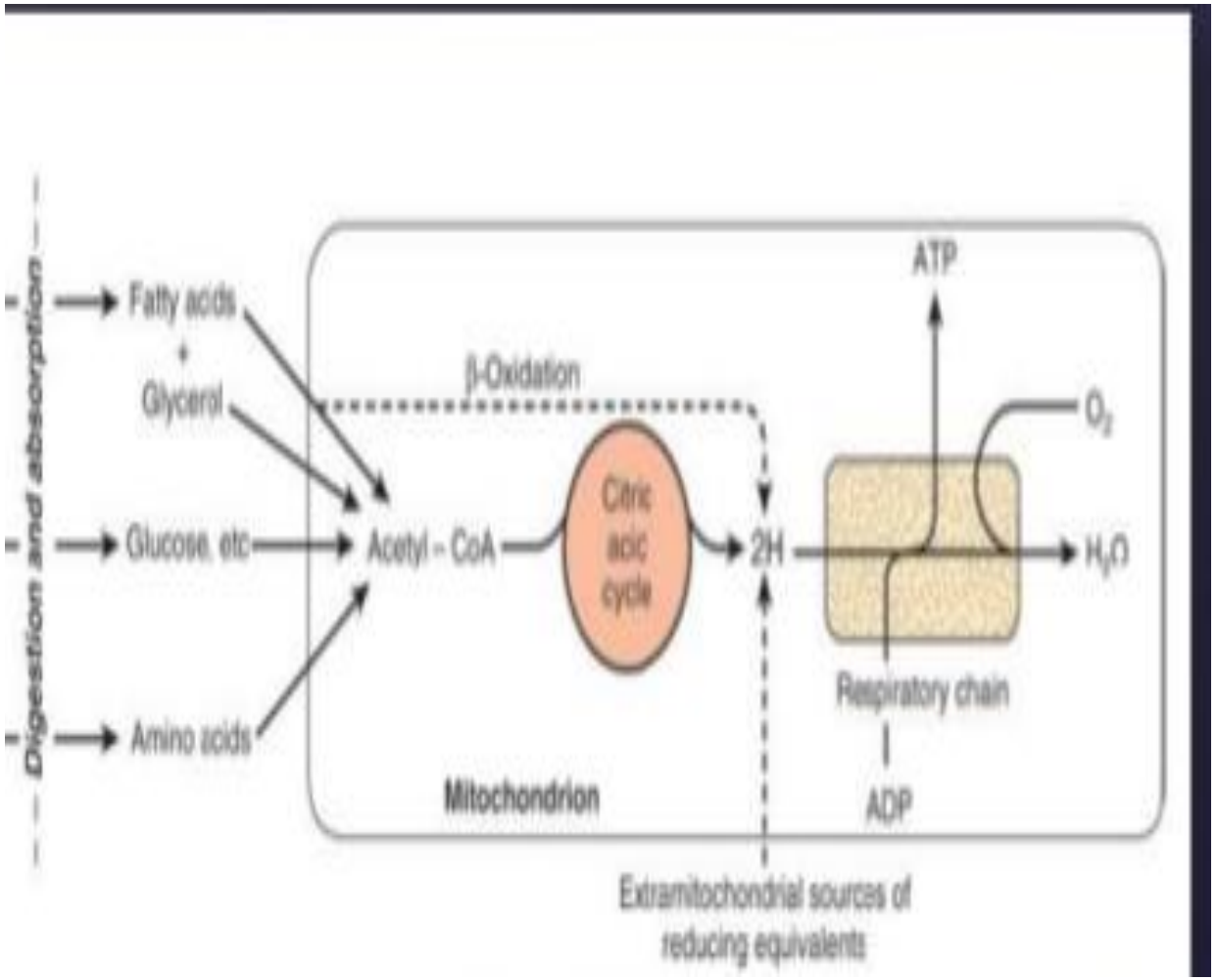
The Respiratory Chain & Oxidative Phosphorylation.



Learning Objectives :

- Define biological oxidation.
- Describe the sources of NADH & $FADH_2$
- Role of Anaerobic Dehydrogenases.
- Enumerate different parts of enzymes & coenzymes that carryout biological oxidation.
- Enlist components of each complex involved in the biological oxidation.
- Describe the transfer of electrons through each complex.

- Describe the transfer of protons from inter mitochondrial membrane to mitochondrial matrix through ATP synthase (Generation of Proton gradient).

- Describe the mechanism of ATP production by ATP synthase (CHEMIOSMOTIC THEORY)

Biological Oxidation and Oxidative Phosphorylation

- The Transfer of Electrons from the reduced Co-enzymes through the respiratory chain to oxygen is known as Biological oxidation.

- Energy released during this process is Trapped as ATP (ADP ATP)
- This coupling of oxidation with phosphorylation is called oxidative phosphorylation. 

