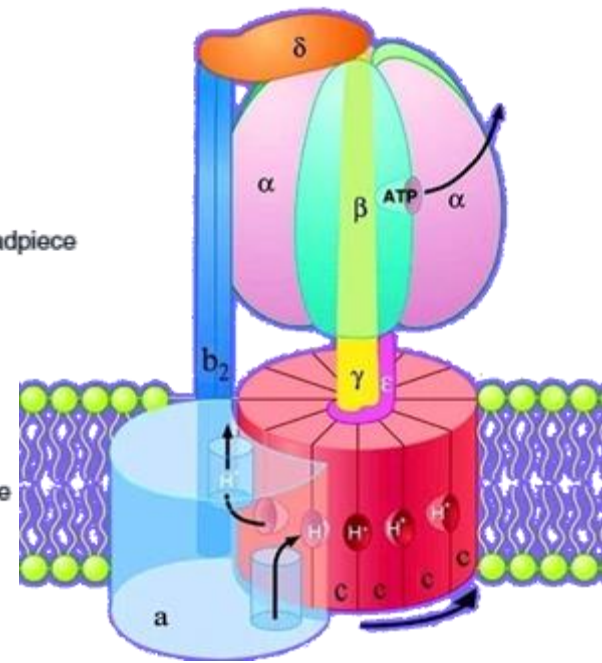
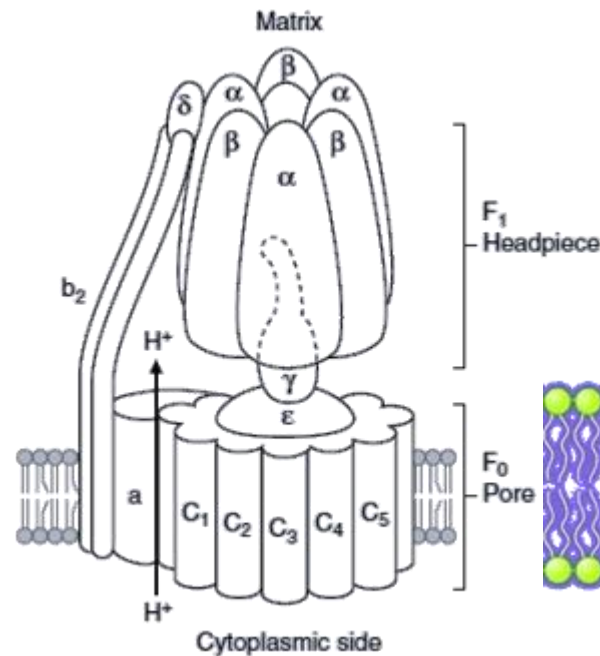


➤ For every 2 electrons passing:

➤ 4H^+ (complex I); 0H^+ (complex II); 4H^+ (complex III), 2H^+ (complex IV)

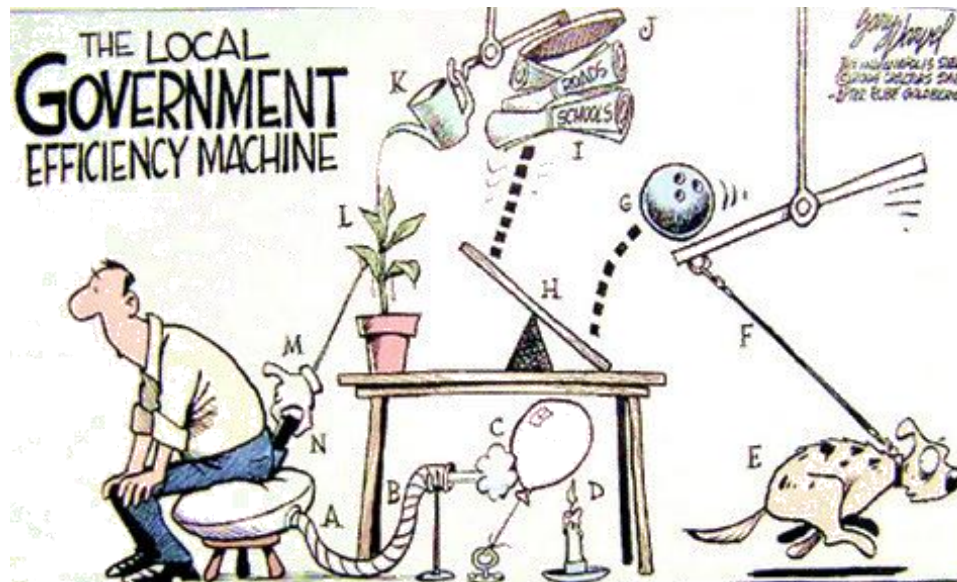
ATP Synthase

- **F₁:**
 - “γ” subunit: rotates
 - “β” subunit: binds
 - “α” subunit: structural
 - 3 conformations: tight (T), loose (L), open (O)
- **F₀:**
 - “a” subunit: point of entry & exit
 - “c” subunit rotates
 - 4H⁺/ATP
 - Can run backwards



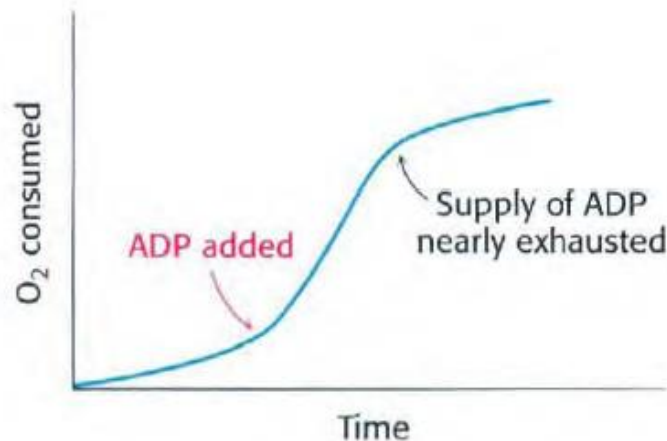
Energy yield from the ETC

- NADH, -53 kcal, ATP?
- FADH₂, -41 kcal, ATP?
- $\Delta G^{\circ'}$ is so negative, never reversible
- ATP machine efficiency, (anions, Ca⁺², heat, phosphate, substrates)
- Electron transport chain is our major source of heat



