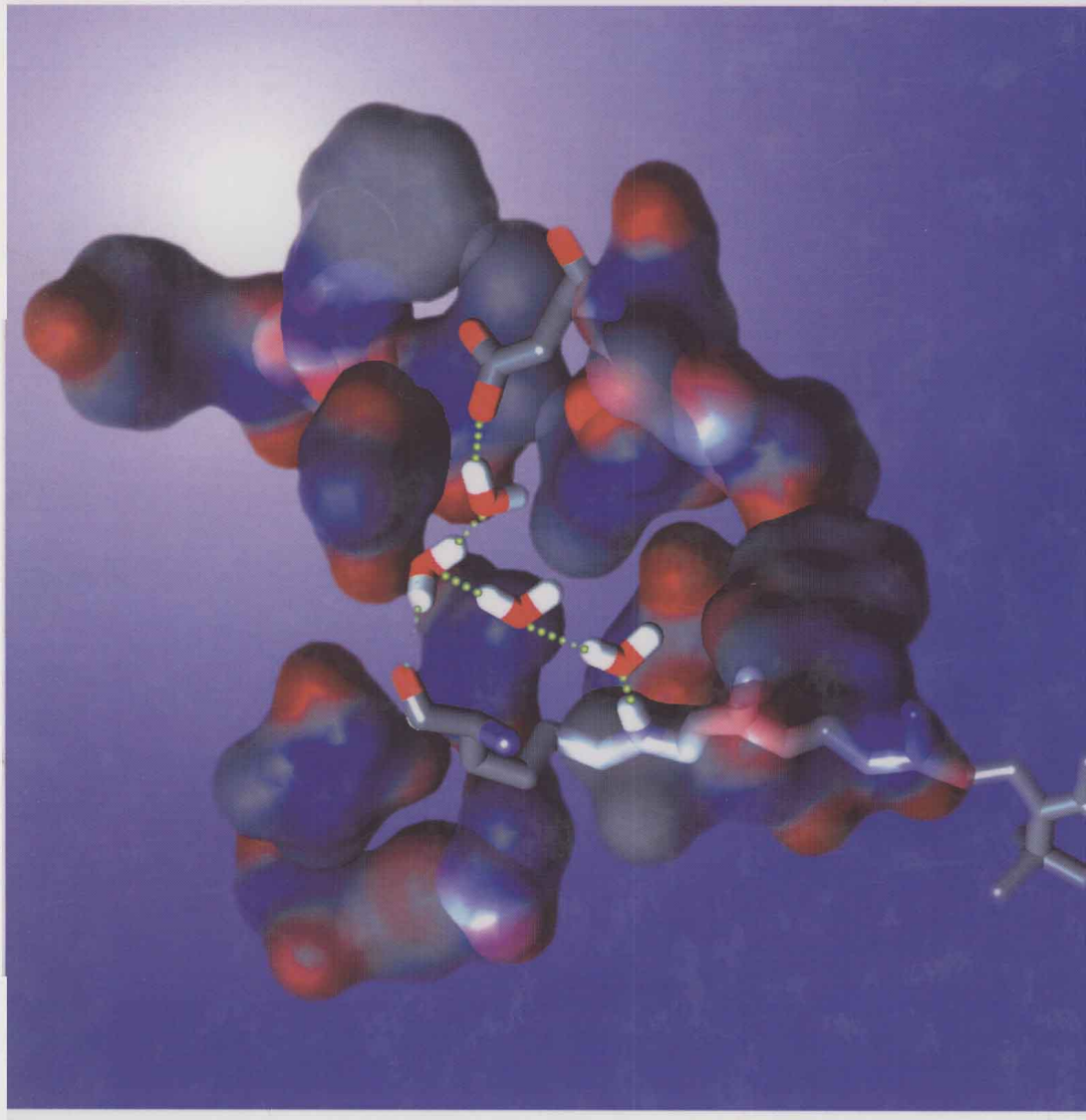
RSC Biomolecular Sciences

Edited by Mårten Wikström

Biophysical and Structural Aspects of Bioenergetics



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Preface

Molecular bioenergetics is a strongly interdisciplinary field of biochemistry, biophysics and molecular biology. It is concerned with how energy derived either from sunlight or from cellular respiration is primarily transduced into an electrochemical proton gradient across a coupling membrane, and how this gradient is subsequently utilised for energy-requiring reactions such as ATP synthesis or active transport. This field thus intimately involves biological membranes and membrane proteins. Bioenergetics has traditionally also included the cellular and tissue levels of organisation, as well as diseases. Pathophysiological, or 'systems' bioenergetics, is indeed today a very active research field, which includes studies of reactive oxygen species ('oxygen radicals'), apoptosis, mitochondrial diseases, and the process of aging. However, this book focuses on the physicochemical core of bioenergetics, which in the last 20 years has advanced greatly by the resolution of 3D structures of several of the protein complexes that catalyse key energy-transducing reactions in chloroplasts, mitochondria, and bacteria.

Molecular bioenergetics is a unique field in many ways. Due to its intrinsic multidisciplinarity, it is an excellent research arena for students who desire a broad education in biochemistry and biophysics, including molecular and structural biology. Such a comprehensive education is unfortunately becoming rare at this time, perhaps due to the current strong research focus on genomics and cell biology. Nevertheless, the necessity of ultimately understanding biological structures and reactions at the atomic level is obvious, which may give some consolation.

