DAVID KEILIN'S RESPIRATORY CHAIN CONCEPT AND ITS CHEMIOSMOTIC CONSEQUENCES

Nobel Lecture, 8 December, 1978

by
PETER MITCHELL
Glynn Research Institute, Bodmin, Cornwall, U. K.

0. INTRODUCTION

It was obviously my hope that the chemiosmotic rationale of vectorial metabolism and biological energy transfer might one day come to be generally accepted, and I have done my best to argue in favour of that state of affairs for more than twenty years. But, it would have been much too presumptuous to have expected it to happen. Of course, I might have been wrong, and in any case, was it not the great Max Planck (1928, 1933) who remarked that a new scientific idea does not triumph by convincing its opponents, but rather because its opponents eventually die? The fact that what began as the chemiosmotic hypothesis has now been acclaimed as the chemiosmotic theory - at the physiological level, even if not at the biochemical level - has therefore aroused in me emotions of astonishment and delight in full and equal measure, which are all the more heartfelt because those who were formerly my most capable opponents are still in the prime of their scientific lives.

I shall presently explain the difference between the physiological and the biochemical levels at which the chemiosmotic theory has helped to promote useful experimental research. But let me first say that my immediate and deepest impulse is to celebrate the fruition of the creative work and benevolent influence of the late David Keilin, one of the greatest of biochemists and - to me, at least - the kindest of men, whose marvellously simple studies of the cytochrome system, in animals, plants and microorganisms (Keilin, 1925), led to the original fundamental idea of aerobic energy metabolism: the concept of the respiratory chain (Keilin, 1929; and see Nicholls, 1963; King, 1966). Perhaps the most fruitful (and surprising) outcome of the development of the notion of chemiosmotic reactions is the experimental stimulus and guidance it has provided in work designed to answer the following three elementary questions about respiratory chain systems and analogous photoredox chain systems: What is it? What does it do? How does it do it? The genius of David Keilin led to the revelation of the importance of these questions. In this lecture, I hope to show that, as a result of the painstaking work of many biochemists, we can now answer the first two in general principle, and that considerable progress is being made in answering the third.

Owing to the broad conceptual background, and the very wide range of practical application of the chemiosmotic theory, I have had to be rather

selective in choosing aspects to review. I have chosen to consider the evolution of the chemiosmotic theory from earlier fundamental biochemical and physicochemical concepts in three perspectives: 1, a middle-distance physiological-cum-biochemical perspective; 2, a longer physicochemical view; and 3, a biochemical close-up. These perspectives involve general considerations of biochemical theory and knowledge, and scope is not available to discuss experimental procedures on this occasion.

1. PHYSIOLOGICAL-CUM-BIOCHEMICAL PERSPECTIVE

A. *Oxidative and Photosynthetic Phosphorylation*

During the two decades between 1940 and 1960, the mechanism of oxidative phosphorylation (by which some 95% of the energy of aerobic organisms is obtained), and the basically similar mechanism of photosynthetic phosphorylation (by which much of the energy available from plant products is initially harvested from the sun) was recognised as one of the great unsolved problems of biochemistry. At the beginning of this period, the work of David Keilin (1925, 1929) on the cytochrome system, and work by Warburg, Wieland and others on the respiratory hydrogen carriers, had already led to the concept of the respiratory chain: a water-insoluble complex of redox carriers, operating serially between the reducing substrates or coenzymes and molecular oxygen (see Nicholls, 1963; King, 1966).

As indicated in Fig. 1, according to Keilin's chemically simple concept of

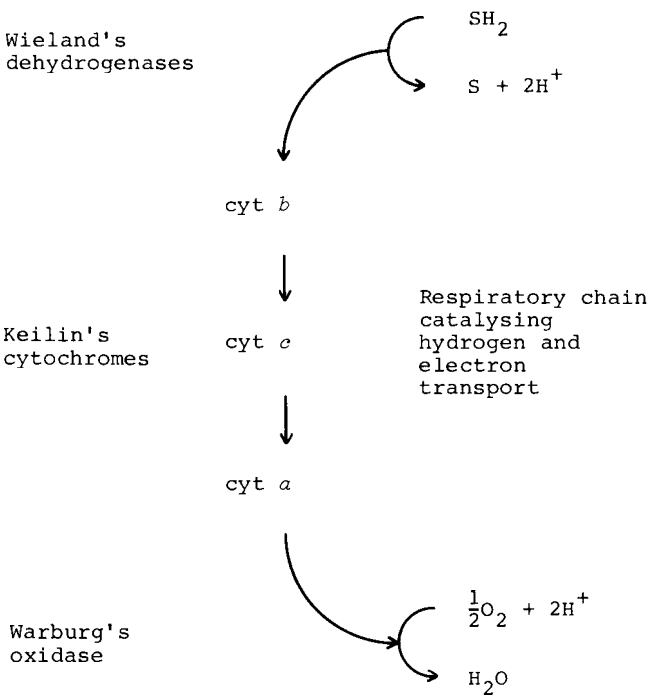


Fig. 1. David Keilin's chemically simple respiratory chain concept.

the respiratory chain, the respiratory-chain carriers (or their complexes of molecular dimensions) were involved chemically only in redox reactions. However, when, following the pioneer work of Kalckar (1937), Belitser & Tsybakova (1939), Ochoa (1940), Lipmann (1941, 1946), Friedkin & Lehninger (1948), and Arnon, Whatley & Allen (1954), attention was directed to the mechanism by which the redox process was coupled to the phosphorylation of ADP in respiratory and photoredox metabolism, it was natural for the metabolic enzymologists who were interested in this problem to use substrate-level phosphorylation as the biochemical model, and to assume that the mechanism of coupling between oxidation and phosphorylation in respiratory and photoredox chains would likewise be explained in terms of the classically scalar idiom of metabolic enzymology (see Slater, 1976).

In 1953, the general chemical coupling hypothesis, summarised in Fig. 2, was given formal expression in a historically important paper by Slater, which defined the reactions of the energy-rich intermediates at several coupling sites along the mitochondrial respiratory chain. Accordingly,

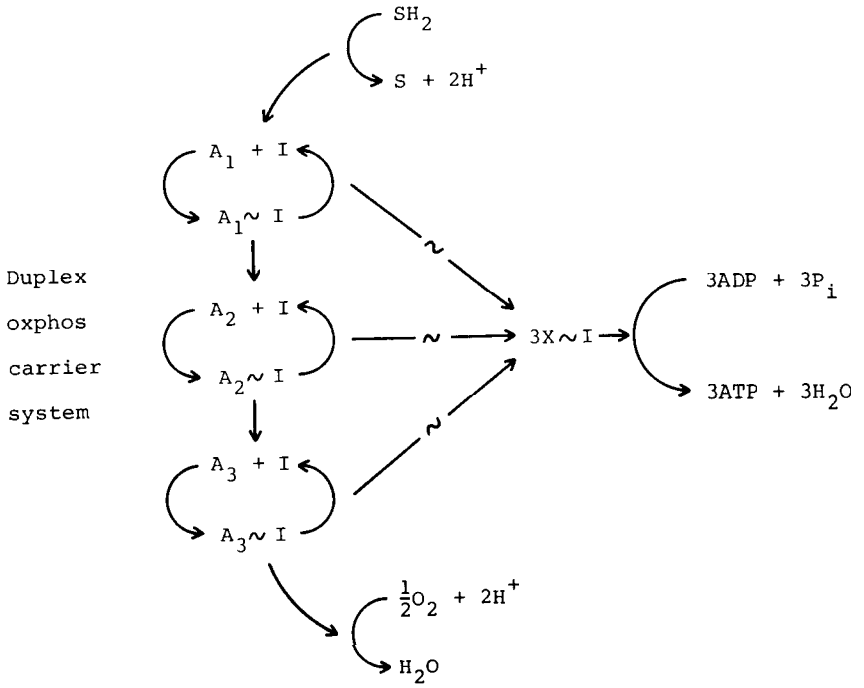


Fig. 2. Phosphorylating respiratory chain: Chemical coupling hypothesis. A~I and X~I represent hypothetical high-energy chemical intermediates; and the symbol ~ represents the so-called high-energy bond.

many expert metabolic enzymologists made it their prime objective to identify the energy-rich intermediates or other coupling factors supposed to be responsible for coupling oxidoreduction to phosphorylation in redox chain systems (Slater, 1953; Boyer et al., 1954; Chance & Williams, 1956;

Slater, 1958; Lehninger, 1959; Slater & Hulsmann, 1959; Chance, 1961; Racker, 1961; Lehninger & Wadkins, 1962; Williams, 1962; Boyer, 1963; Green et al., 1963; Hatefi, 1963; Ernster & Lee, 1964; Lardy et al., 1964; Griffiths, 1965; Racker, 1965; Sanadi, 1965; Slater, 1966; Chance et al., 1967). This development caused Keilin's chemically-simple concept of the respiratory chain to be almost universally rejected in favour of a chemically duplex concept according to which respiratory chain components participated directly, not only in the known redox changes, but also in other chemical changes involving the energy-rich intermediates - just as the phosphorylating glyceraldehyde-3-phosphate dehydrogenase is involved in both oxidative and phosphorylative reactions.