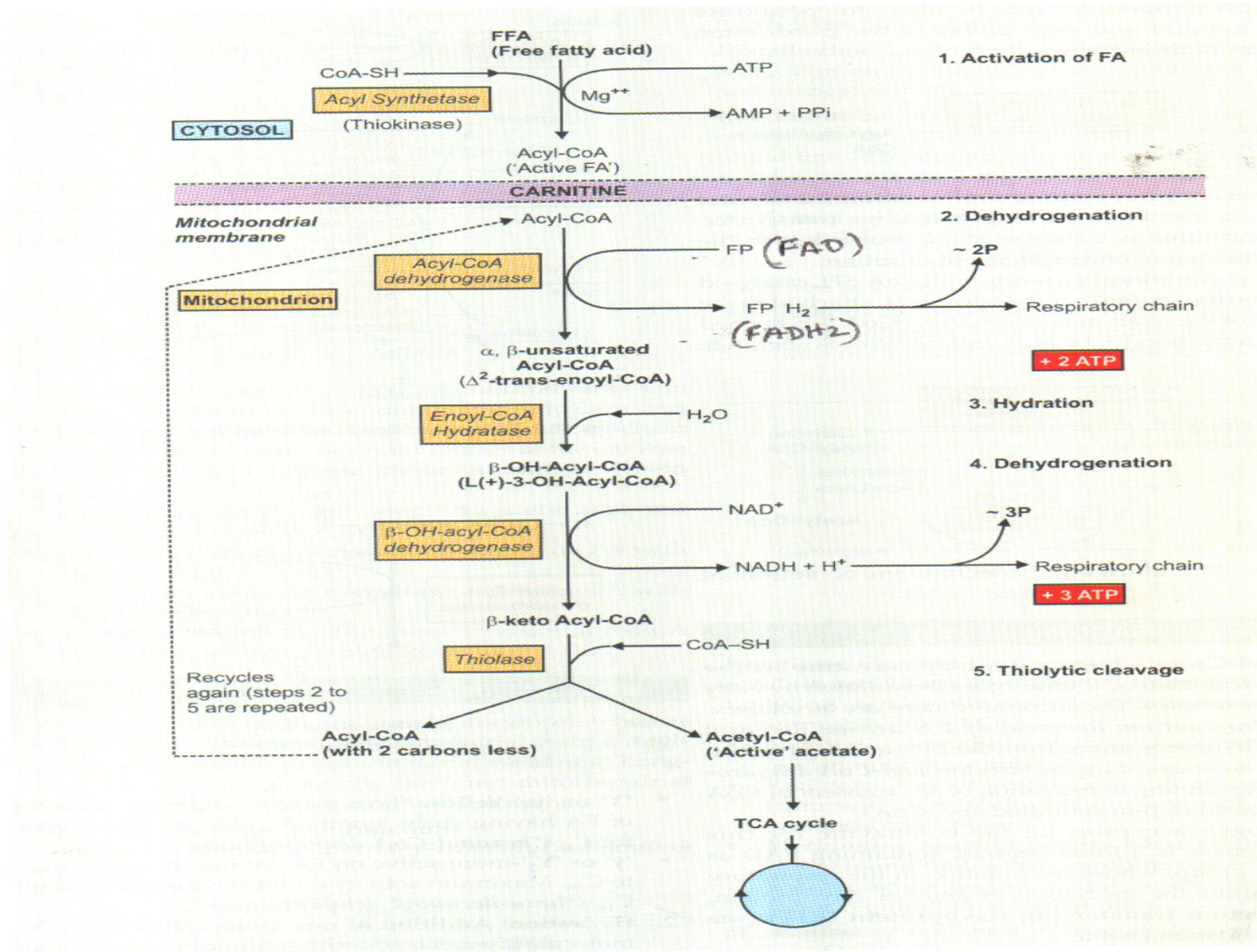


Fig. 25.3: β-oxidation of fatty acids

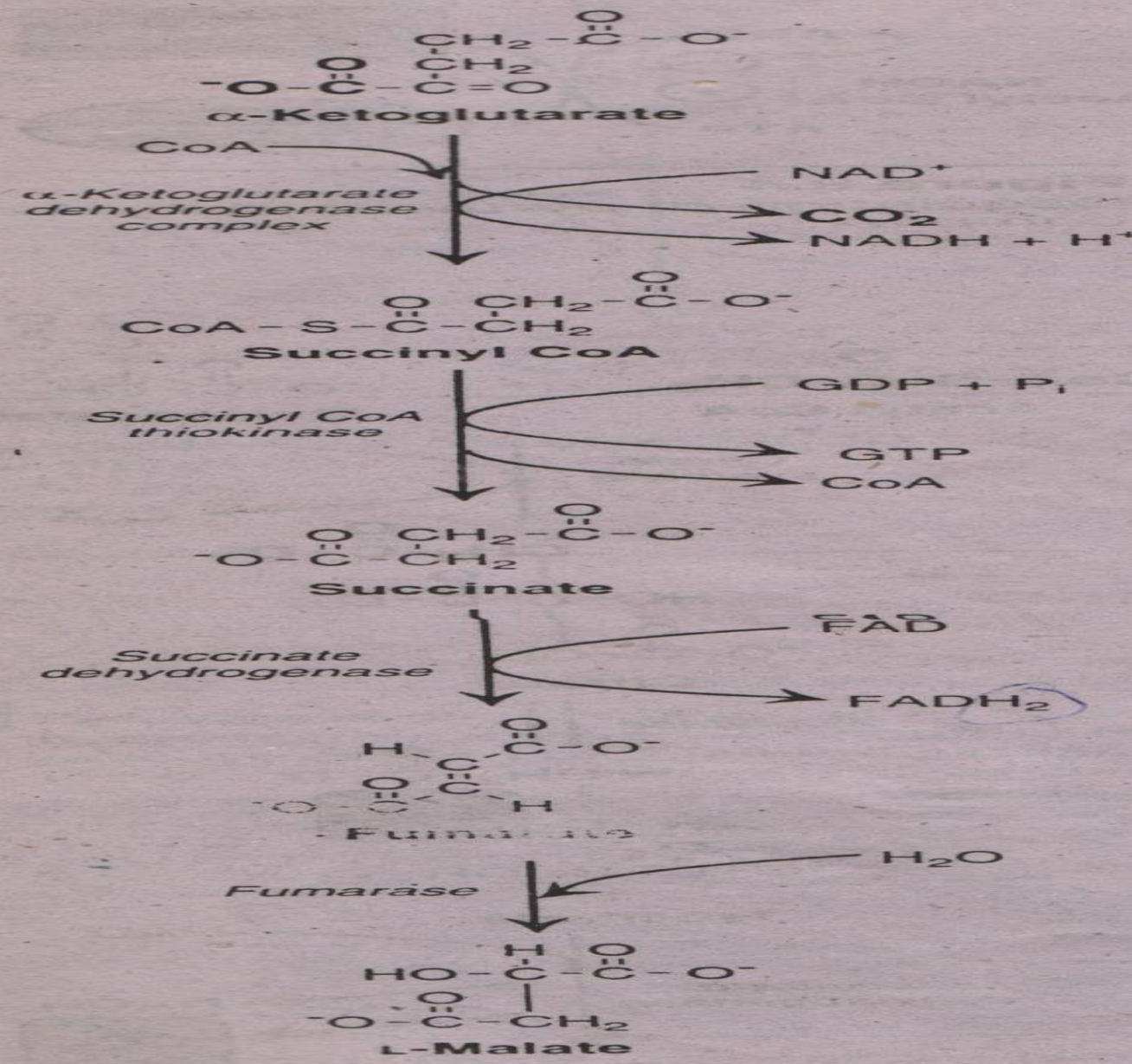
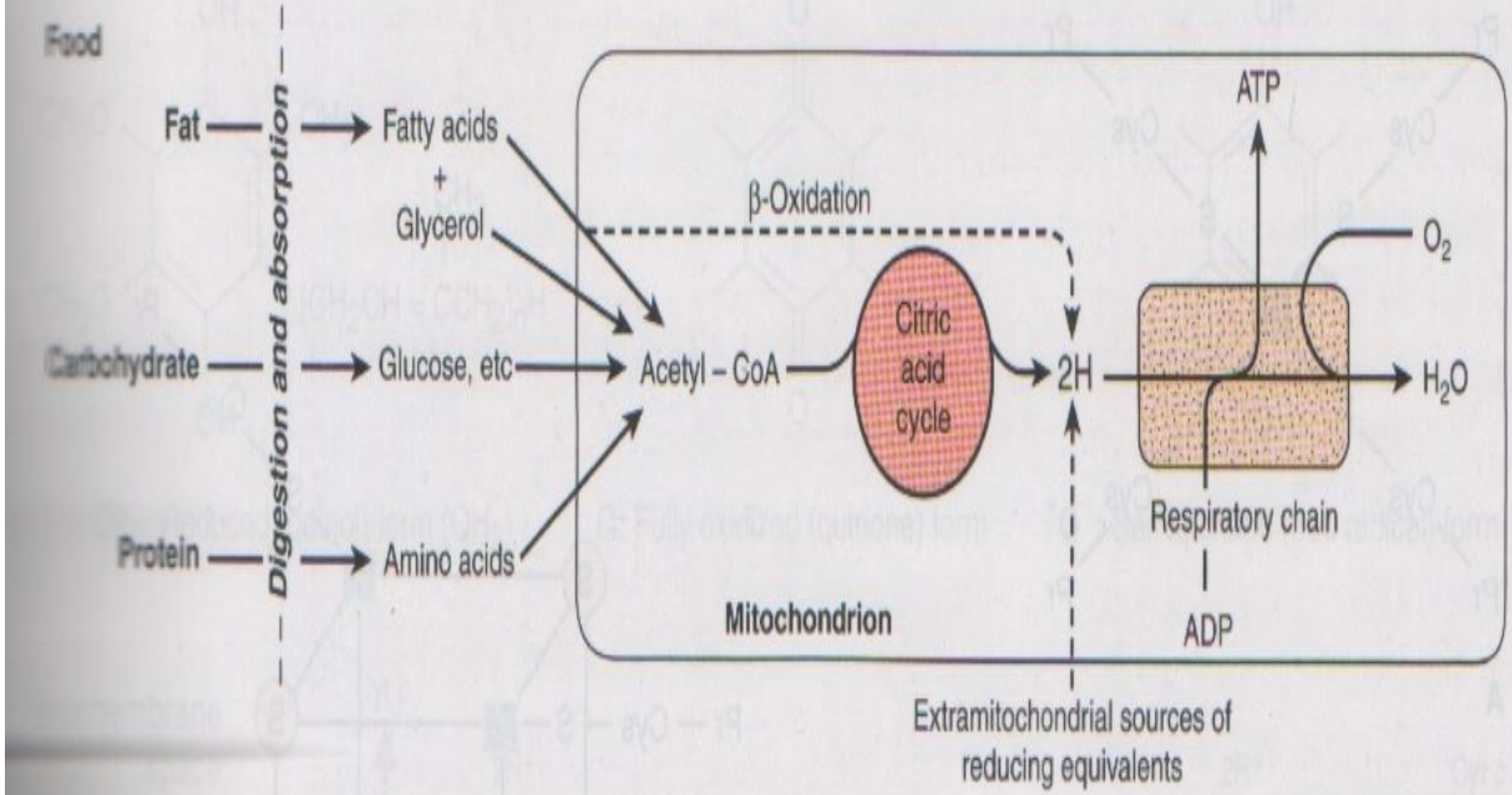


Figure 9.6
Formation of malate from α-ketoglutarate.


