Chemiosmotic Hypothesis

Chemiosmotic hypothesis was proposed by Peter Mitchell (1960). It states that a proton-motive force was responsible for driving the synthesis of ATP. In this hypothesis, protons would be pumped across the inner mitochondrial membrane as electrons went through the electron transfer chain. This would result in a proton gradient with a lower pH in the inter-membrane space and an elevated pH in the matrix of the mitochondria. An intact inner mitochondrial membrane which is impermeable to protons is a requirement of such model. Proton gradient and membrane potential are the proton-motive force that is used to drive ATP synthesis. In effect, the pH gradient acts as a battery which stores energy to produce ATP.

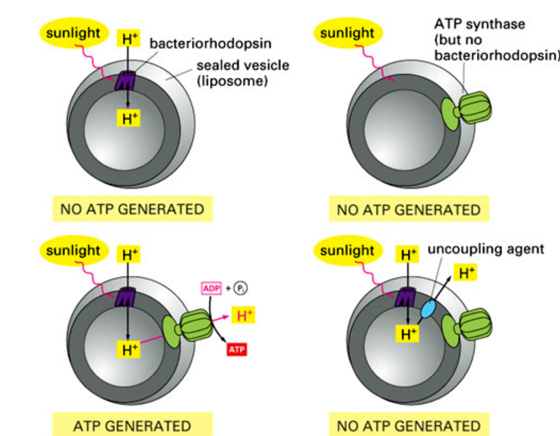
Over the past several years, Mitchell's chemiosmotic hypothesis has been widely accepted as the mechanism of coupling of electron transport and ATP synthesis. He was awarded Nobel Prize in Chemistry in 1978. This is result of accumulating experimental evidence supporting hypothesis.

Some of the evidence supporting Mitchell's chemiosmotic hypothesis is as follows.

Electron transport generates a proton gradient. The pH measured on the outside is lower than that measured inside the mitochondria.Only a proton gradient is needed to synthesize ATP. Electron transport is not required as long as there is another mechanism for generating a pH gradient.

A reconstitution experiment carried out by Racker and Stoeckenius (1974) showed that the generation of a proton gradient can result in ATP synthesis in a totally artificial system. In their experiment, mitochondrial ATPase complex from beef heart was inserted into artificial lipidbilayer. Also inserted in this bilayer was a membrane fragment containing protein, bacteterio-rhodopsin from purple bacteria *Halobacterium*, so called because the bacterio-rhodopsin gives the membrane a purple color. Bacterio-rhodopsin is a light-driven proton pump. Therefore, shining light on this artificial purple membrane formed a proton gradient, which was used by beef heart mitochondrial ATPase to synthesize ATP.

The electron transfer chains and the ATPases are asymmetrically oriented in the inner mitochondrial membrane. Asymmetric orientation is required to establish pH gradient. Random arrangement would not result in net gradient of protons and therefore, no proton-motive force for synthesis of ATP.



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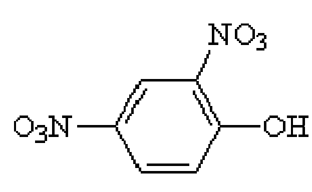

2,4-dinitrophenol
DNP

Compounds called uncouplers were found to collapse pH gradient by shuttling protons back across the membrane through the compounds. One such uncoupler, dinitophenol is shown above. In the presence of the uncoupler electron transport continues, but no ATP synthesis occurs.

This uncoupling of electron transport and ATP synthesis is useful to an organism. Such uncoupling can generate an energetically wasteful byproduct, heat. This occurs normally in many in hibernating animals, in newborn humans, and in mammals adapted to the cold. It occurs in a specialized tissue known as brown adipose tissue. An uncoupling protein thermogenin can accomplish this uncoupling and thus allow heat to be generated.

According to Hinkle et al (1991), value for ATP per NADH is 2.5 and ATP per $FADH_2$ is 1.5; although we are familiar with the numbers ATP per NADH = 3 and ATP per $FADH_2$ = 2.
The different values of 30 or 32 ATP/glucose depend on the method used to transport cytoplasmic NADH, formed by glycolysis, into the mitochondria, i.e. the shuttles.

Source: http://fig.cox.miami.edu/~cmallery/255/255etc/chemiosm.htm