By the end of the two and a half decades between 1940 and 1965, the field of oxidative phosphorylation was littered with the smouldering conceptual remains of numerous exploded energy-rich chemical intermediates; the remarkable uncoupling action of 2,4-dinitrophenate and of other chemically unrelated reagents, and of physical membrane-lytic treatments, remained obscure; and the process of hypothesis-building, needed to keep faith with the chemical-coupling notion, reached such fantastic proportions as to be hardly intelligible to those outside the field (see Mitchell, 1961 c, 1966, 1967 a). Nevertheless, the quest for the energy-rich intermediates continued through the nineteensixties and persisted into the nineteenseventies with only a minor broadening of the conception of the type of coupling mechanism favoured by many of the metabolic enzymologists (Painter & Hunter, 1970; Storey, 1970, 1971; Slater, 1971, 1974, 1975; Chance, 1972, 1974; Hatefi & Hanstein, 1972; Wang, 1972; Cross & Boyer, 1973; Boyer et al., 1973, 1977; Ernster et al., 1973, 1974; Green, 1974; Weiner & Lardy, 1974; Griffiths et al., 1977; Nordenbrand et al., 1977). This conceptual broadening, which began to occur during the early nineteensixties, stemmed from ingenious suggestions by Boyer, Chance, Ernster, Green, Slater, Williams and others (see Boyer, 1965; Slater, 1971, 1974; Ernster et al., 1973). As indicated by Fig. 3, they assumed that coupling may be achieved through a direct conformational or other non-osmotic physical or chemical interaction - that might, for example, involve protons as a localised anhydrous chemical intermediate (Williams, 1962, 1970; and see Ernster, 1977 a; Mitchell, 1977 a), or might involve electrical interaction (Green, 1974) - between the redox carrier proteins and certain catalytic components associated with ATP synthesis in the supposedly duplex respiratory chain system, often described as the "phosphorylating respiratory chain".

Soon after 1950, it began to be recognised that the water-insoluble property of preparations of respiratory chain and photoredox chain complexes was related to the circumstance that, in their native state, these complexes were part of the lipid membrane system of bacteria, mitochondria and chloroplasts. But, such was the lack of liaison between the students of transport and the students of metabolism, that the significance of this fact for the field of oxidative and photosynthetic phosphorylation was

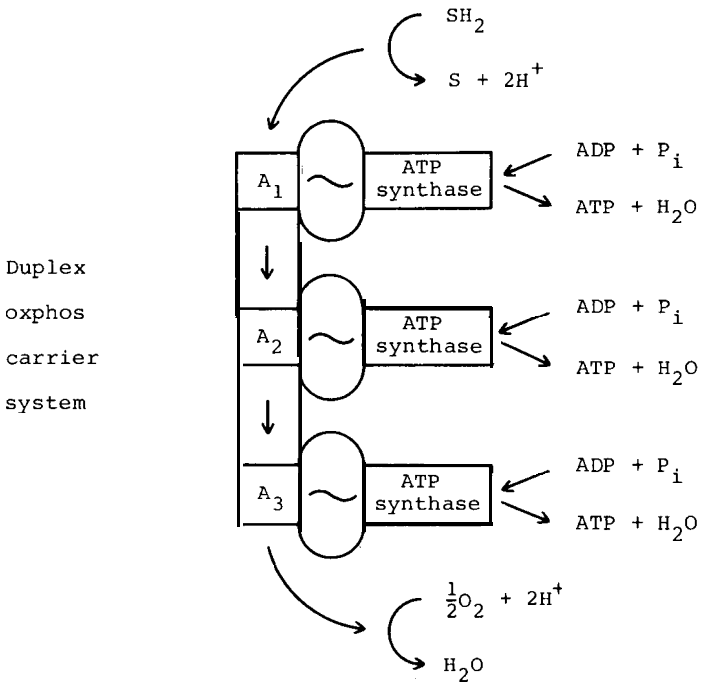


Fig. 3. Phosphorylating respiratory chain: Local interaction coupling hypothesis. The symbol ~ represents a localised "high-energy" chemical intermediary or physical state.

not appreciated, despite suggestive clues provided, for example, by Lundegardh (1945), Robertson & Wilkins (1948), Ussing (1949), Davies & Ogston (1950), Conway (1951) and me (Mitchell, 1954). These clues suggested that some osmotic type of protonic coupling mechanism might be feasible (see Robertson, 1960, 1968; Lehninger, 1962). It was in this context that I began to take an active outsider's interest in this fundamental problem of energy metabolism in the nineteenfifties (and occasionally talked to David Keilin about it), while I was mainly engaged in trying to develop general principles of coupling between metabolism and transport, by means of the biochemical concepts of chemiosmotic group-translocation reactions and vectorial metabolism (Mitchell, 1954, 1956, 1957, 1959, 1961a, b; Mitchell & Moyle, 1956, 1958a, b). I shall define these concepts more fully later. For the moment, suffice it to remark that it was these essentially biochemical concepts (Mitchell, 1961 a, b, 1962, 1963, 1967b, c, 1970a, b, 1972b, 1973 a, b, c, 1977c), and not my relatively subsidiary interest in energy metabolism, that led me to formulate the coupling hypothesis, summarised in Fig. 4, which came to be known as the chemiosmotic hypothesis. As it happened, the main protonmotive ATPase principle of this hypothesis was first outlined at an international meeting held in Stockholm in 1960 (Mitchell, 1961b). My motivation was simply a strategic conjectural one. There was a chance worth exploring that the chemiosmotic rationale might provide a generally acceptable conceptual framework in the field of membrane bioenergetics and oxidative phosphorylation, and that, if so, it

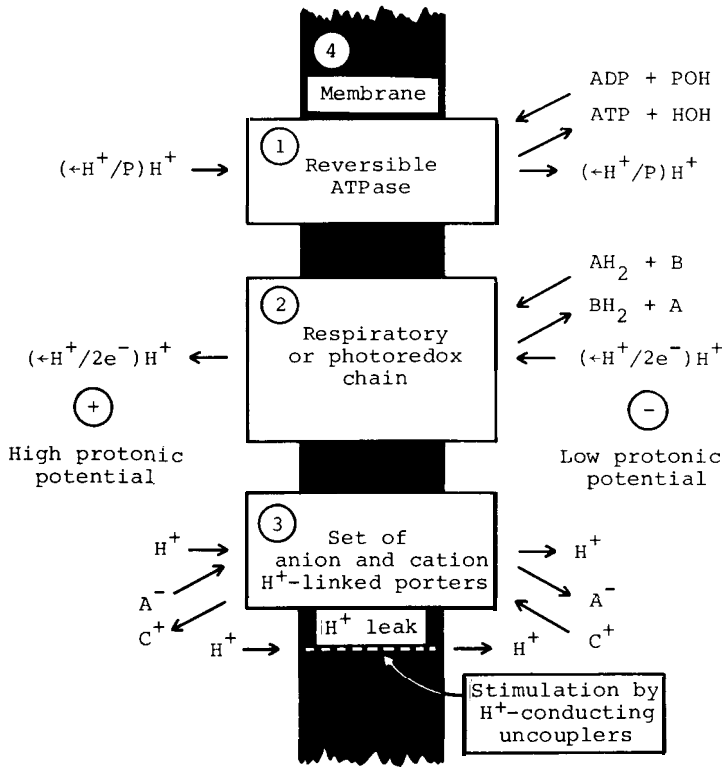


Fig. 4. Chemiosmotic hypothesis: Physiological level.

might encourage more adventurous and successful interdisciplinary research by improving communication and acting as a kind of navigational aid (see Mitchell, 1961c, 1963, 1976a, 1977b).

There are two conceptual levels at which the chemiosmotic rationale has helped to promote useful experimental research.