Food
Fat
Carbohydrate
Protein
Digestion and absorption
Fatty acids
+
Glycerol
Glucose, etc
Amino acids
β-Oxidation
Acetyl – CoA
Citric acid cycle
2H
ATP
O_2
H_2O
Respiratory chain
ADP
Mitochondrion
Extramitochondrial sources of reducing equivalents

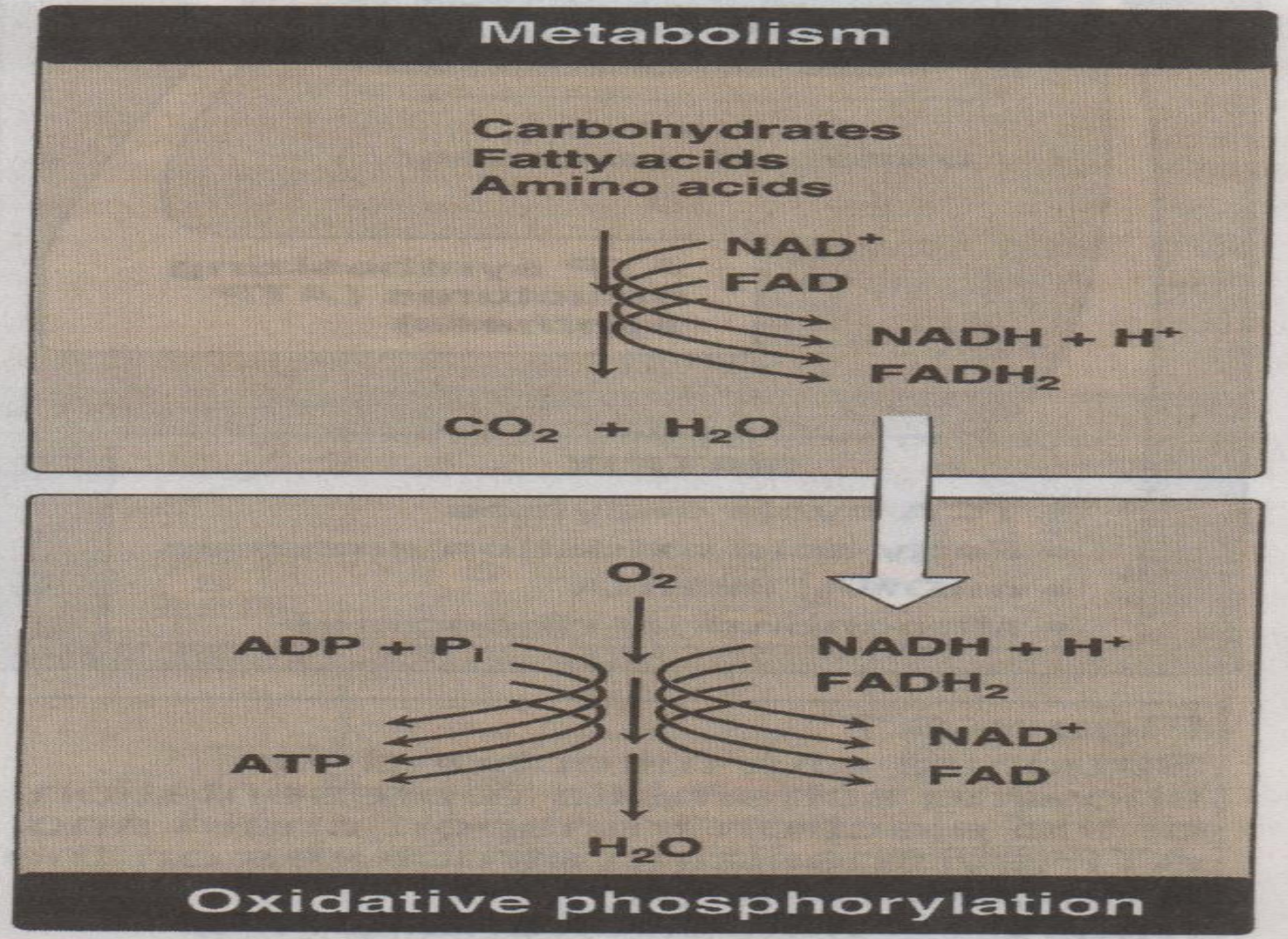
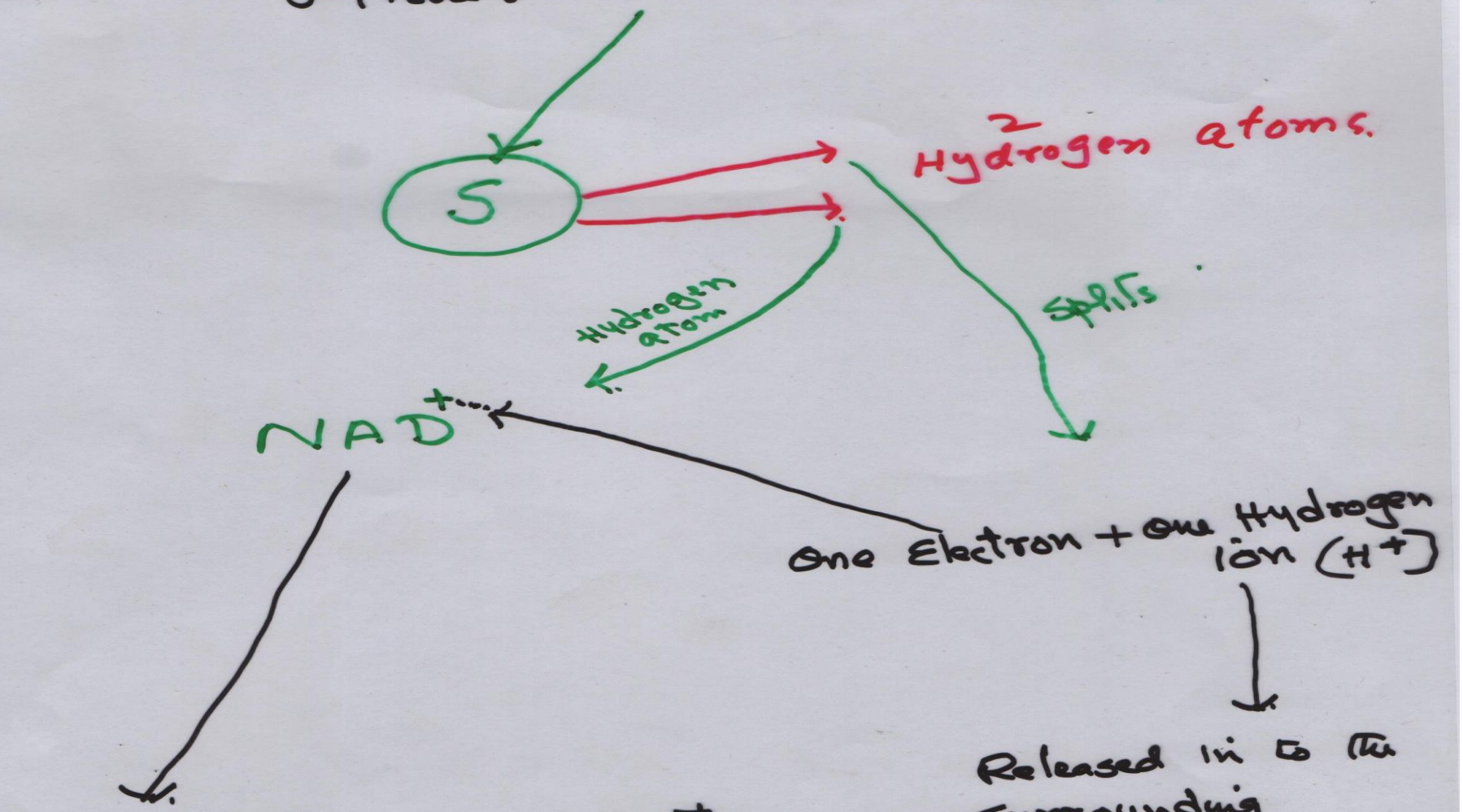


Figure 6.6
The metabolic breakdown of energy-yielding molecules.

