

Mechanisms of Redox-Linked Proton Translocations: An Introduction

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Received May 1, 1991

The present volume is a collection of short reviews concentrating on the mechanisms of redox-linked proton translocation in biological systems. The authors were asked to concentrate on mechanism rather than phenomenology although, with the notable exception on the Q-cycle, this is an area where little is known at the molecular level.

The concept that redox reactions can be linked to the translocation of protons evolved from early work of gastric secretion and plant ion transport (see Weber, 1986). It was Mitchell who made the conceptual leap to a specific mechanism involving vectorial chemistry (Mitchell, 1961, 1966, 1968). The clear predictions of the model were increasingly used as a basis for successful experimentation so that in the late seventies the focus of attention changed to the mechanisms underlying the phenomena, in particular the molecular basis of proton translocation. Originally, Mitchell (1966) proposed a loop arrangement of the respiratory chain whereby electron transport over any particular span occurred as two half reactions, one proton-associated and one electron-translocating. A half-loop system, involving electron translocation between protonated reductant and deprotonated oxidant on opposite sides of a membrane, had been developed earlier by Lundegardh (1951, 1952). With the complete loop, proton stoichiometry could be one or two protons per two-electron transfer equivalent depending on the nature of the carrier. Problems of stoichiometry and the "anomalous" kinetic behavior of the cytochromes *b* in loop 2 of the electron transport chain led to the development of the Q-cycle mechanism (Mitchell, 1975) for the *bc*₁ and *bf*₁ complexes of the mitochondrial and photosynthetic redox chains.

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The success of the concept of redox-linked proton translocation by direct-coupled ligand conduction is discussed by West in this volume. It is clear that the best established cases for this type of mechanism are the Q-cycles of chloroplasts, mitochondria, and certain bacteria (see Trumpower, 1990). It is less certain how this type of mechanism applies to other redox-linked systems. Weiss and Friedrich (this volume) discuss the problems of involving flavin and coenzyme Q in proton translocation by the nicotinamide adenine dinucleotide reductase (complex I). Jackson (this volume) argues that proton translocation by the nicotinamide adenine dinucleotide transhydrogenase can also be compatible with direct mechanisms of coupling. The position with cytochrome oxidase is not so clear. Wilson and Bickar (this volume) discuss the various proposals for "direct" and "indirect" coupling in the context of evidence for redox-linked conformational changes in the enzyme. Redox-linked proton translocation by plasma membrane systems is also addressed by Crane *et al.* (this volume). These systems activate proton release in both plant and animal cells by mechanisms which can include Na^+/H^+ antiport, H^+ ATPase, and possibly protonated electron carriers in the membrane.

It is clear that several different mechanisms have evolved in living systems to serve the unifying chemiosmotic concept. The non redox-linked systems of Archaeobacteria, the mechanism of proton translocation by the F_1F_0 ATPase, as well as the adaption of certain organisms to a primary sodium-motive mechanism suggest that it is unlikely that we should expect a single evolved mechanism for proton translocation in redox-linked systems. It is hoped that this mini-review volume will stimulate some experimental testing of the various models proposed and serve as a basis for fresh speculation.

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