The level represented by Fig. 4 is essentially physiological. It aims to answer the question: what does it do? At this conceptual level one makes use of the general principle of coupling by proticity, the protonic analogue of electricity. Separate protonmotive redox (or photoredox) and reversible protonmotive ATPase complexes are conceived as being plugged through a topologically closed insulating membrane between two proton-conducting aqueous media at different protonic potential. Thus, coupling may occur, not by direct chemical or physical contact between the redox and reversible ATPase systems, but by the flow of proticity around an aqueous circuit connecting them. I use the word proticity for the force and flow of the proton current by analogy with the word electricity, which describes the force and flow of an electron current (Mitchell, 1972 a, 1976 a). However, the total protonic potential difference Δp has both electric ($\Delta\psi$) and chemical activity (ΔpH) components, according to the equation:

$$\Delta p = \Delta\psi - Z\Delta\mathrm{pH} \qquad (1)$$

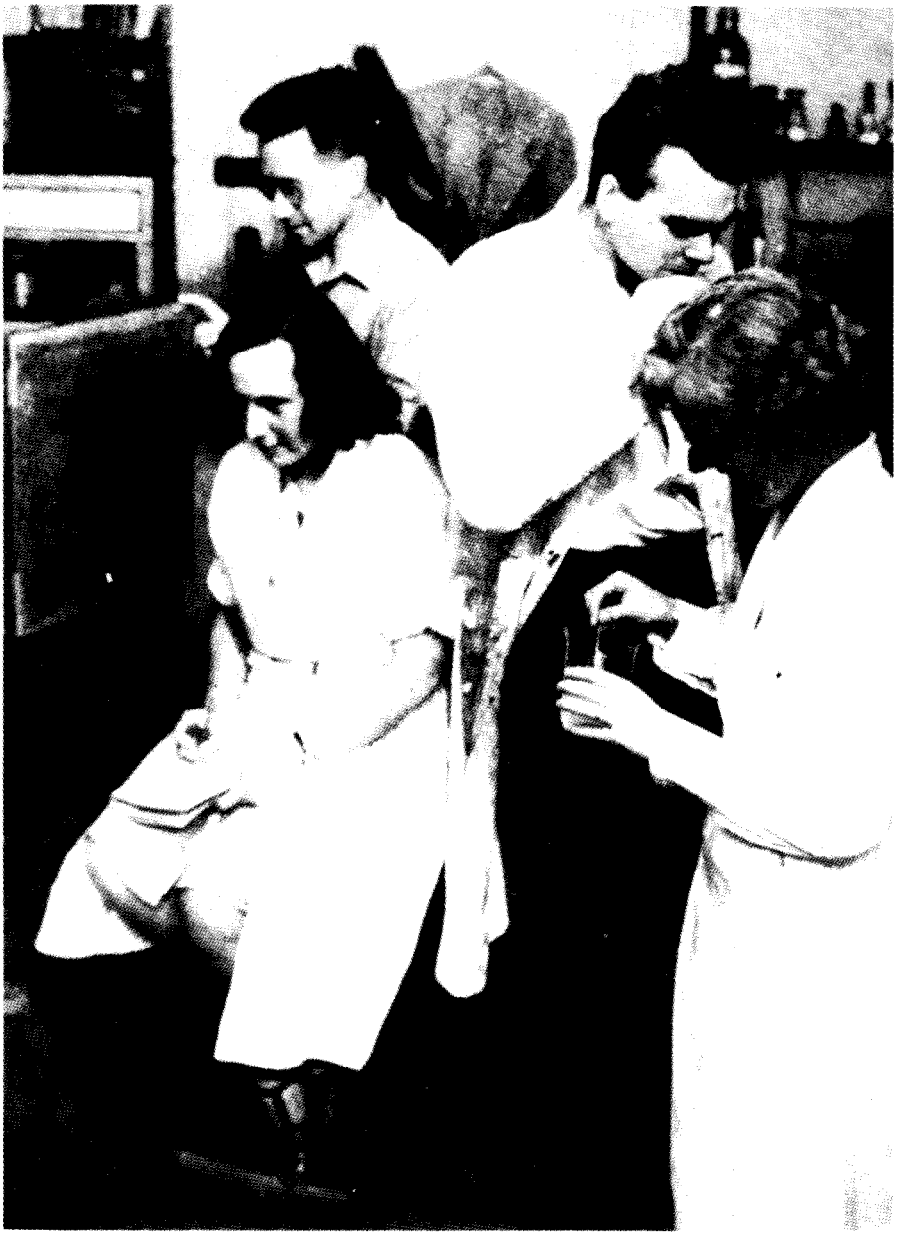


Fig. 6. Research at the bench in 1942 or 1943. Department of Biochemistry, Cambridge, England. From left to right: Joan Keilin, Jim Danielli. Peter Mitchell, Mary Danielli.

ologist and was involved: first, in studies of a functional aspect of the plasma membrane of bacteria, which I called the osmotic barrier (Mitchell, 1949); and soon after, in studies of the specific uptake and exchange of inorganic phosphate and arsenate through a catalytic system present in the osmotic barrier of staphylococci (Mitchell, 1954; and see Mitchell & Moyle, 1956). This enabled me to give my full attention to the functional and

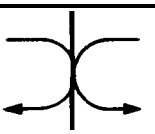
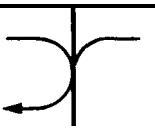
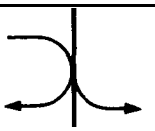
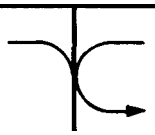
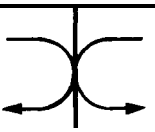
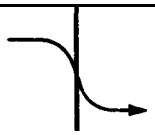
EXAMPLE	CHEMI-OSMOTIC PROCESS LEFT PHASE	PHOSPHOKINASE IN MEMBRANE	RIGHT PHASE	GROUPS TRANS-PORTED
1	ATP ADP		S SP	P-
2	ATP ADP + SP		S	S-
3	ATP + S ADP		SP	S- P-
4	ATP		S ADP + SP	ADP- P-
5	ADP		S + ATP SP	ADP-
6	ATP SP		S ADP	ADP- S-
7	ATP + S		ADP + SP	ADP- P- S-

Table 1. Alternative translocation-specific chemiosmotic processes catalysed by a hypothetical phosphokinase in a membrane (from Mitchell & Moyle, 1958b).

could be at the microscopic level, by pairing and enclosure of a 'microscopic internal phase' between neighbouring catalytic units, thus giving rise to a chemical coupling effect. As illustrated in Fig. 11 A, we cited as possible examples the NADP-linked isocitrate dehydrogenase and the malic enzyme, which catalyse consecutive oxidation and decarboxylation reactions (with oxalosuccinate and oxaloacetate respectively as intermediates trapped in the microscopic internal phase). We pointed out that such pairing of catalytic units could be developed in three dimensions for branching or cycling reaction sequences in enzyme complexes (Mitchell &

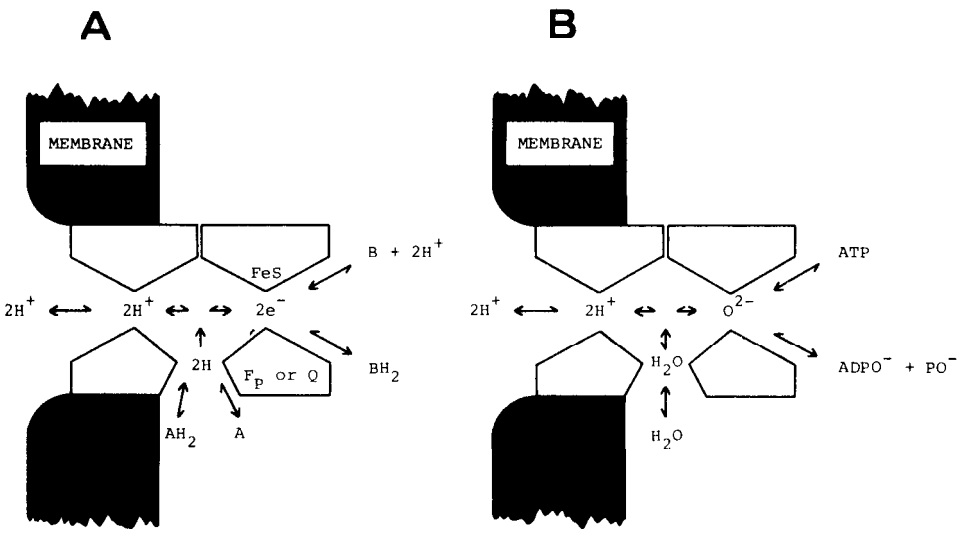


Fig. 12. Macroscopic and microscopic topological principles developed together in: A, protonmotive redox loop; B, protonmotive ATPase (hydrodehydration loop).