This book is by no means a comprehensive treatise, but rather a 'snapshot' of recent research and the state-of-the-art of this field. Yet, the reader can get a much broader insight into this and related fields from the extensive citations in each chapter. The book is comprised of 16 articles written by a group of active and authoritative researchers. The emphasis is on structure, and particularly on how the molecular structures may 'come alive' during their bioenergetic function. A functional description (mechanism) on the atomic level goes beyond static structures of single conformational states, and therefore requires a deeper level of understanding, which can be obtained by time-resolved biophysical methods, by quantum-mechanical and classical dynamics calculations and simulations, or by trapping series of transient intermediate states and solving their 3D structures, as for the case of bacteriorhodopsin (see cover picture). Such research is often strongly hypothesis-driven: the formulation of mechanistic models is a strong driving force in science the importance of which must not be underestimated.

I am very grateful to all the authors for their contributions to this book, to Dr. Janos Lanyi for kindly providing the cover picture, and especially to Mrs. Annie

Jacob and Miss Katrina Turner of the Royal Society of Chemistry for their patience and humour, which made the editor's work pleasant.

Mårten Wikström
Helsinki, May 2005

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CHAPTER 1

Principles of Molecular Bioenergetics and The Proton Pump of Cytochrome Oxidase

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1 Introduction: General Principles of Bioenergetic Systems

All of the bioenergetic enzymes described in this book can couple an exergonic or free-energy yielding reaction to the electrogenic movement of charged species across the membrane, generating a protonmotive force. In the case of bacteriorhodopsin, the driving reaction is the absorption of a photon, for the bc_1 complex, the oxidation of ubiquinol by cytochrome c is the driving force, and for the respiratory oxidases, the reduction of O_2 to H_2O provides the impetus. In this book, the principles utilized by a number of these systems are detailed with an emphasis on recent structural studies.

It is convenient to classify two classes of mechanisms used to generate a transmembrane voltage:

(1) Mechanisms utilizing an oxidoreduction loop.
(2) True ion (proton) pumps.

1.1 Oxidoreduction Loops

The principle of coupling different chemical reactions is central to biology and is accomplished in a number of ways. Many of the systems that generate a protonmotive force can be understood in terms of Mitchell's chemiosmotic oxidoreduction loop.[1] This is illustrated by the example shown in Figure 1, which shows a redox loop formed from the anaerobic respiratory system comprised of formate dehydrogenase and nitrate reductase enzymes from *E. coli*. Recently, the structures of each of these two enzymes were determined.[2,3] The topology of the catalytic active sites assures that the

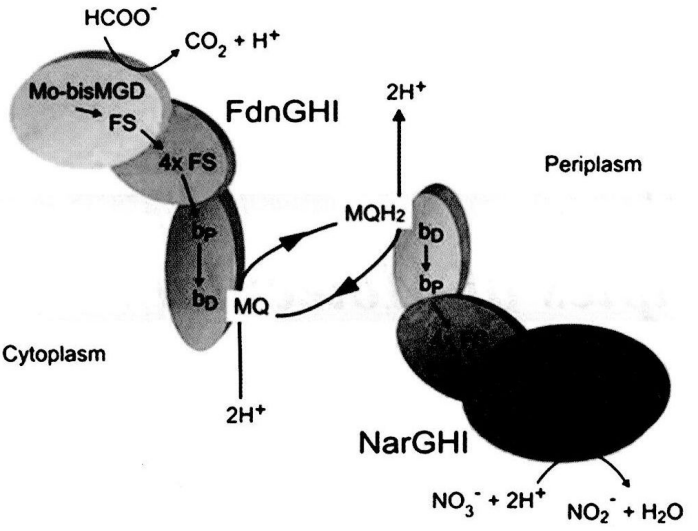

Figure 1 *Proposed mechanism for the protonmotive force generating redox loop by nitrate reductase (NarGHI) and formate dehydrogenase (FdnGHI) from* E. coli.[3] *MQ and* MQH_2 *are menoquinone and menaquinol, respectively;* b_D *and* b_P *indicate the distal and proximal hemes, respectively; FS indicates [Fe-S] clusters; Mo-bisMGD is the molybdenum cofactor. Note that only electrons cross the membrane resulting in the transmembrane voltage*

net reaction results in the generation of a protonmotive force.[3] Formate dehydrogenase oxidizes formate on the periplasmic side of the membrane (the positive or P-side) and electrons are delivered through a series of metal centers to a menaquinone reductase site located near the cytoplasmic surface (the negative or N-side of the membrane). The formate dehydrogenase, thus, separates the oxidative and reductive half-reactions on opposite sides of the membrane. Protons are released in the periplasm upon formate oxidation and protons are taken up from the cytoplasm upon the reduction of menaquinone. The actual charge crossing the chemiosmotic barrier is the electron.

Reduced menaquinol is a neutral, hydrophobic compound and can diffuse freely within and across the membrane bilayer. The nitrate reductase enzyme has a menaquinol oxidation site located near the periplasm, whereas the site where nitrate is reduced to nitrite is located on the opposite side of the membrane. Electrons are transferred across the membrane between these active sites to couple the two half-reactions catalyzed by the enzyme (see Figure 1). The full reaction of nitrate reductase, therefore, is coupled to the release of protons in the periplasm, the uptake of protons from the cytoplasm and the transfer of charges, in the form of electrons, across the membrane.

The net reaction of both of these enzymes together results in the transfer of four protons from the cytoplasm to the periplasm for each formate oxidized and nitrate reduced. Points to note are

(1) The actual charges crossing the membrane are electrons and not protons.
(2) The net transfer of protons is due to the vectorial placement of the enzyme active sites so that the oxidation and reduction half-reactions occur on opposite sides of the membrane.

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