Anaerobic Dehydrogenase



So $NAD \rightarrow NADH + H^+$

2a

NAD Linked Dehydrogenases:-

Anaerobic Dehydrogenases catalyse removal of hydrogen from substrate.

The coenzymes NAD or FAD act as hydrogen acceptor. when the substrate is oxidised, the co-enzyme is reduced.

$$AH_2 + NAD^+ \longrightarrow A + NADH + H^+$$

FAD — Linked Dehydrogenases :-

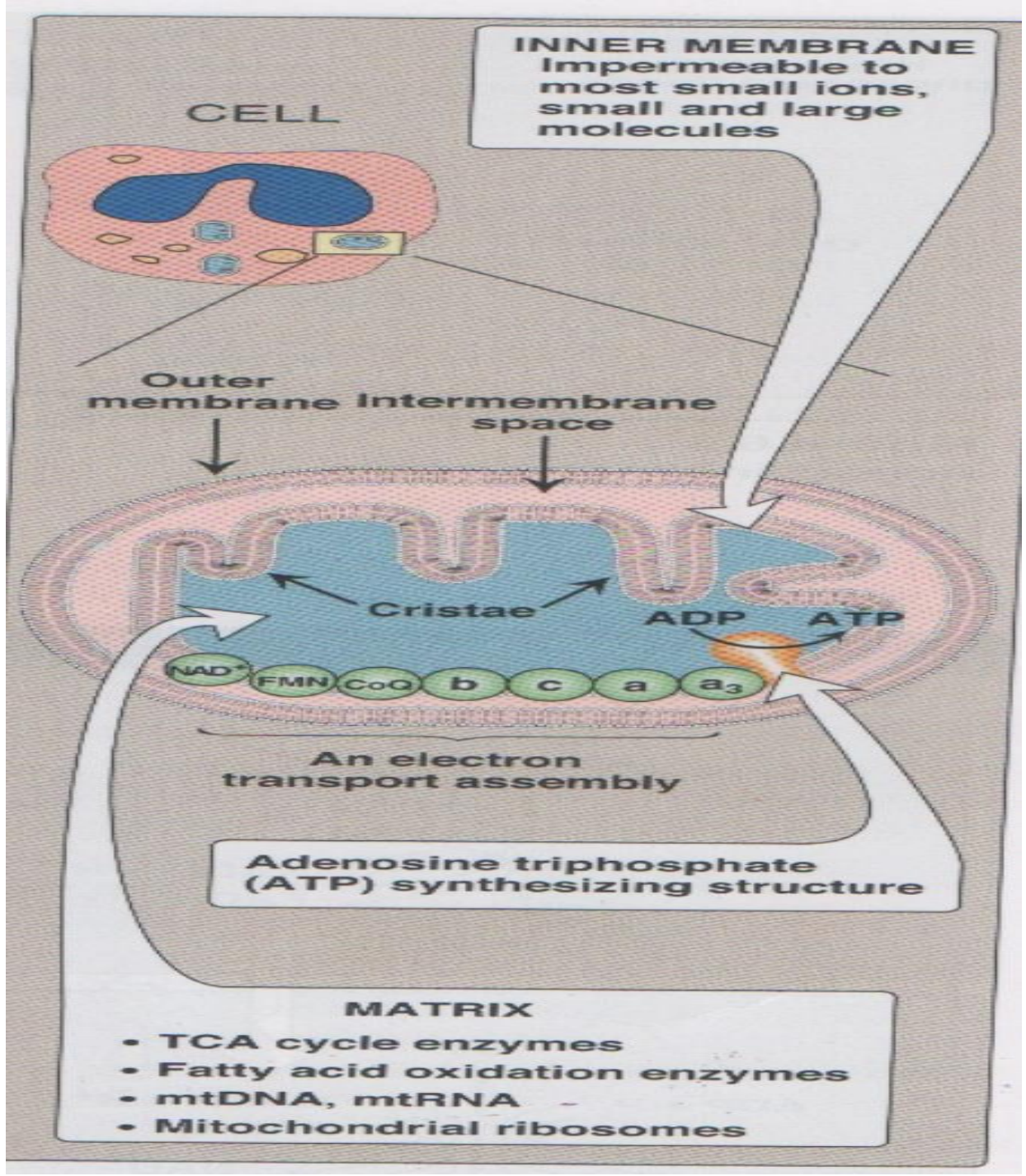
When FAD is the co-enzyme, Both the hydrogen atoms are attached to the Flavin ring.

FMN ::

is the component of E.T.C, accepting the hydrogen atoms from NADH2.

- $NADP^+$ Linked Dehydrogenase :-

NADPH can't be oxidised for the production of energy, but take part in reductive biosynthetic reactions e.g, Fatty acids and cholesterol synthesis.


CELL
INNER MEMBRANE
Impermeable to most small ions, small and large molecules
Outer membrane
Intermembrane space
Cristae
ADP
ATP
NAD+
FMN
CoQ
b
c
a
a3
An electron transport assembly
Adenosine triphosphate (ATP) synthesizing structure
MATRIX
• TCA cycle enzymes
• Fatty acid oxidation enzymes
• mtDNA, mtRNA
• Mitochondrial ribosomes

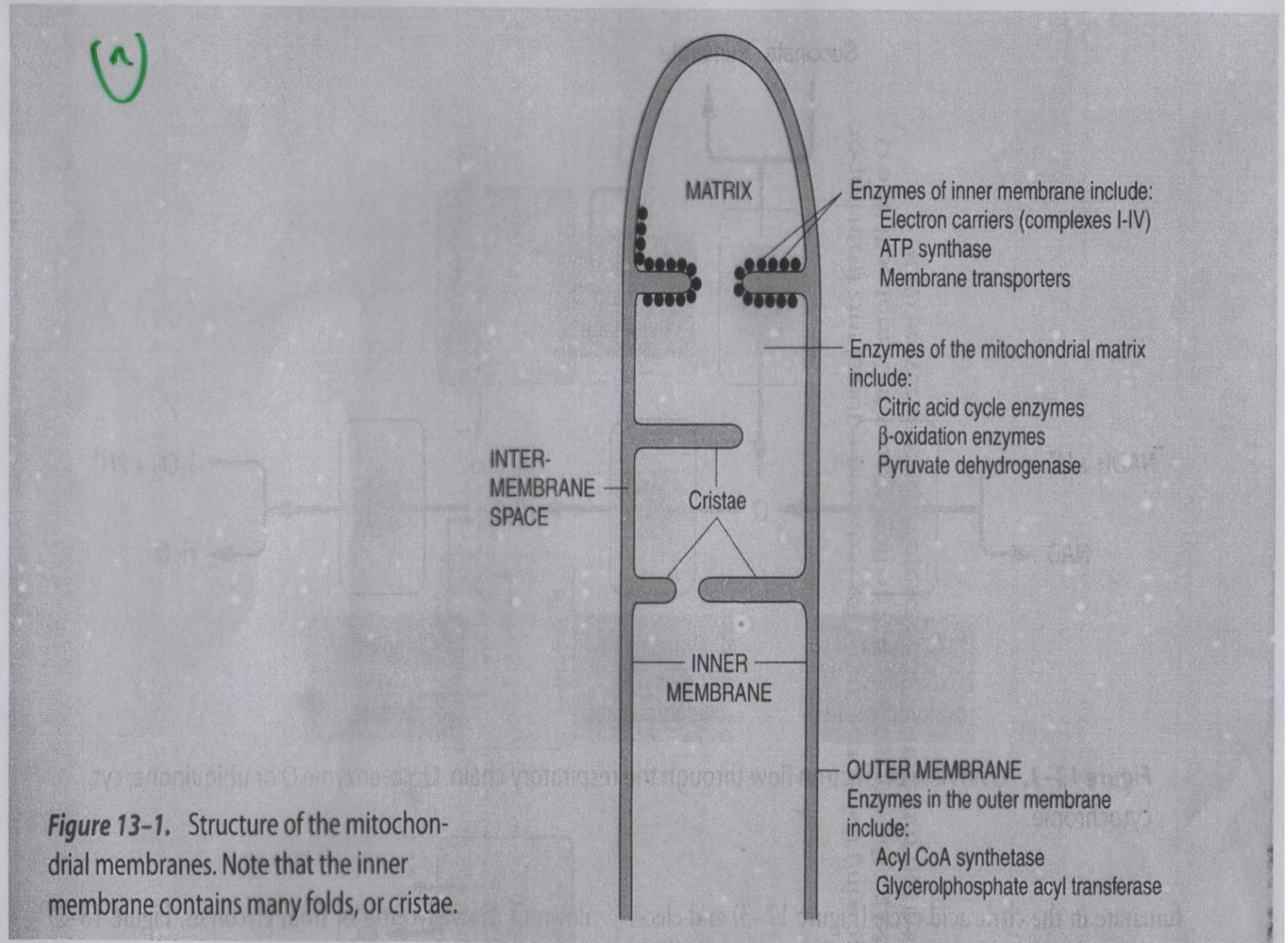


Figure 13–1. Structure of the mitochondrial membranes. Note that the inner membrane contains many folds, or cristae.