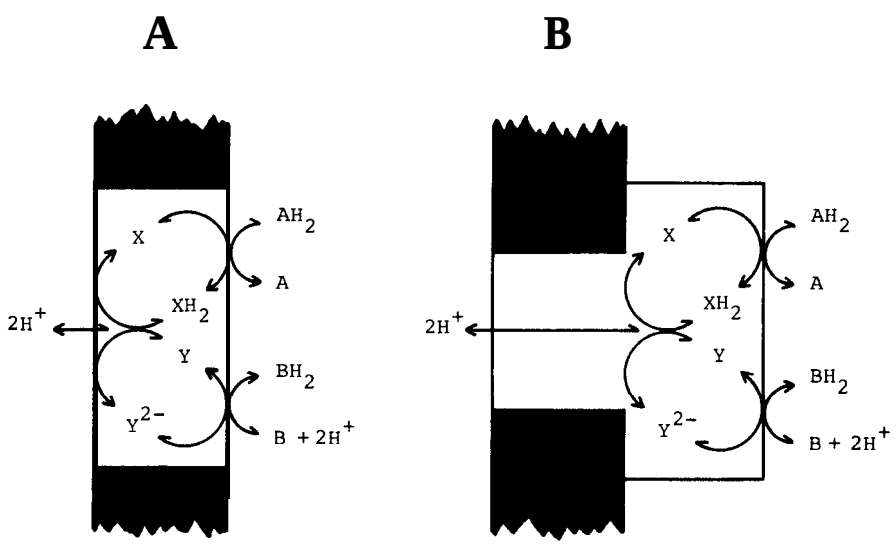


Fig. 13. Direct redox loop mechanism in cycling carrier idiom: A, plugged through the membrane; B, connected through a proton-conducting component (following Mitchell, 1966 and 1968).

C. The Protonmotive Respiratory Chain and Photoredox Chain: What is it? How does it do it?

Let us return to the theme of David Keilin's respiratory chain in the light of the essentially biochemical concept of direct group-translocating or group-conducting chemiosmotic mechanisms.

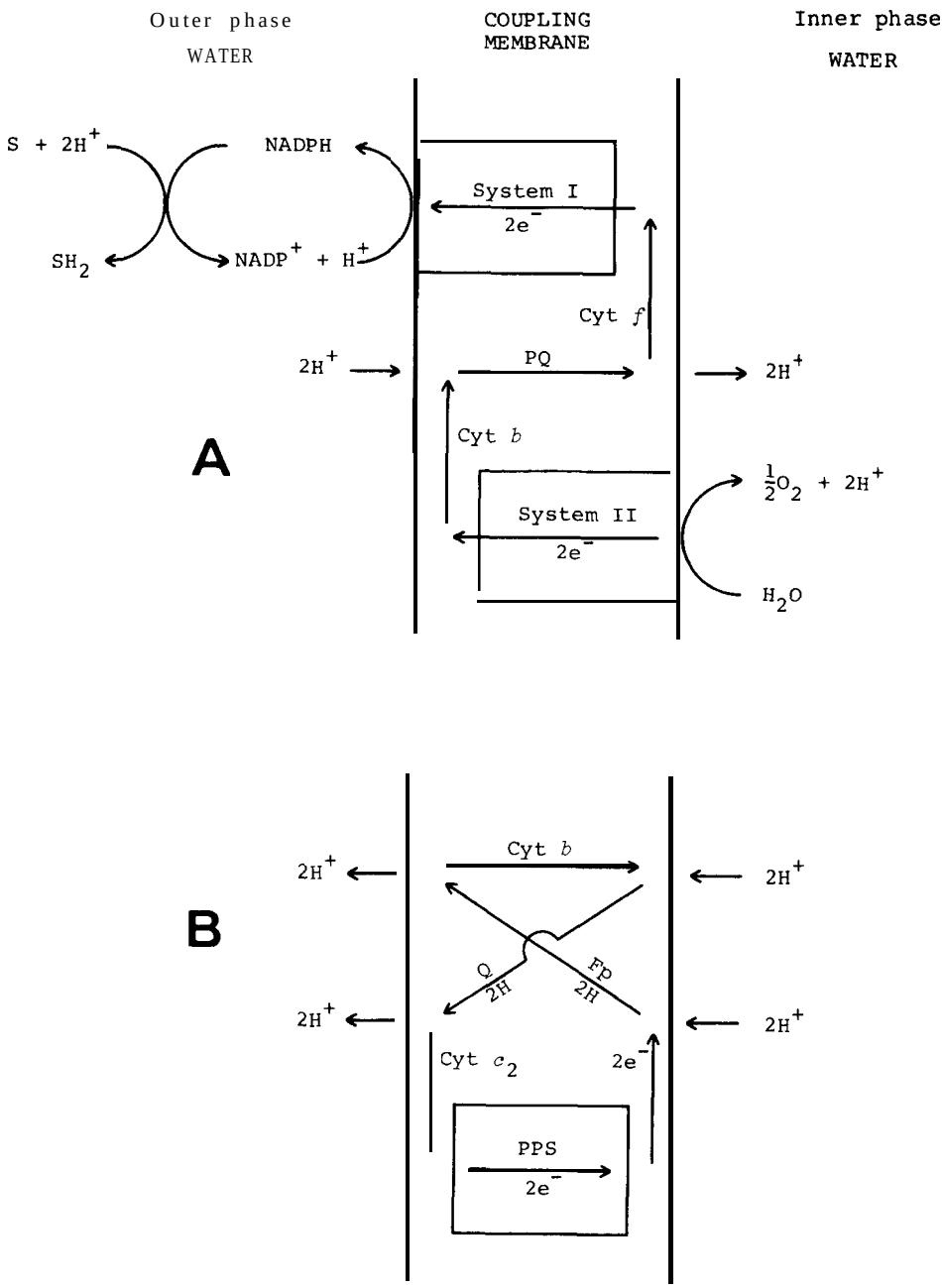


Fig. 16. Suggested protonmotive photoredox chain systems: A, for chloroplast non-cyclic photoredox activity; B, for bacterial cyclic photoredox activity. System I, System II and PPS stand for photosynthetic pigment systems (after Mitchell, 1966, 1967a).

discuss in a little more detail later, summarise recent knowledge about the mitochondrial respiratory chain (A), the chloroplast non-cyclic photoredox chain (B), and the reversible ATPases (F_0F_1 and CF_0CF_1), driven by these systems. It is noteworthy that these schemes show remarkable similarities.

diffusion of hydrogen atoms and electrons in opposite directions, adding up to net proton translocation across the coupling membrane.

2. A LONG PHYSICOCHEMICAL VIEW OF CHEMICOMOTIVE SYSTEMS

The first protonmotive device conceived by man was the electromotive hydrogen-burning fuel cell, invented by the remarkable William Grove in 1839. It is, perhaps, not self evident that such a fuel cell for generating electricity is also, potentially, a generator of proticity. This is illustrated by the diagrams of the hydrogen-burning fuel cell shown in Fig. 18. It simply depends where one opens the circuit to conduct away the power for external use. In A, the circuit is opened in the electron conductor to give electricity. In B, the circuit is opened in the proton conductor to give proticity (Mitchell, 1967a).

The fuel cell is a beautiful example of the truth of the principle, enunciated by Pierre Curie at the end of the last century (Curie, 1894), that effects cannot be less symmetric than their causes. The phenomena of transport in the fuel cell arise from the intrinsically vectorial disposition of the chemical reactions at the anisotropic metal/aqueous catalytic electrode interfaces (Liebhafsky & Cairns, 1968). Thus, the scalar group-potential differences of the chemical reactions are projected in space as vectorial chemical fields of force corresponding to the chemical group-potential gradients directed across the electrode interfaces. These simple considerations illustrate nicely the nonsensical character of the question asked by certain theoreticians in the context of the coupling between transport and metabolism around 1960, and still persisting in some circles: how can scalar chemical reactions drive vectorial transport processes? The answer is plainly: they can't (Mitchell, 1962, 1967b).

