TDC 3RD SEMESTER
MAJOR

THEORIES OF OXIDATIVE PHOSPHORELATION

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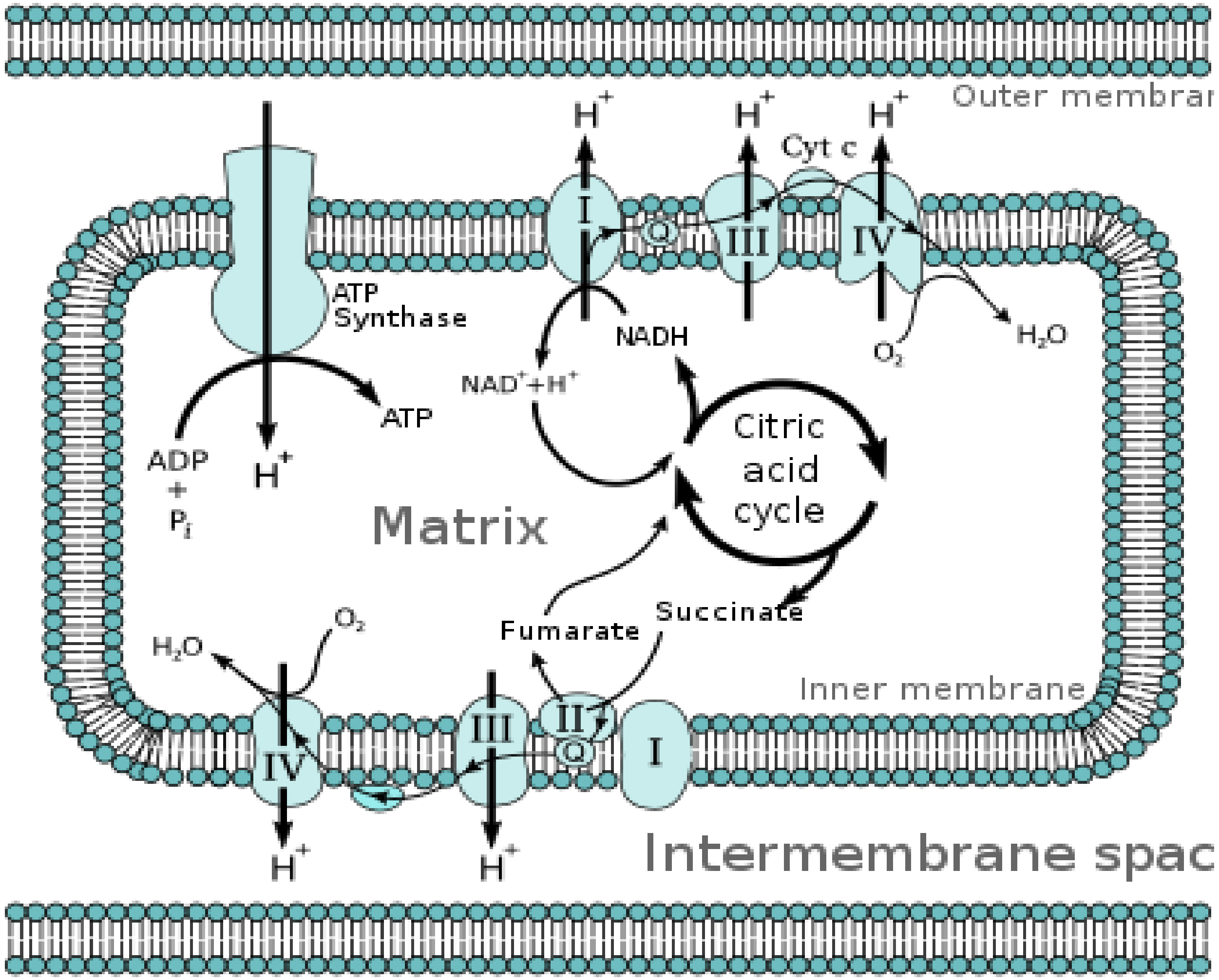
Oxidative phosphorylation

- **Oxidative phosphorylation (or electron transport-linked phosphorylation) is the metabolic pathway in which cells use enzymes to oxidize nutrients, thereby releasing the chemical energy stored within in order to produce adenosine triphosphate (ATP). In most eukaryotes, this takes place inside mitochondria. Almost all aerobic organisms carry out oxidative phosphorylation.**

During oxidative phosphorylation, electrons are transferred from electron donors to electron acceptors such as oxygen in redox reactions. These redox reactions release the energy stored in the relatively weak double bond of O_2, which is used to form ATP. In eukaryotes, these redox reactions are catalyzed by a series of protein complexes within the inner membrane of the cell's mitochondria, whereas, in prokaryotes, these proteins are located in the cell's intermembrane space. These linked sets of proteins are called electron transport chains. In eukaryotes, five main protein complexes are involved, whereas in prokaryotes many different enzymes are present, using a variety of electron donors and acceptors.