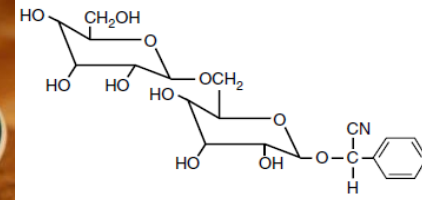
Regulation – the need for ATP

- What OxPhos needs? (NADH, O₂, ADP, and Pi)
- In skeletal muscles, 20% drop in ATP concentration
- In the heart, Ca⁺² activates TCA enzymes for extra push (NADH, ATP), no drop
- ET is tightly coupled to phosphorylation (simultaneously)
- ADP is the most important factor in determining the rate
- The regulation of the rate of oxidative phosphorylation by the ADP level is called respiratory control



Regulation – inhibition (coupling)

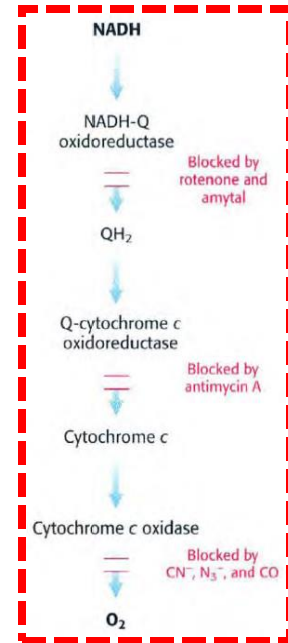
- Can occur at any stage
- Specific inhibitors:
 - ✓ Cyanoglycosides such as amygdalin are present in edible plant pits
 - ✓ Oligomycin prevents the influx of H^+ through ATP synthase (tight coupling)



Amygdalin, a cyanoglycoside

Anit-cancerous drug

Specific inhibitor	Target
Rotenone (insecticide) & Amytal (sedative)	NADH-Q oxidoreductase
Antimycin A (antibiotic)	Q-cytochrome c oxidoreductase
Cyanide (CN ⁻), Azide (N ₃ ⁻), & (CO)	Cytochrome c oxidase
Oligomycin (antibiotic)	ATP synthase



المسألة الرئيسية < محليات



أشهر جرائم القتل العائلية في المملكة

جرائم القتل العائلية

جرائم القتل العائلية - فيما يلي قائمة بأشهر جرائم القتل العائلية التي حدثت في الأردن خلال السنوات الماضية ، والتي كان لكل منها وقع الصدمة حين وقوعها لما تمثلته من فعل غريب على المجتمع وأعرافه ، فضلا عن مخالفتها الشرائع السماوية والقوانين النافذة والطبيعة الإنسانية بعامة.

قصة السباين

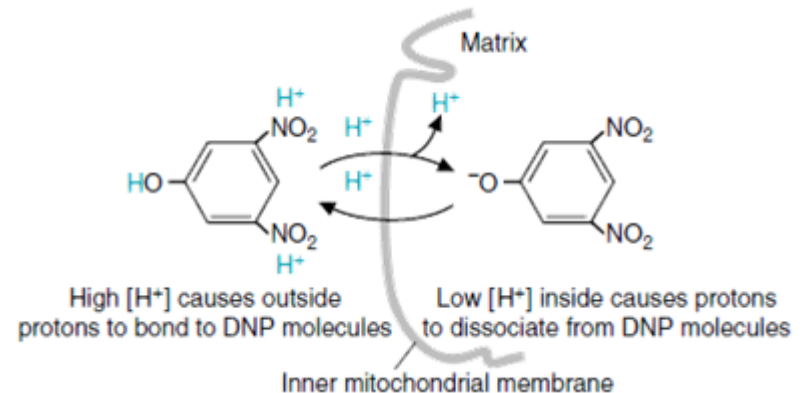
أول جريمة من نوعها برتكها أب ضد ولديه ، إذ قام الأب بوضع مادة السباين في كأس الحليب وطلب من طفليه أن يشربا منه ، حيث فارقا الحياة بعد 10 دقائق من مغادرة الام المنزل ليعود وتجدهما جثتين هامدين.

وقد ادّين الأب بعقوبة الاعدام شنقا الا ان والده اسقط الحق الشخصي كونه وليا عن الطفلين وحكم عليه بالاشغال المؤبدة.

Regulation – Uncoupling

Unregulated – chemical uncouplers

- What is uncoupling?
- How does it occur? Dissipation of PMF
- What is the result?
- Is it physiological or not?
- 2,4-dinitrophenol (DNP) & other acidic aromatic compounds
- What changes happen? \uparrow O_2 consumption, \uparrow NADH oxidation
- Soviet soldiers were given DNP, FDA banned DNP (1938)



Regulation – Uncoupling

Regulated - Uncoupling proteins (UCPs)

- Short-circuiting ATP synthase
- UCP₁ (thermogenin):
 - ✓ Brown adipose tissue, non-shivering thermogenesis
 - ✓ Infants: neck, breast, around kidneys
 - ✓ Fatty acids directly activates UCP₁
- UCP₂ (most cells); UCP₃ (skeletal muscle); {UCP₄, UCP₅} (brain)
- Obesity tendency in some populations