The idea of electrochemical cells and circuits was generalised by Guggenheim in 1933 to include the chemically motivated transport of any two species of chemical particle around a suitably conducting circuit. Guggenheim's rather abstract thermodynamic treatment effectively showed that chemical transport can be coupled reversibly to chemical transformation by splitting the chemical reaction spatially into two half reactions, connected internally by a specific conductor of one chemical species, and connected externally by a specific conductor of another chemical species needed to complete the overall reaction (see Mitchell, 1968). When we include the leading in and out of the reactants and resultants, as in the fuel cell of Fig. 18, we see that there have to be two internal specific ligand conductors arranged in a looped configuration between the interfaces where the chemical half reactions occur (Mitchell, 1967a). Obviously, the external specific ligand conduction process - for example, the flow of protons in Fig. 18 B - must be the sum of the internal specific ligand conduction processes - for example the flow of hydrogen atoms one way and of electrons the opposite way in Fig. 18 B.

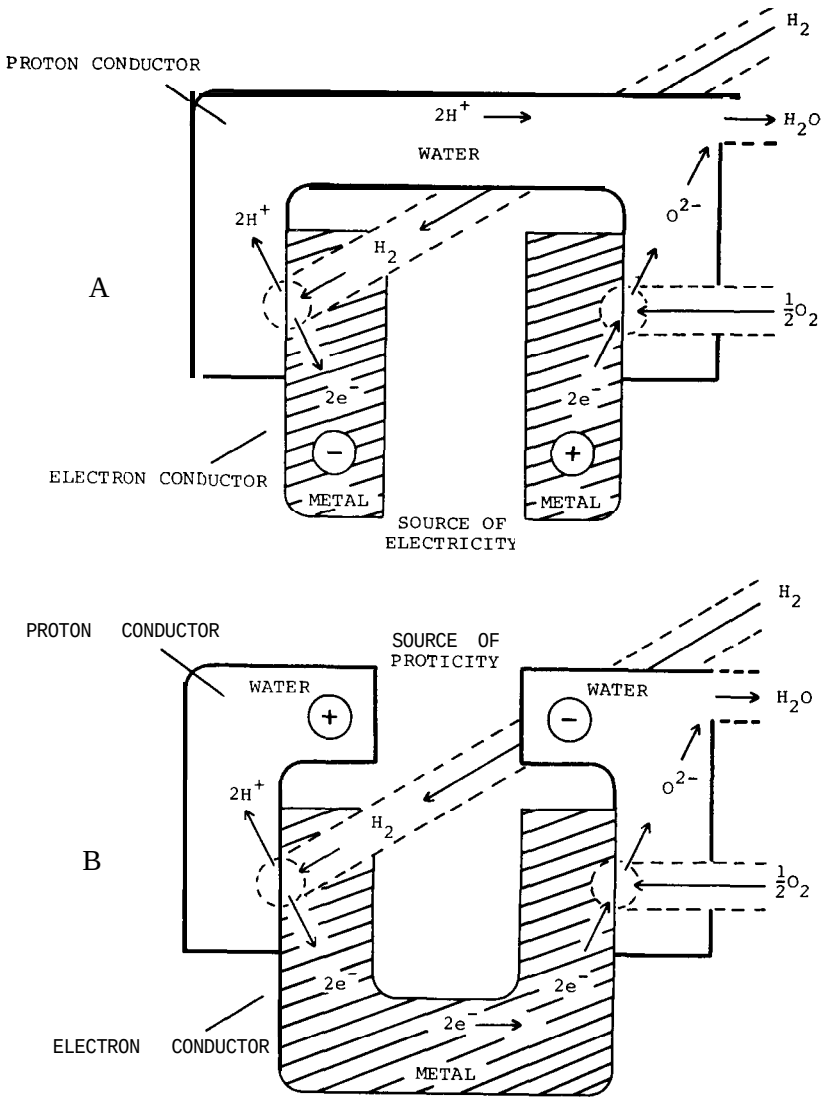
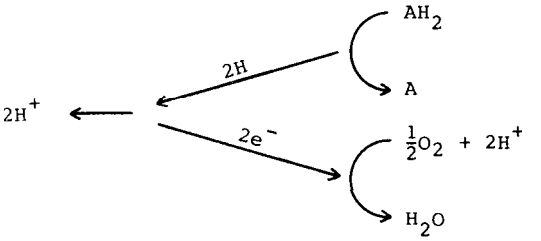


Fig. 18. Hydrogen-burning fuel cell: A, generating electricity; B, generating proticity (after Mitchell, 1967a).

The specification of chemical group conduction in an enzyme or catalytic carrier complex may usefully be considered to correspond to the specification of an internal ligand conduction reaction of a chemicomotive cell, the other internal and external circuit components of which may be determined by the topological arrangement of the specific group-conducting complex, relative to other osmotic or diffusion-regulating systems. Thus, as the name chemiosmotic implies, the intrinsic osmotic property of a

chemical group-translocation or group-conduction reaction in biology represents its chemicomotive potentiality, which may be exploited (through natural selection) by appropriate topological organisation.

For example, the notion of the protonmotive redox loop is based on this type of development of the specific ligand-conducting group-translocation concept



(2)

As indicated in equation (2), the internal (trans osmotic barrier) ligand conductors in the redox-loop complex are conceived as being specific for hydrogen atoms that diffuse down their potential gradient one way, and for electrons that diffuse down their (electrochemical) potential gradient the opposite way - exactly as in the fuel cell of Fig. 18 B, and as illustrated further in Fig. 19. The outer circuit consists of the aqueous proton conductors on either side of the insulating lipid membrane (Mitchell, 1966).

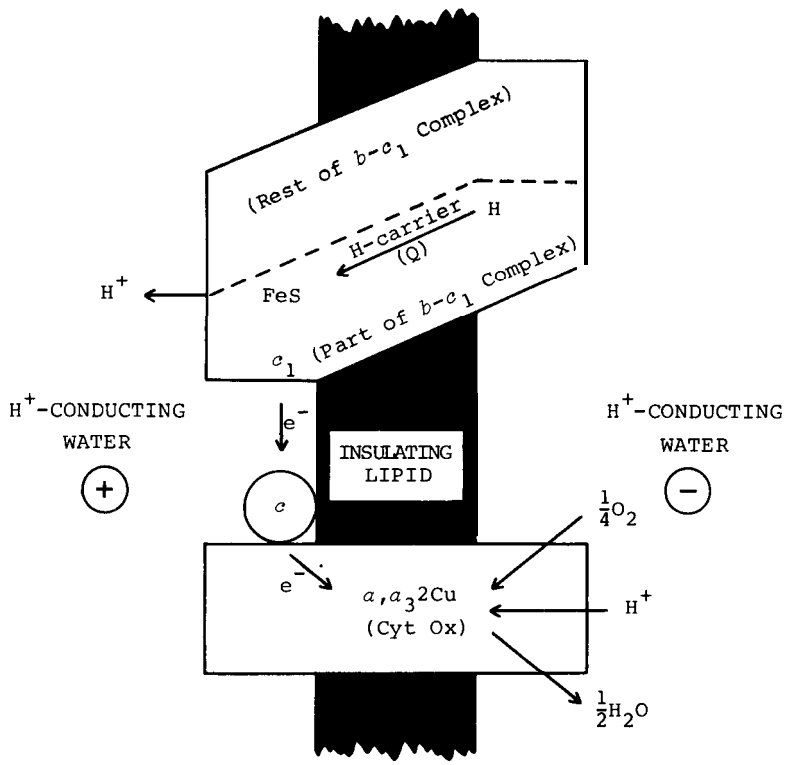


Fig. 19. Fuel cell-like terminal redox loop of respiratory chain (after Mitchell, 1967a).

quinone (PQ) cycle may operate in chloroplasts (see Bendall, 1977). Another significant feature of the diagrams of Fig. 17 is the inclusion of ironsulphur centres (FeS), which, following the beautiful pioneer work of Helmut Beinert, are now thought to have as important a role in electron transport as the haem nuclei of cytochromes (Sands & Beinert, 1960; Beinert, 1977).

The representation of the respiratory and photoredox chains as a set of physically compact complexes (that may be partially resolved and reconstituted) stems from work by Keilin & King (1958), by Takemori & King (1962), by the Madison group, led by Green and Hatefi (see Hatefi 1966), and by Efraim Racker's group (see Racker, 1976). They originally defined four complexes: NADH-Q reductase, succinate-Q reductase, QH,-cytochrome c reductase (the cytochrome ***b-c,*** complex) and cytochrome oxidase-functionally linked by ubiquinone and cytochrome c. Racker's group added the F_oF_1 and CF_0CF_1 complexes, which are physically and chemically separate from the redox complexes (Racker, 1976,1977; Jagendorf, 1977; Kozlov& Skulachev, 1977; Kagawa, 1978; Senior, 1979).