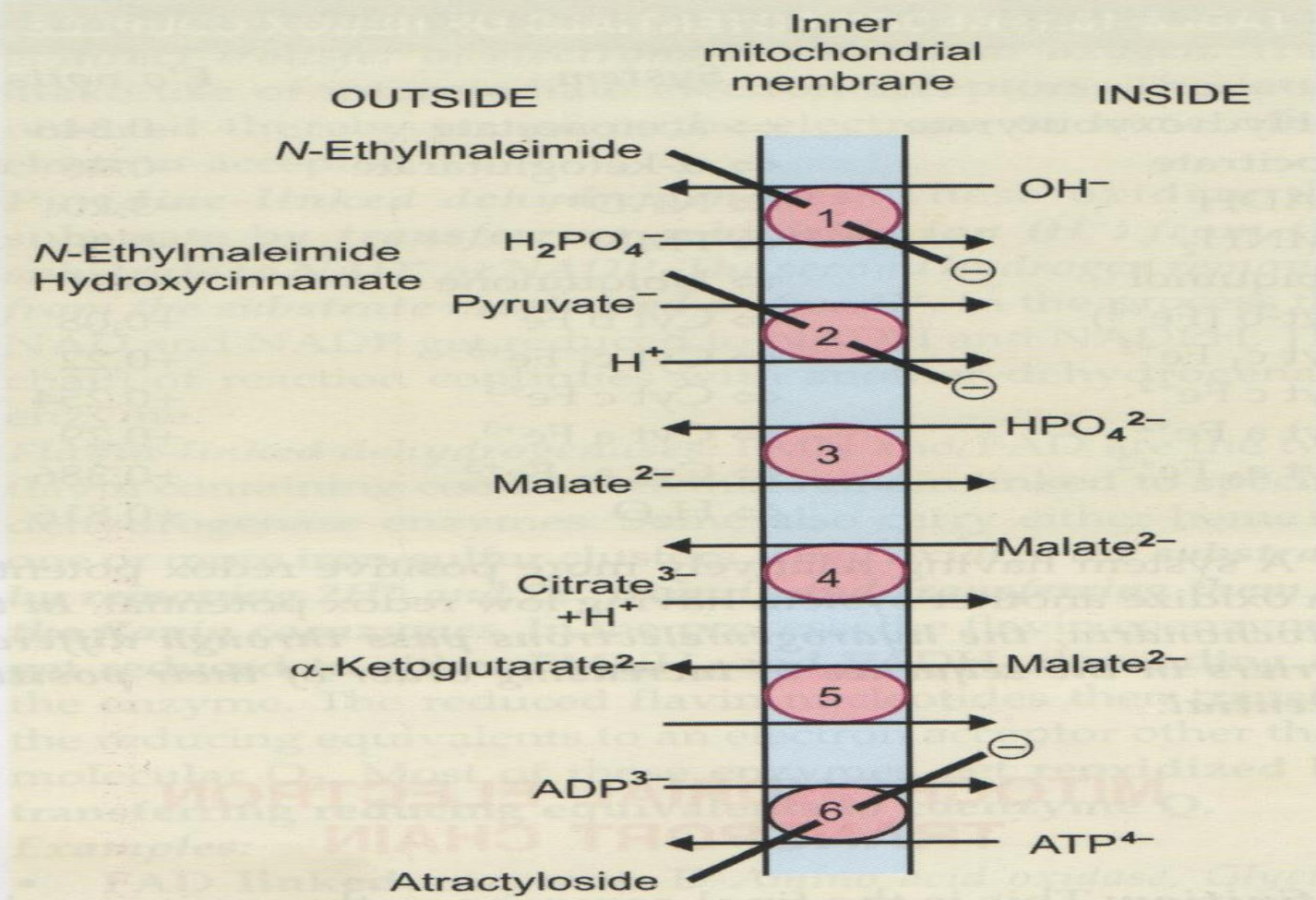


FIG. 10.1: SHOWS SOME OF THE TRANSPORTER SYSTEM IN INNER MITOCHONDRIAL MEMBRANE AND THEIR INHIBITORS. TRANSPORTER SYSTEMS IN THE INNER MITOCHONDRIAL MEMBRANE. (1) PHOSPHATE TRANSPORTER; (2) PYRUVATE SYMPORT; (3) DICARBOXYLATE TRANSPORTER; (4) TRICARBOXYLATE TRANSPORTER; (5) α-KETOGLUTARATE TRANSPORTER; (6) ADENINE NUCLEOTIDE TRANSPORTER. N-ETHYL-MALEIMIDE, HYDROXYCINNAMATE, AND ATRACTYLOSIDE INHIBIT (–) THE INDICATED SYSTEMS

E.T.C

- All the components of E.T.C are located in the inner membrane of mitochondria (except Cyt-C)

- In E.T.C, The electrons are transffered from NADH and FADH to electron carriers.
- `
- Four distinct multi-Protien complexes named as Complex-I,II,III and IV , which are connected by two mobile carriers i.e Co-Q and Cyt-C and
- Complex-V (ATP-Synthase) involved in the production of ATP