The energy transferred by electrons flowing through this electron transport chain is used to transport protons across the inner mitochondrial membrane, in a process called electron transport. This generates potential energy in the form of a pH gradient and an electrical potential across this membrane. This store of energy is tapped when protons flow back across the membrane and down the potential energy gradient, through a large enzyme called ATP synthase; this process is known as chemiosmosis. The ATP synthase uses the energy to transform adenosine diphosphate (ADP) into adenosine triphosphate, in a phosphorylation reaction. The reaction is driven by the proton flow, which forces the rotation of a part of the enzyme; the ATP synthase is a rotary



The electron transport chain in the cell is the site of oxidative phosphorylation. The NADH and succinate generated in the citric acid cycle are oxidized, releasing the energy of O2 to power the ATP synthase

Classical Theories of Oxidative Phosphorylation | Respiration

The following points highlight the top three classical theories of oxidative phosphorylation. The theories are: 1. The Chemical Coupling Theory

2. The Conformational Coupling Theory and

3. The Chemiosmotic Coupling Theory

Classical Theory 1. The Chemical Coupling Theory:

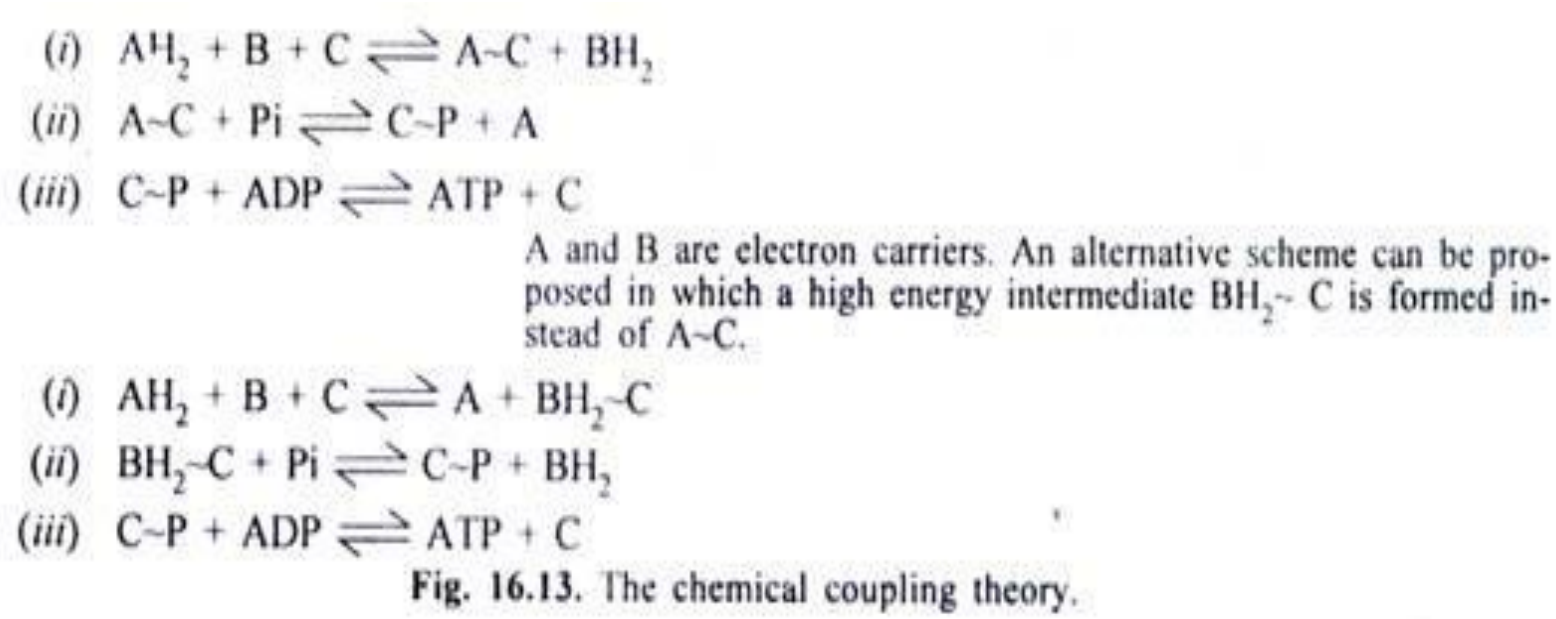
This theory was first proposed by Slater in 1953 and is based on the principles of substrate-level phosphorylation as illustrated by reaction sequence for glyceraldehyde-3-phosphate dehydrogenase in glycolysis resulting in the formation of one ATP molecule and 3-phosphoglyceric acid, (For details see glycolysis).