The lipid coupling membrane through which the redox and ATPase complexes are plugged is now considered to be very mobile laterally (see Hackenbrock & Höchli, 1977; King, 1978; Heron et al., 1978), in accordance with the fluid membrane concept of Singe& Nicholson (197 1).

There are about equal numbers of cytochrome b-c_1 and cytochrome oxidase complexes in mitochondrial respiratory chains. Counting all the different Q-linked dehydrogenases (NADH dehydrogenase, succinate dehydrogenase, electron transfer flavoprotein dehydrogenase, choline dehydrogenase, glycerol-l-phosphate dehydrogenase, etc.), there are about as many dehydrogenase complexes as there are cytochrome b-c_1 complexes. Thus, there is no special significance of the number four in the redox complexes of Green's group. There is, however, a special significance of two complexes: the cytochrome b-c_1 complex and the cytochrome oxidase complex, which are functionally linked by cytochrome c, and make up the protonmotive cytochrome system. This remarkably compact system serves all the Q-linked dehydrogenases, only one of which, the NADH dehydrogenase, is, so far, known to be protonmotive itself (Ragan, 1976).

There are generally at least ten Q molecules per cytochrome b-c_1 complex, so providing for the redox pool function of Q, identified by Kroger & Klingenberg (1973). However, recent work by Ragan and colleagues (Ragan & Heron, 1978; Heron et al., 1978) on functional interaction between NADH-Q reductase and cytochrome b-c_1 complexes in liposomal membranes confirms the thesis of King (1966,1978) that the most active redox-functional units are binary dehydrogenase-cytochrome b-c_1 complexes containing bound Q. Thus, it may be that the Q pool function arises more from rapid lateral lipid mobility, giving rise to a dynamic association-dissociation equilibrium of binary dehydrogenase-cytochrome b-c_1 complexes with associated Q, than to the lateral diffusion of free Q molecules between dehydrogenase and cytochrome b-c, complexes.

Hauska (1977a,b) and Lenaz et al. (1977) have argued that Q and PQ are sufficiently mobile across the lipid phase of liposomes to account for the observed rates of condution of H atoms across mitochondrial and chloroplast coupling membranes by the Q and PQ pools. It seems likely, however, that, in accordance with the ideas of King, and with the concept of the Q cycle (see Mitchell, 1975), the conduction of H atoms across the osmotic barrier may occur preferentially via specific ligand-conducting Q and PQ domains associated with Q-binding or PQ-binding proteins in the cytochrome *b*-c_1 (or *b*-*f?)* complexes, and in the neighbouring dehydrogenase (or PSII?) complexes (Trumpower, 1976,1978,1979; Gutman, 1977; Yu et al., 1977a,b,1978; King, 1978; Ragan & Heron, 1978; Heron et al., 1978; Hauska, 1977b).

The possible conduction of H atoms by flavin mononucleotide (FMN) in NADH dehydrogenase is based only on the known H-binding property of the flavin group (Mitchell, 1972a; Garland et al., 1972; Gutman et al., 1975). The very wide gap between the redox midpoint potentials of FeS1 and FeS2, and the effects of Δp in poising these centres, are difficult to reconcile with the arrangement shown in Fig. 17A (Ohnishi, 1979). As indicated in Fig. 21, I suggest rather speculatively that a protein-bound

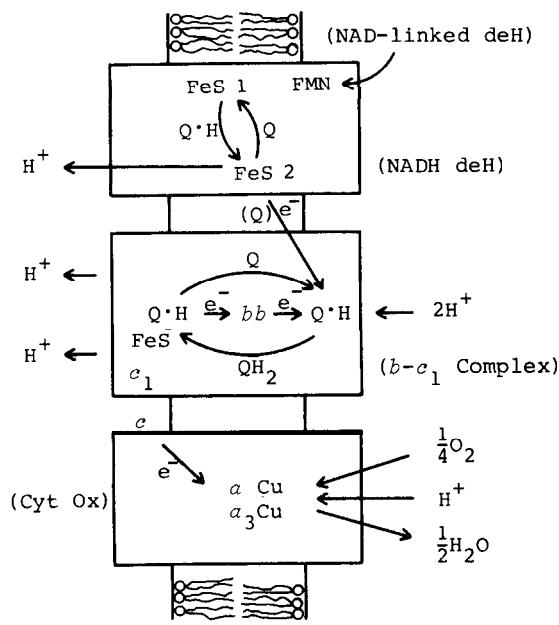


Fig. 2 1. Speculative suggestion for involvement of the Q· H/Q couple in NADH-Q reductase, and connection to cytochrome system.

Q·H/Q couple, acting between FeS1 and FeS2, might possibly account better for the general behaviour of the protonmotive NADH dehydrogenase, and for its requirement (Lenaz et al., 1975) for a specific homologue of Q.

The notion of the net conduction of O^{2-} groups by $(ADP^{-} + P^{-})/ATP$ antiport in F_1 and CF_1 (Mitchell, 1972b, 1977a) is based on the precedent of the mitochondrial ADP/ATP antiporter, which is known to conduct ADP and ATP only in specific protonation states (Klingenberg, 1977). The protonmotive NAD(P) transhydrogenase, not shown in Fig. 17, may likewise translocate protons by the effective antiport of the phosphate groups of NAD and NADP, in different protonation states determined by the redox states of the nicotinamide groups (Mitchell, 1972b).

In summary, the bioenergetically efficient mechanisms, represented in outline by Fig. 17, depend on two main principles: 1, the semi-fluid bimolecular lipid membrane and the plug-through complexes form a condensed, continuous non-aqueous (protonically insulating) sheet that acts as the osmotic barrier and separates the aqueous proton conductors on either side; 2, components of the complexes plugged through the membrane catalyse the highly specific vectorially organised conduction of electrons, H atoms, H^{+} ions and O^{2-} groups. As examples of specific ligand *binding*, we have the electron-accepting action of cytochromes or ironsulphur centres, the hydrogen-accepting action of flavoproteins or Q-proteins, and the O^{2-} - accepting action of the $ATP/(ADP^{-} + P^{-})$ couple. But the action of specific ligand *conduction* in the plug-through chemiosmotic complexes requires additional dynamic topological, physical and chemical specifications that facilitate the diffusion of the ligands along uniquely articulated pathways down through-space or through-bond fields of force.

There is still much to be understood about the biochemical details of the specific ligand-conduction processes, even for electron conduction (King, 1978; Dockter et al., 1978). But, I think it is fair to say that the protonmotive property of the mitochondrial cytochrome system and the photosysterns of chloroplasts can probably be correctly explained, in general principle, by the direct ligand-conduction type of chemiosmotic mechanism. The same may be said of the protonmotive property of the photosystems of bacterial chromatophores (Crofts & Bowyer, 1978; Dutton et al., 1978), and of certain bacterial redox chains (see Hamilton & Haddock, eds, 1977; Jones et al., 1978). The mechanism of the protonmotive ATPase is more controversial; but, at all events, mechanistic conjectures of the direct chemiosmotic type seem to me to be strategically valuable because they stimulate rational experimental research and thereby add to our biochemical knowledge, even if they ultimately turn out to be wrong.

4. CONCLUSION AND PROSPECT

The students of membrane biochemistry and bioenergetics have endured a long period of uncertainty and conceptual upheaval during the last thirty years - a time of great personal, as well as scientific, trauma for many of us.

The present position, in which, with comparatively few dissenters, we have successfully reached a consensus in favour of the chemiosmotic

theory, augurs well for the future congeniality and effectiveness of experimental research in the field of membrane biochemistry and bioenergetics. At the time of the most intensive testing of the chemiosmotic hypothesis, in the nineteensixties and early nineteenseventies, it was not in the power of any of us to predict the outcome. The aspect of the present position of consensus that I find most remarkable and admirable, is the altruism and generosity with which former opponents of the chemiosmotic hypothesis have not only come to accept it, but have actively promoted it to the status of a theory. According to their classically Popperian view (see Mitchell, 1977b), the chemiosmotic theory is worth accepting, for the time being, as the best conceptual framework available (Slater, 1977). Thus to have falsified the pessimistic dictum of the great Max Planck is, I think, a singularly happy achievement.

Returning, finally, to the theme of the respiratory chain, it is especially noteworthy that David Keilin's chemically simple view of the respiratory chain appears now to have been right all along - and he deserves great credit for having been so reluctant to become involved when the energy-rich chemical intermediates began to be so fashionable. This reminds me of the aphorism: "The obscure we see eventually, the completely apparent takes longer".