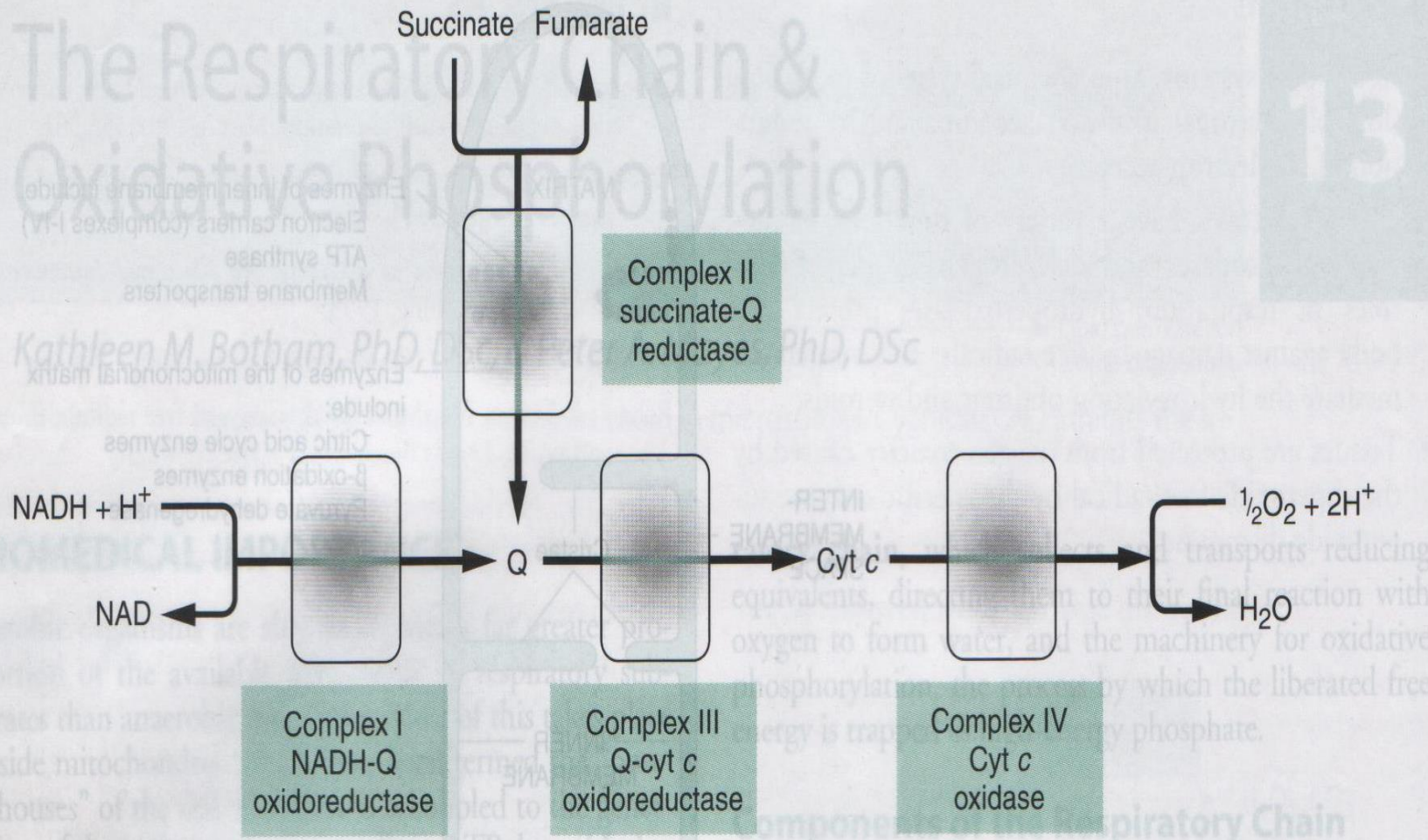


Figure 13–3. Overview of electron flow through the respiratory chain. Q, co-enzyme Q or ubiquinone; cyt, cytochrome.

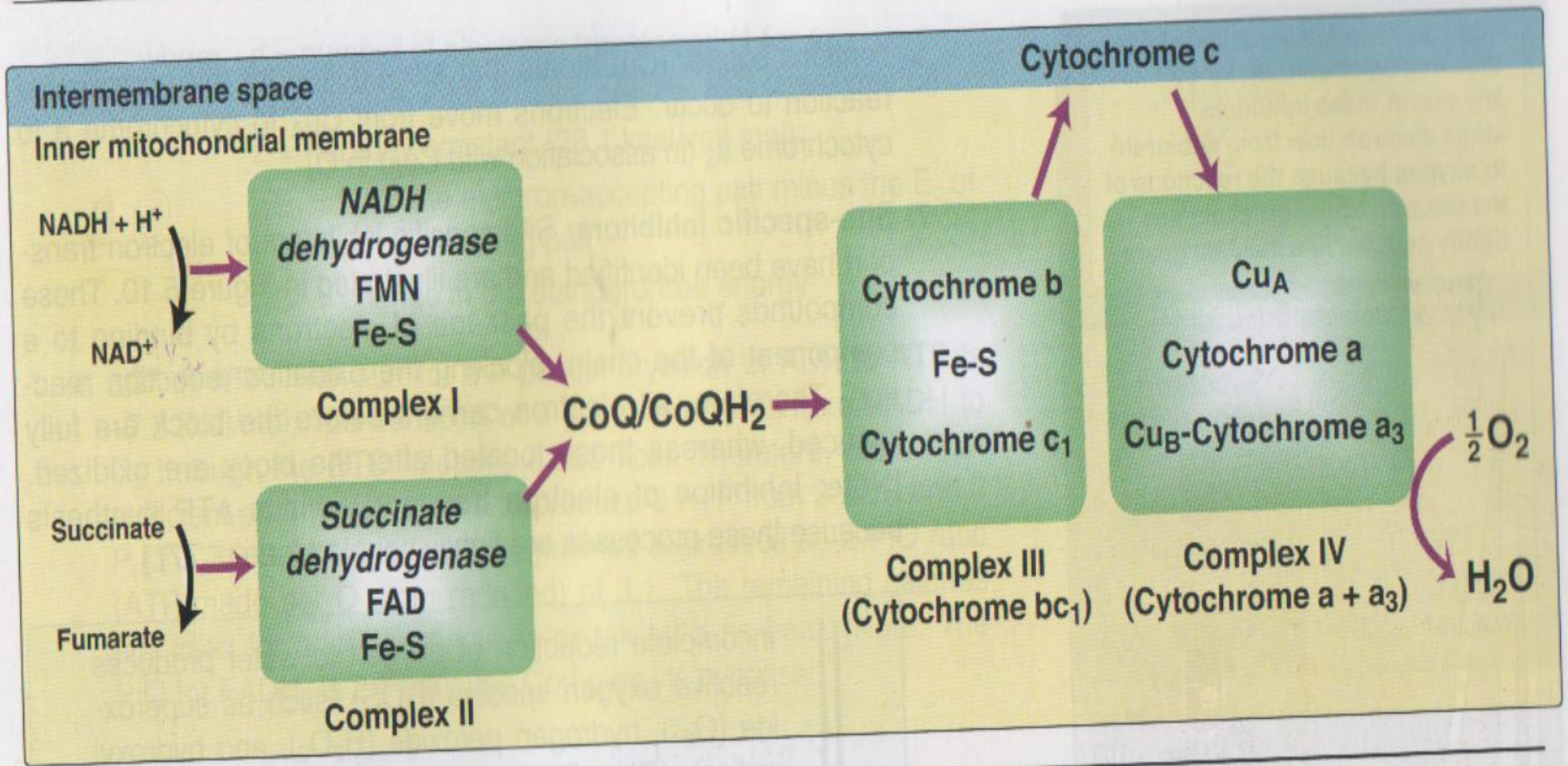


Figure 6.8
Electron transport chain. The flow of electrons is shown by the magenta arrows. NAD(H) = nicotinamide adenine dinucleotide; FMN = flavin mononucleotide; FAD = flavin adenine dinucleotide; Fe-S = iron-sulfur center; CoQ = coenzyme Q.