According to this theory (Fig. 16.13) a reduced electron carrier of the respiratory chain (e.g., AH2) reacts with an oxidised carrier (e.g., B) which is adjacent to it with sufficient free energy drop occurring to allow the reaction of A with an unknown compound C to give a non phosphorylated high energy intermediate compound A~C. B is reduced to BH2.

In the next sequential exchange reactions, C is transferred to phosphate to form a phosphorylated intermediate C~P. The electron carrier A becomes free and oxidised.

Finally, phosphate from C~P is transferred to ADP to give ATP. The unknown compound C becomes free and recycled.

Alternatively, there may be a parallel scheme of reaction in which the high-energy non- phosphorylated intermediate is formed with BH_2 instead A (Fig. 16.13).



(*i*) $AH_2 + B + C \rightleftharpoons A{\sim}C + BH_2$

(*ii*) $A{\sim}C + Pi \rightleftharpoons C{\sim}P + A$

(*iii*) $C{\sim}P + ADP \rightleftharpoons ATP + C$

A and B are electron carriers. An alternative scheme can be proposed in which a high energy intermediate $BH_2{\sim}C$ is formed instead of $A{\sim}C$.

(*i*) $AH_2 + B + C \rightleftharpoons A + BH_2{\sim}C$

(*ii*) $BH_2{\sim}C + Pi \rightleftharpoons C{\sim}P + BH_2$

(*iii*) $C{\sim}P + ADP \rightleftharpoons ATP + C$

Fig. 16.13. The chemical coupling theory.

The chemical coupling theory did not find much support because no phosphorylated intermediates or high-energy intermediates of the respiratory carriers have yet been identified unequivocally.

Classical Theory # 2. The Conformational Coupling Theory:

This theory was first put forward by Boyer in 1964 and according to this the free energy liberated during electron transport is conserved as a conformational change in the protein component of a respiratory electron carrier or complex of carriers and this change is associated in some way with the phosphorylation of ADP to form ATP.

Boyer suggested that conformational change in an electron carrier probably brought a carboxyl and sulphydryl group very close to each other to form an acyl-s-linkage (Fig. 16.14 A) and that this was the 'high-energy intermediate' which could drive ATP synthesis.