ACKNOWLEDGEMENTS

I am especially indebted to my research associate, Jennifer Moyle, for constant discussion, criticism and help. Many colleagues have contributed to the evolution of ideas and knowledge traced in this lecture. In particular, I would like to mention the influence of Tsoo King, after the premaature death of David Keilin in 1963. I would also like to acknowledge that it was Bill Slater who persuaded me to become more deeply involved in practical research on oxidative phosphorylation in 1965, when Jennifer Moyle and I first commenced work at the Glynn Research Laboratories. I thank Jim Danielli for the photograph shown in Fig. 6; I thank Jack Dunitz and Ulrich Müller-Herold for help in researching the dictum of Max Planck (1928, 1933); and I thank Bernie Trumpower and Carol Edwards for informing me, prior to publication of their work, that factor OxF is probably a reconstitutively active form of the Rieske ironsulphur protein, thus influencing the representation of the Q cycle in Fig. 17A. I am grateful to Robert Harper and Stephanie Key for help in preparing the manuscript, and to Glynn Research Ltd for general financial support.

REFERENCES

Arnon, D. I., Whatley, F. R. and Allen, M. B. (1954) J. Am. Chem. Soc. 76, 6324-6328.

Azzone, G. F., Pozzan, T. and Bragadin, M. (1977) BBA Library ***14,*** 107- 116.

Beinert, H. (1977) BBA Library 14, 11-21.

Belitser, V. A. and Tsybakova, E. T. (1939) Biokhimia 4, 516-535.

Bendall, D. S. (1977) in *Internat. Rev. of Biochem. Plant Biochem. II* (Northcote, D. H., ed.) vol. 13, pp. 41-78, University Park Press, Baltimore.

Bowman, B. J., Mainzer, S. E., Allen, K. E., and Slayman, C. W. (1978) Biochim. Biophys. Acta 512, 13-28.

Bayer, P. D., Falcone, A. B. and Harrison, W. H. (1954) Nature ***174,*** 401-404.

Boyer, P. D. (1963) Science 141, 1147-1153.

Bayer, P. D. (1965) in *Oxidases and Related Redox Systems* (King, T. E. et al., eds) vol. 2, pp. 994-1008, John Wiley, New York.

Boyer, P. D., Cross, R. L. and Momsen, W. (1973) Proc. Nat. Acad. Sci. U.S.A. 70, 2837-2839.

Boyer, P. D. (1974) BBA Library 13, 289-301.

Boyer, P. D., Chance, B., Ernster, L., Mitchell, P., Racker, E. and Slater, E. C. (1977) Ann. Rev. Biochem. 46, 955-1026.

Chance, B. and Williams, G. R. (1956) Adv. Enzymol. 27, 65-134.

Chance, B. (1961) J. Biol. Chem. 236, 1569-1576.

Chance, B., Lee, C. P. and Mela, L. (1967) Fed. Proc. 26, 1341-1354.

Chance, B. (1972) FEBS Lett. 23, 3-20.

Chance, B. (1974) Ann. N.Y. Acad. Sci. 227, 613-626.

Chappell, J. B. (1968) Brit. Med. Bull. 24, 150-157.

Conway, E. J. (1951) Science 113, 270-273.

Crofts, A. R. and Bowyer, J. (1978) in *The Proton and Calcium Pumps* (Azzone, G. F. et al., eds) pp. 55-64, Elsevier / North-Holland, Amsterdam.

Cross, R. L. and Boyer, P. D. (1973) in *Mechanisms in Bioenergetics* (Azzone, G. F. et al., eds) pp. 149- 155, Academic Press, New York.

Curie, P. (1894) J. Phys., 3ème Ser. 393-415.

Davies, R. E. and Ogston, A. G. (1950) Biochem. J. 46, 324-333.

Delhez, J., Dufour, J.-P., Thines, D. and Goffeau, A. (1977) Eur. J. Biochem. 79, 319-328.

DePierre, J. W. and Ernster, L. (1977) Ann. Rev. Biochem. 46, 201-262.

Dockter, M. E., Steinmann, A. and Schatz, G. (1978) J. Biol. Chem. 253, 31l-317.

Drachev, L. A., Kaulen, A. D. and Skulachev, V. P. (1978) FEBS Lett. 87, 161-167.

Dutton, P. L., Bashford, C. L., van den Bergh, W. H., Banner, H. S., Chance, B., Jackson, J. B., Petty, K. M., Prince, R. C., Sorge, J. R. and Takamiya, K. (1978) in *Photosynthesis 77, Proc. Fourth Internat. Congr. Photosynth.* (Hall, D. O. et al., eds) pp. 159- 171, Biochem. Soc., London.

Dutton, L., Leigh, J. and Scarpa, A., eds (1978) *Frontiers of Biological Energetics,* Academic Press, New York.

Ewards, G. E. and Huber, S. C. (1978) in *Photosynthesis 77, Proc. Fourth Internat. Congr. Photosynth.* (Hall, D. O. et al., eds) pp. 95- 106, Biochem. Soc., London.

Ernster, L. and Lee, C. P. (1964) Ann. Rev. Biochem. 33, 729-788.

Emster, L., Juntti, K. and Asami, K. (1973) J. Bioenerg. 4, 149-159.

Ernster, L., Nordenbrand, K., Chude, O. and Juntti, K. (1974) in *Membrane Proteins in Transport and Phosphorylation* (Azzone, G. F. et al., eds) pp. 29-41, North-Holland, Amsterdam.

Ernster, L. (1977a) in *Living Systems as Energy Converters* (Buvet, R. et al., eds) pp. 115-118, North-Holland, Amsterdam.

Emster, L. (1977b) in *Bioenergetics of Membranes* (Packer, L. et al., eds) pp. 373-376, Elsevier / North-Holland, Amsterdam.

Friedkin, M. and Lehninger, A. L. (1948) J. Biol. Chem. 174, 757-758.

Garland, P. B., Clegg, R. A., Downie, J. A., Gray, T. A., Lawford, H. G. and Skyrme, J. (1972) FEBS Symp. 28, 105-117.
Glagolev, A. N. and Skulachev, V. P. (1978) Nature 272, 280-282.
Green, D. E., Beyer, R. E., Hansen, M., Smith, A. L. and Webster, G. (1963) Fed. Proc. 22, 1460- 1468.
Green, D. E. (1974) Biochim. Biophys. Acta 346, 27-78.
Griffiths, D. E. (1965) in *Essays in Biochemistry* (Campbell, P. N. and Greville, G. D., eds) vol. 1, pp. 91- 120, Academic Press, London.
Griffiths, D. E., Hyams, R. L. and Bertoli, E. (1977) FEBS Lett. 74, 38-42.
Grove, W. R. (1839) Phil. Mag., Ser. 3, 14, 127-130.
Guggenheim, E. A. (1933) *Modern Thermodynamics by the Methods of Willard Gibbs,* Methuen, London.
Gutman, M., Beinert, H. and Singer, T. P. (1975) in *Electron Transfer Chains and Oxidutive Phosphorylation* (Quagliariello, E. et al., eds) pp. 55-62, North-Holland, Amsterdam.
Gutman, M. (1977) in *Bioenergetics of Membranes* (Packer, L. et al., eds) pp. 165-175, Elsevier/North-Holland, Amsterdam.
Hackenbrock, C. R. and Höchli, M. (1977) FEBS Symp. 42, 10-36.
Hall, D. O., Coombs, J. and Goodwin, T. W., eds (1978) *Photosynthesis 77, Proc. Fourth Internat. Congr. Photosynth.,* Biochem. Soc., London.
Hamilton, W. A. and Haddock, B. A., eds (1977) Symp. Soc. Gen. Microbial. 27.
Harold, F. M. (1977a) Curr. Top. Bioenerg. 6, 83-149.
Harold, F. M. (1977b) Ann. Rev. Microbial. 31, 181-203.
Hatefi, Y. (1963) Adv. Enzymol. 25, 275-328.
Hatefi. (1966) Compr. Biochem. ***14,*** 199-231.
Hatefi, Y. and Hanstein, W. G. (1972) J. Bioenerg. 3, 129-136.
Hauska, G. (1977a) in *Bioenergetics of Membranes* (Packer, L. et al., eds) pp. 177- 186, Elsevier/North-Holland, Amsterdam.
Hauska, ***G.*** (1977b) in *Photosynthesis 77, Proc. Fourth Internat. Congr. Photosynth.* (Hall. D. O. et al., eds) pp. 185-196, Biochem. Soc., London.
Heaton, G. M., Wagenvoord, R. J., Kemp, A. and Nicholls, D. G. (1978) Eur. J. Biochem. 82, 515-521.
Heldt, H. W. (1976) in *The Intact Chloroplast* (Barber, J., ed) pp. 215-234, Elsevier, Amsterdam.
Heron, C., Ragan, C. I. and Trumpower. B. L. (1978) Biochem. J. 174, 791-800.
Hill. R. and Bendall, F. (1960) Nature ***186,*** 136-137.
Hinkle, P. C. and McCarty, R. E. (1978) Scientific American 238, 104-123.
lngledew, W. J., Cox, J. C. and Halling, P. J. (1977) FEBS Microbiology Letters 2, 193-197.
Jagendorf, A. T. (1967) Fed. Proc. 26, 1361-1369.
Jagendorf, A. T. (1977) in *Encyclopedia of Plant Physiol.* New Series (Trebst, A. and Avron, M., eds) vol. 5, pp. 307-377, Springer Verlag, Berlin.
Jones, C. W., Brice, J. M. and Edwards, C. (1978) FEBS Symp. 49, 89-97.
Junge, W. (1977) Ann. Rev. Plant Physiol. 28, 503-536.
Junge, W., Auslinder, W., McGeer, A. and Runge, T. (1979a) Biochim. Biophys. Acta, 546, 121-141.
Junge, W., McGeer, A. J., AuslBnder, W. and Kolla, J. (1979b) in *29th Mosbach Colloq.* (Schäfer, G. and Klingenberg, M., eds) in press, Springer Verlag, Berlin.
Kagawa, Y. (1978) Biochim. Biophys. Acta 505, 45-93.
Kalckar, H. (1937) Enzymologia 2, 47-52.
Keilin, D. (1925) Proc. Roy. Soc. B 98, 312-339.
Keilin, D. (1929) Proc. Roy. Soc. B 104, 206-252.
Keilin, D. and King, T. E. (1958) Nature 181, 1520- 1522.
King, T. E. (1966) Adv. Enzymol. 28, 155-236.
King, T. E. (1978) FEBS Symp. 45, 17-31.
Klingenberg, M. (1977) BBA Library ***14, 275-282.***
Konstantinov. A. A. and Ruuge, E. K. (1977) FEBS Lett. *81,* 137-141.