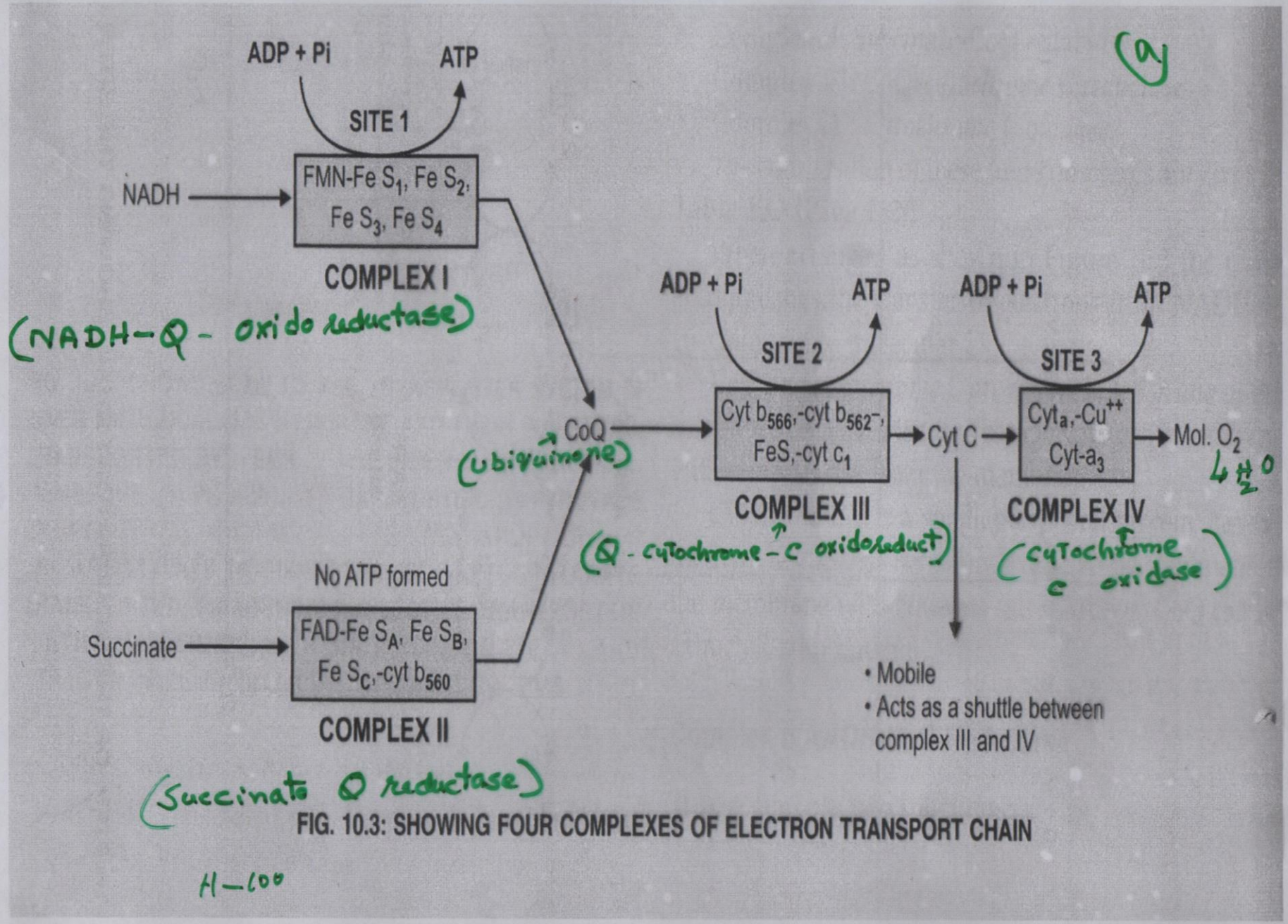


FIG. 10.3: SHOWING FOUR COMPLEXES OF ELECTRON TRANSPORT CHAIN

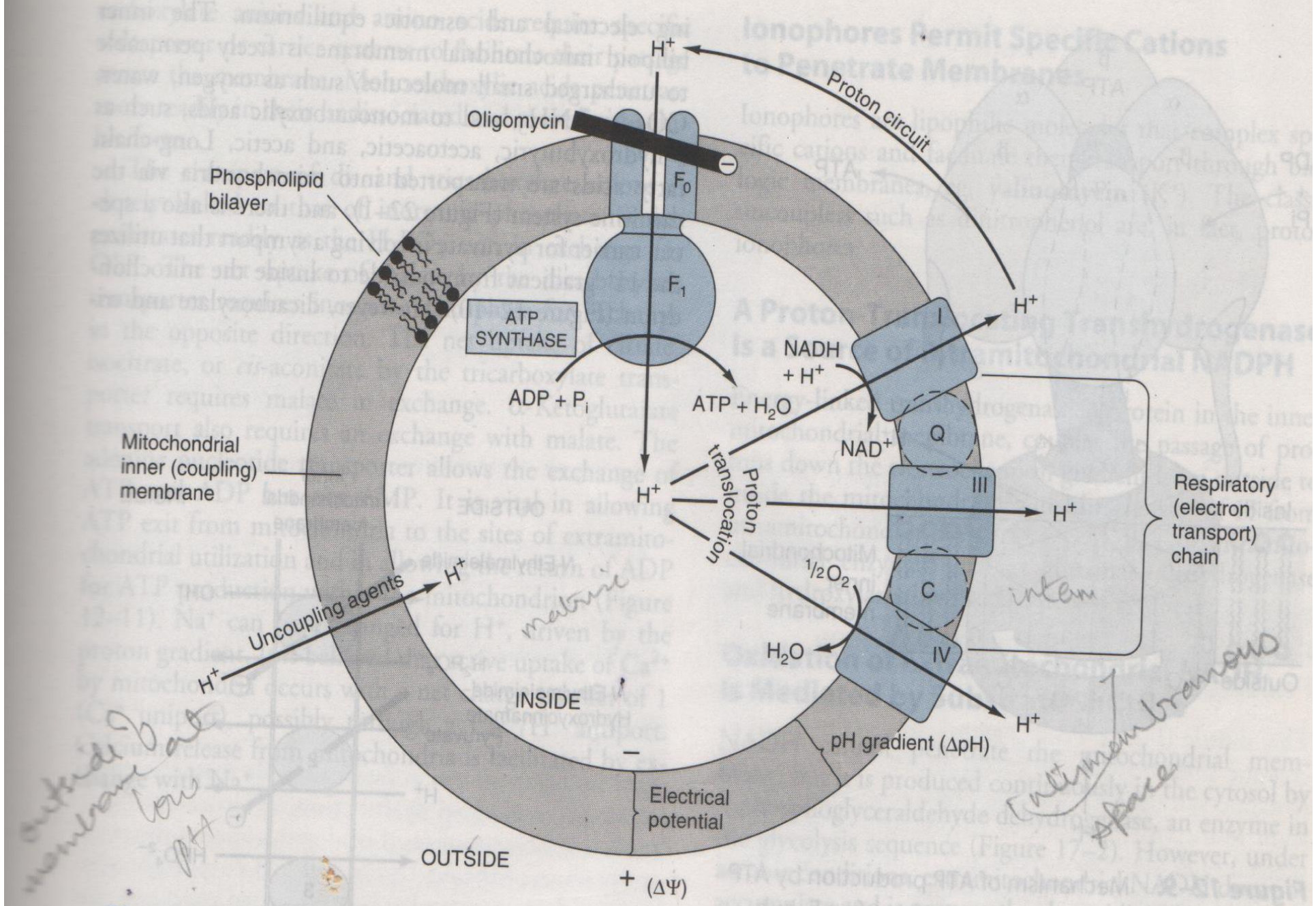


Figure 12–8. Principles of the chemiosmotic theory of oxidative phosphorylation. The main proton circuit is created by the coupling of oxidation in the respiratory chain to proton translocation from the

- The flow of electrons through E.T.C from electron donors e.g NADH to electron acceptor e.g oxygen is

EXERGONIC process i.e it releases energy.

- The synthesis of ATP is ENDERGONIC process ,which requires an input of energy.

- The Free proton plus hydride ion carried by NADH are transferred to NADH dehyrogenase, embaded in inner mitochondrial membrane.(complex-I)
- Than the FMN accept two hydrogen atoms

  ($2e^- + 2H^+$)becoming $FMNH_2$, then to iron of iron sulphur centre, and then two COQ
- Up to CoQ, Hydrogen atoms are transferred but from CoQ onward , only electrons are transferred.

  $2H^+$ goes in to the medium.

- As electrons flow, they lose energy.
- Part of this energy is used to pump protons across the inner mit membrane in to intermembrane space.
- Rest is used for production of Heat.

- The small energy change (+0.113V) does not allow complex II to pump protons, So does not contribute in ATP formation.

  FAD $FADH_2$

- Fumerate → Succinate

  This enzyme system is present in complex II, so this reaction of TCA take place in complex II

- Up to CoQ, H is transferred but from CoQ onward , only electrons are transferred.

  $2H^+$ goes in to the medium.

