Preface

This special issue is devoted to enzymes that link proton movement to energy transduction, with particular emphasis on the structural basis for this linkage. Included are redox enzymes that link proton movement to organic reaction chemistry, flagellar proteins that link proton movement to mechanical motion, and enzymes, the ATP synthase and V-ATPase, that link proton movement to organic reaction chemistry through an intervening mechanical movement.

The first review discusses the structural basis for proton pumping by bacteriorhodopsin, which links transmembrane proton movement to photochemistry and is generally considered the paradigm of proton pumps. Whereas bacteriorhodopsin is structurally quite simple and well-understood, NADH-ubiquinone oxidoreductase, the topic of the second review, is structurally quite complex and is one of the least well-understood protonmotive enzymes at this point in time. As future research narrows the gap in our understanding of these two enzymes, it will be interesting to see whether the latter, more complex enzyme utilizes conformational changes embodied in the simplest proton pump. Transhydrogenase, the topic of the third review, provides an interesting example of proton movement occurring some distance from a conformational change that controls hydride ion transfer between bound nucleotides.

Formate dehydrogenase and the succinate-quinone oxidoreductases use quinones as hydrogen accepting cofactors. Although these enzymes are not energy transducing when acting by themselves, they can form a protonmotive loop when sequentially linked to a second enzyme, such that quinone is reduced and hydroquinone is oxidized on opposite sides of a membrane. In such a protonmotive loop, protons are moved through the membrane by hydroquinone diffusion. The cytochrome bc_1 complex also uses a hydroquinone, ubiquinol, to carry protons between quinone reduction and quinol oxidation sites within the enzyme on opposite sides of the membrane. Proton conduction pathways to and from the hydrophobic environment in which the quinone redox reactions occur are discussed in three reviews on these enzymes.

Cytochrome *c* oxidase uses the energy from reduction of oxygen to pump protons across the membrane in which it resides. This requires entry of protons to the site where water is synthesized and movement of protons through the membrane. Since cytochrome *c* oxidase has no diffusible hydrogen carrier these proton movements must occur through channels in the protein and these must be gated to confer directionality on the proton movements. The crystal structures of cytochrome *c* oxidase have revealed the channels by which protons enter the enzyme, but how protons exit and how directionality is controlled are not yet understood. The possible mechanisms are discussed in a review on this enzyme.

Electrostatic interactions play a key role in protonmotive enzymology, and as crystal structures of protonmotive enzymes become available, it is possible to apply structure-based electrostatic calculations to these enzymes. A review has thus been included in which principles of charge stabilization within membrane proteins are discussed for a photosynthetic reaction center, cytochrome *c* oxidase, and quinol-fumarate oxidoreductase.

Two reviews are devoted to ATP synthase, which is perhaps the best known protonmotive enzyme. This enzyme uses proton movement to drive rotary motion of subunits, which in turn causes a nucleotide binding change that results in ATP synthesis. One review summarizes current understanding of this 'mechanoenzymatic' mechanism, while a second discusses the function of two regulatory subunits, γ and ε, in regulation of the chloroplast ATP synthase. Reversal of the ATP synthase reaction results in proton movement driven by ATP hydrolysis, and the structurally similar V-ATPases use this reaction to acidify organelles and to pump protons across the plasma membrane of many eukaryotic cells. The structural basis for this proton movement is also reviewed.

Approximately four decades ago Peter Mitchell introduced the notion that protonmotive force could do work. The chemiosmotic mechanism of energy transduction did not gain immediate acceptance, but with the clarity of hindsight, the principles seem so obvious as to be self-evident. The last review in this special issue is thus devoted to one of the clearest examples of 'working protons', flagellar movement.

B.L. Trumpower
Biochemistry Department of Medical School,
Hanover, NH 03755, USA
E-mail address: bernard.l.trumpower@dartmouth.edu

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