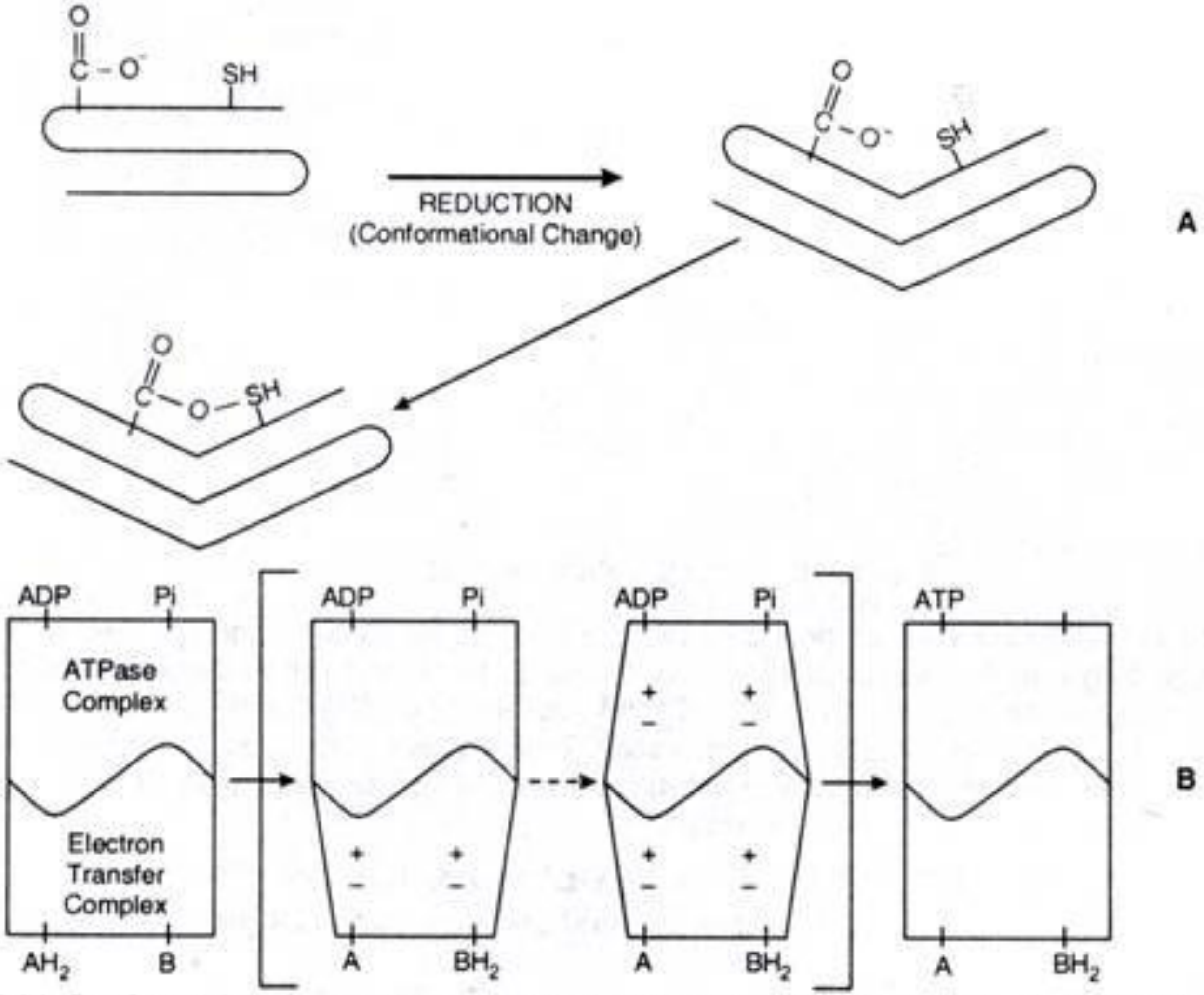


Fig. 16.14. Conformational coupling theory. A, Boyer's original theory. B, Green and Ji's electromechanochemical model.

Based on conformational coupling theory Green and Ji (1972) have given their electro-mechanochemical coupling theory which envisaged conformational changes in enzyme complexes rather than in individual carriers.

According to their model the transport of electrons brings about a conformational change in one of the electron transport complexes in the form of mechanical and electrical strain components. Similar mechanical and electrical changes are in turn induced in an ATPase Complex. The reverse conformational change now leads to the synthesis of ATP bringing back the electron transport complex and the ATPase complex in their original form (Fig. 16.14 B).

Classical Theory # 3. The Chemiosmotic Coupling Theory:

This theory was first put forward **by Nobel laureate Peter Mitchell in 1961** and is most convincing of all the three theories to explain the mechanism of mitochondrial oxidative phosphorylation. It is also equally applicable to chloroplastic photophosphorylation

The main feature of this theory (Fig. 16.15) is a membrane located reversible ATPase. The membrane is mitochondrial in case of oxidative phosphorylation and chloroplastic in case of photophosphorylation.

The ATPase reversibly catalyses the following reaction:

This reaction is assumed to be anisotropic so that the active centre is accessible to H+ but not OH– from the outer side of the membrane. On the other hand it is accessible only to OH– but not H+ from the inner side of the membrane. The active centre is assumed to be relatively inaccessible to water and the membrane almost impermeable to ions.

It is quite obvious from the ATPase catalysed reversible reaction that the removal of H^+ and OH^- would favour the reaction towards ATP synthesis.

According to Mitchell H^+ and OH^- can be removed by membrane bound electron transport chain and the operation of ATPase in the following way:

a. The oxidation of the reduced electron carrier e.g., AH_2 to A with the simultaneous reduction of O to H_2O leads to the accumulation of H^+ on the inner side and OH^- on the outer side of the membrane.

These accumulations of H+ on the inner side of the membrane pull OH– from the ATPase catalysed reaction. Similarly, accumulation of OH– on the outer side of the membrane pulls H+ from the ATPase catalysed reaction. Thus, the equilibrium is shifted in favour of ATP synthesis (Fig. 16.15). The dehydrating force which drives the ATPase catalysed reaction in the direction of ATP synthesis is derived from the chemical potential differential of the OH– and H+ across the membrane.