COENZYME Q

- Quinone derivative with isoprenoid tail
- lipid soluble component of ETC
- Mobile carrier
- Can accept hydrogen atoms from

  Complex I

  Complex II and mitochonrial dehydrogenases

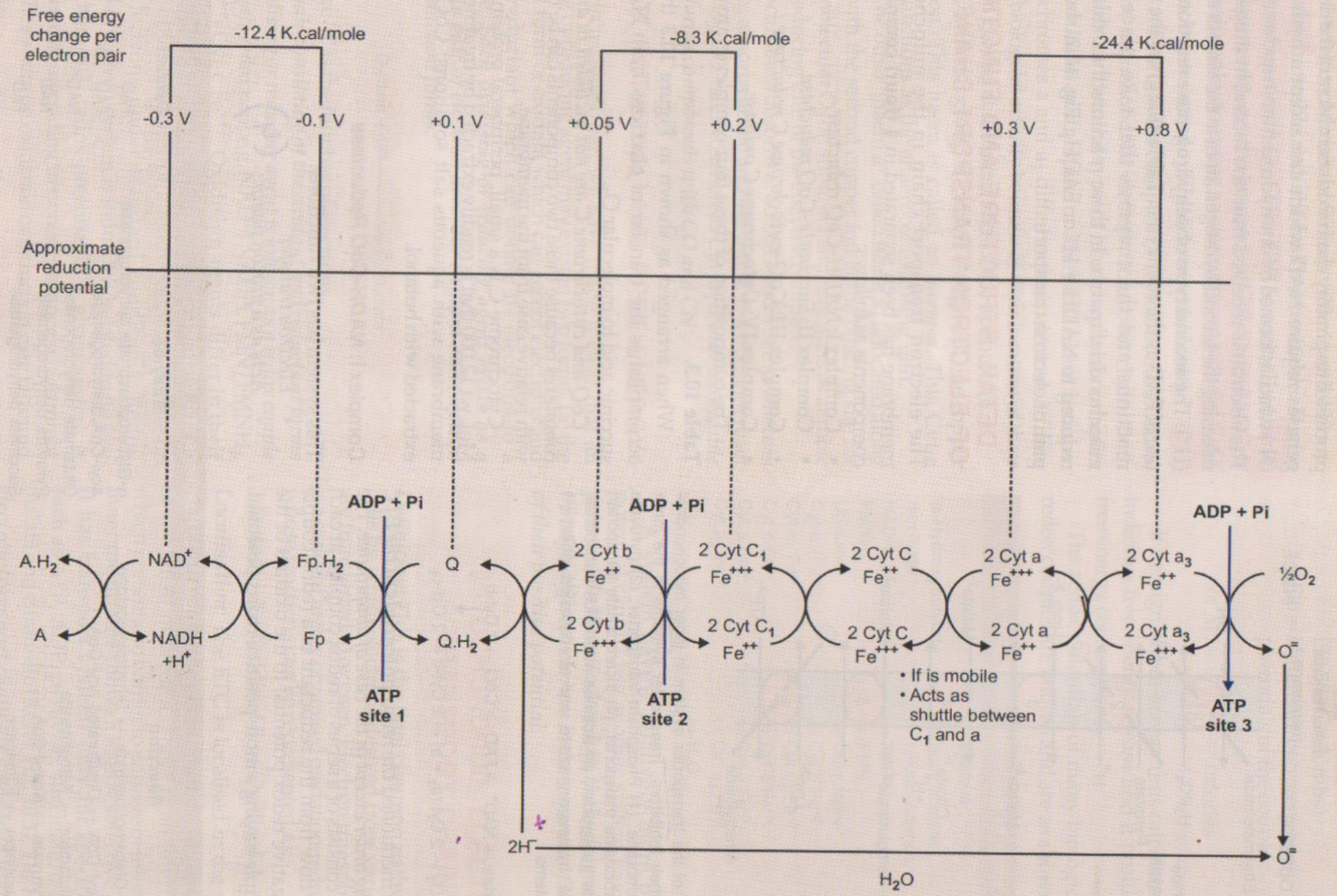


Fig. 10.2: The electron transport system of the respiratory chain showing the sites of formation of 3ATP molecules

RELEASE OF FREE ENERGY DURING ELECTRON TRANSPORT

The free energy released as electrons are transferred along the ETC from an electron donor (reducing agent or reductant) to an electron acceptor (oxidizing agent or oxidant) is used to pump protons at Complexes I, III and IV.

[Note: The electrons can be transferred as hydride ions (:H-) to NAD+ : as hydrogen atoms (**.**H) to FMN, CoQ, and FAD: or as electrons (e-) to cytochromes.]

Incomplete reduction of oxygen to water produces reactive oxygen species (ROS), such as superoxide ($O_2^{-}\cdot$), hydrogen peroxide (H_2O_2), and hydroxyl radicals ($OH\cdot$). ROS damage DNA and proteins and cause lipid peroxidation. Enzymes such as *superoxide dismutase* (*SOD*), *catalase*, and *glutathione peroxidase* are cellular defenses against ROS.

CHEMIOSMOTIC HYPOTHESIS
(Mitchell Hypothesis)

- Explains how the free energy generated by the transport of electrons by the ETC is used to produce ATP from ADP+ Pi.

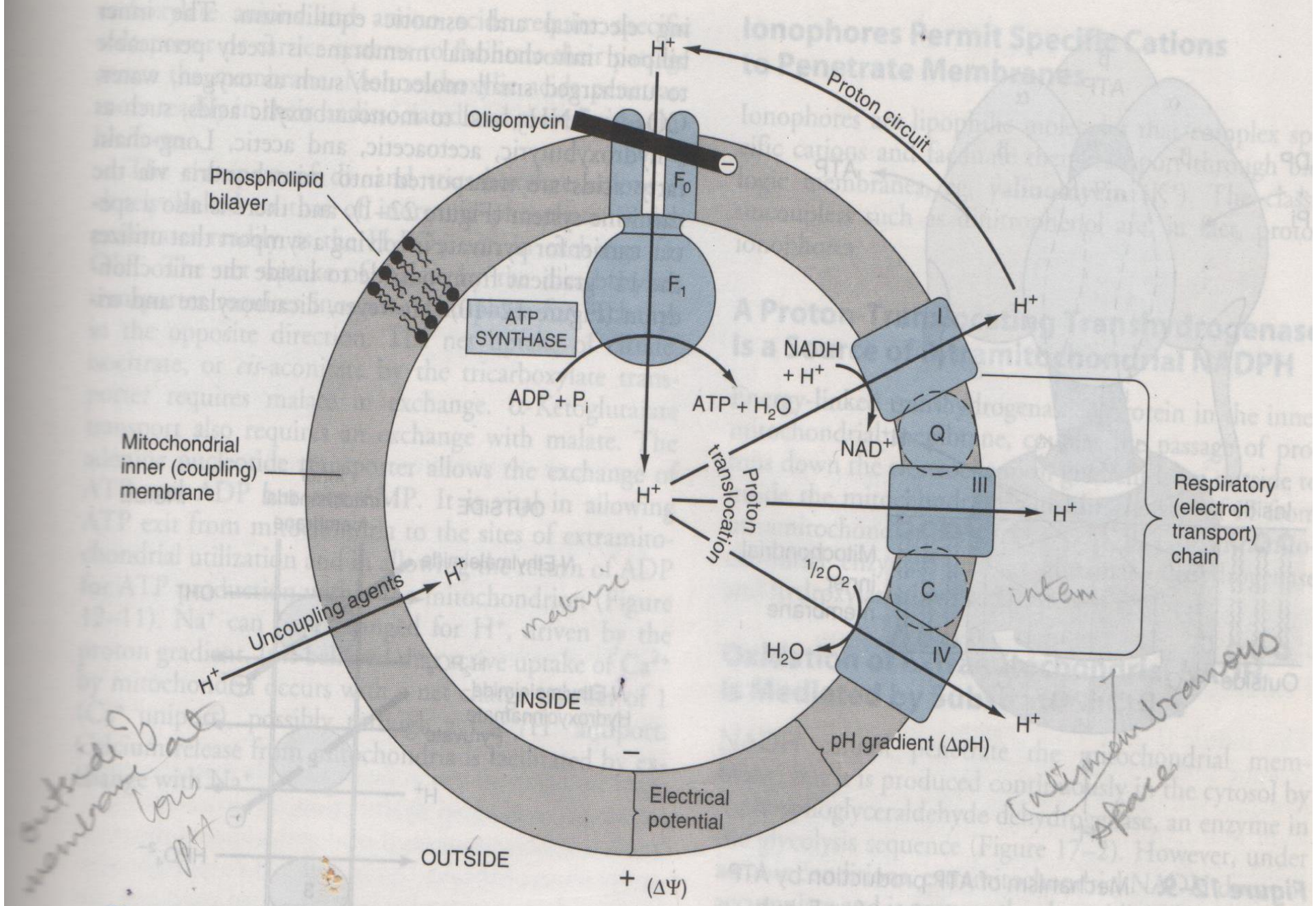


Figure 12–8. Principles of the chemiosmotic theory of oxidative phosphorylation. The main proton circuit is created by the coupling of oxidation in the respiratory chain to proton translocation from the