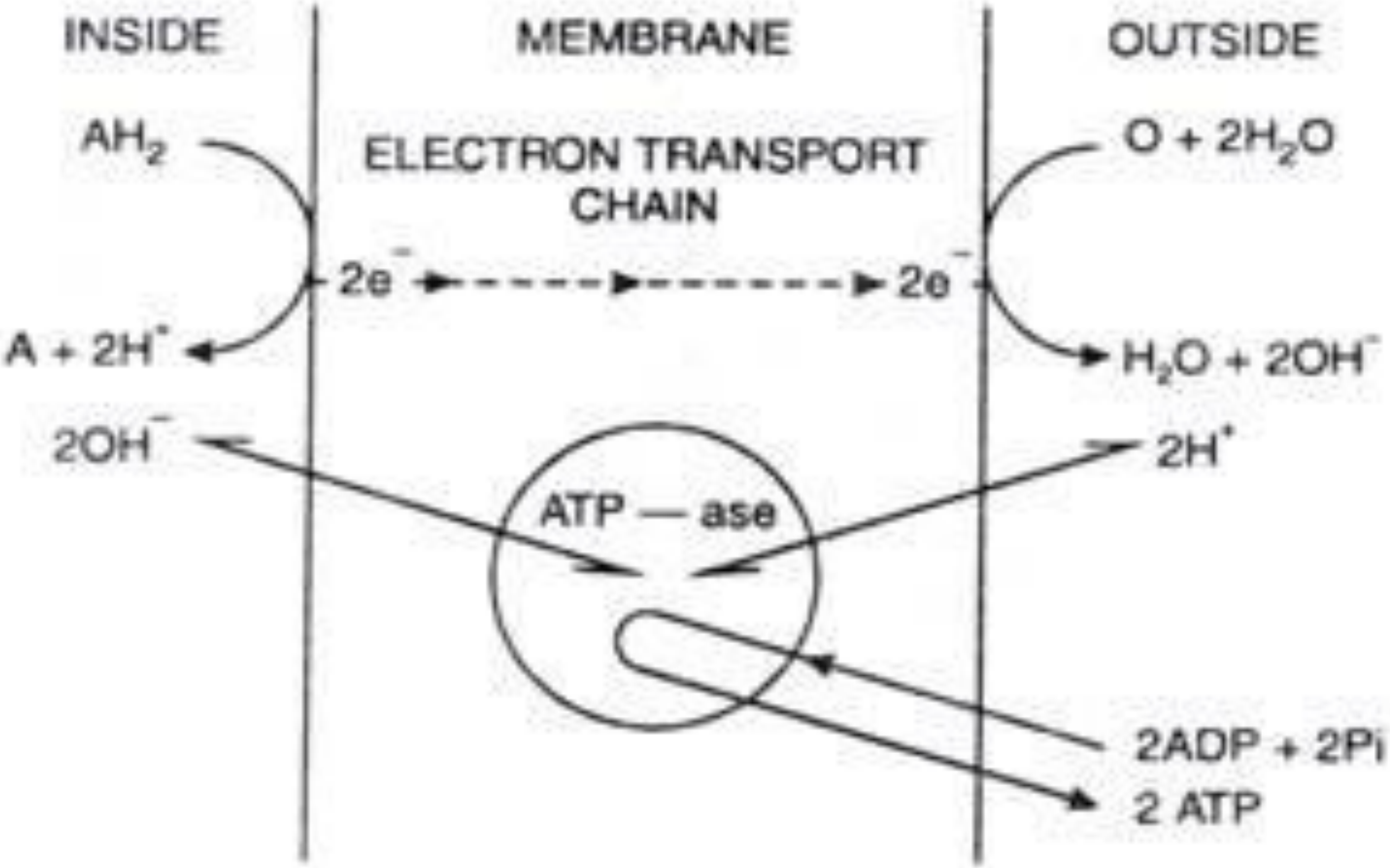


Fig. 16.15. Mitchell's chemi-osmotic hypothesis.

Mitchell’s hypothesis also predicted the existence of membrane transporters or specific exchange diffusion carriers which has been shown to be correct. These carriers permit reversible exchange of anions (e.g. Cl–) for OH– and cations (e.g., K+) for H+ and regulate the pH and osmotic differential across the membrane. These systems permit the movements of essential metabolites without breaking the membrane potential which is essential for ATPase catalysed reaction in the direction of ATP synthesis.

THANKYOU