Kozlov, I. A. and Skulachev, V. P. (1977) Biochim. Biophys. Acta 463, 29-89.
Kröger, A. and Klingenberg, M. (1973) Eur. J. Biochem. 34, 358-368, and 39, 313-323.
Kundig, W., Ghosh, S., and Roseman, F. D. (1964) Proc. Nat. Acad. Sci. U. S. A. 52, 1067-1074.
Lardy, H. A., Connelly, J. L. and Johnson, D. (1964) Biochemistry 3, 1961- 1968.
Lehninger, A. L. (1959) Rev. Modern Physics 31, 136-146.
Lehninger, A. L. (1962) Physiol. Rev. 42, 467-517.
Lehninger, A. L. and Wadkins, C. L. (1962) Ann. Rev. Biochem. 31, 47-78.
Lenaz, G., Pasquali, P., Bertoli, E., Parenti-Castelli, G. and Folkers, K. (1975) Archs. Biochem. Biophys. 169, 2 17-226.
Lenaz, G., Mascarello, S., Laudi, L., Cabrini, L., Pasquali, P., Parenti-Castelli, G., Sechi, A. M. and Bertoli, E. (1977) in *Bioenergetics of Membranes* (Packer, L. et al., eds) pp. 189-198, Elsevier / North-Holland, Amsterdam.
Liebhafsky, H. A. and Cairns, E. J. (1968) *Fuel Cells and Fuel Batteries,* John Wiley, New York.
Lipmann, F. (1941) Adv. Enzymol. I, 99-162.
Lipmann, F. (1946) in *Currents in Biochemical Research* (Green, D. E., ed.) pp. 137-148, Interscience, New York.
Lipmann, F. (1960) in *Molecular Biology* (Nachmansohn, D., ed.) pp. 37-47, Academic Press, New York.
Lundegardh, H. (1945) Arkiv. Bot. 32 A 12, 1-139.
Manson, M. D., Tedesco, P., Berg, H. C., Harold, F. M. and Van der Drift, C. (1977) Proc. Nat. Acad. Sci. U. S. A. 74, 3060-3064.
Matsuura, S., Shioi, J. -i. and Imae, Y. (1977) FEBS Lett. 82, 187-190.
Mitchell, P. (1949) in *The Nature of the Bacterial Surface* (Miles, A. A. and Pirie, N. W., eds) pp. 55-75, Blackwell, Oxford.
Mitchell, P. (1954) Symp. Soc. Exp. Biol. 8, 254-261.
Mitchell, P. (1956) Discuss. Farad. Soc. 21, 278-279 and 282-283.
Mitchell, P. and Moyle, J. (1956) Discuss. Farad. Soc. 21, 258-265.
Mitchell, P. (1957) Nature 180, 134- 136.
Mitchell, P. and Moyle, J. (1958a) Nature 182, 372-373.
Mitchell, P. and Moyle, J. (1958b) Proc. Roy. Phys. Soc., Edinburgh 27, 61-72.
Mitchell, P. (1959) Biochem. Soc. Symp. 16, 73-93.
Mitchell, P. (196 la) in *Membrane Transport and Metabolism* (Kleinzeller, A. and Kotyk, A., eds) pp. 22-34, Academic Press, New York.
Mitchell, P. ***(196 1*** b) in *Biological Structure and Function, Proc. First IUB/IUBS Internat. Symp,,* Stockholm, 1960 (Goodwin, T. W. and Lindberg, O., eds) vol. 2, pp. 581-599, Academic Press, London.
Mitchell, P. (1961c) Nature ***191,*** 144-148.
Mitchell, P. (1962) J. Gen. Microbial. 29, 25-37.
Mitchell, P. (1963) Biochem. Soc. Symp. 22, 142-168.
Mitchell, P. and Moyle, J. (1965) Nature 208, 147-151.
Mitchell, P. (1966) *Chaiosmotic Coupling in Oxidative and Photosynthetic Phosphorylation,* Glynn Research, Bodmin, Cornwall, England.
Mitchell, P. (1967a) Fed. Proc. 26, 1335-1340.
Mitchell, P. (1967b) Compr. Biochem. 22, 167-197.
Mitchell, P. (1967c) Adv. Enzymol. 29, 33-85.
Mitchell, P. and Moyle, J. (1967) Biochem. J. 105, 1147-1162.
Mitchell, P. (1968) *Chaiosmotic Coupling and Energy Transduction,* Glynn Research, Bodmin, Cornwall, England.
Mitchell, P. and Moyle, J. (1968) Eur. J. Biochem. 4, 530-539.
Mitchell, P. (1970a) Membr. Ion Transp. I, 192-256.
Mitchell, P. (1970b) Symp. Sot. Gen. Microbial. 20, 121-166.
Mitchell, P. (1972a) FEBS Symp. 28, 353-370.
Mitchell, P. (1972b) J. Bioenerg. 3, 5-24.
Mitchell, P. (1973a) J. Bioenerg. 4, 63-91.

Mitchell, P. (1973b) in *Mechanisms in Bioenergetics* (Azzone, G. F. et al., eds) pp. 177-201, Academic Press, New York.
Mitchell, P. (1973c) FEBS Lett. 33, 267-274.
Mitchell, P. (1975) in *Electron Transfer Chains and Oxidative Phosphorylation* (Quagliariello, E. et al., eds) pp. 305-316, North-Holland, Amsterdam.
Mitchell, P. (1976a) Biochem. Soc. Trans. 4, 399-430.
Mitchell, P. (1976b) J. Theoret. Biol. 62, 327-367.
Mitchell, P. (1977a) FEBS Lett. 78, l-20.
Mitchell, P. (1977b) Ann. Rev. Biochem. 46, 996-1005.
Mitchell, P. (1977c) Symp. Soc. Microbial. 27, 383-423.
Mitchell, P. (1979) Eur. J. Biochem. 95, l-20.
Moore, A. L. (1978) FEBS Symp. 49, 141-147.
Moyle, J., Mitchell, R. and Mitchell, P. (1972) FEBS Lett. 23, 233-236.
Moyle, J, and Mitchell, P. (1977) FEBS Lett. 84, 135-140.
Moyle, J. and Mitchell, P. (1978a) FEBS Lett. 88, 268-272.
Moyle, J. and Mitchell, P. (I978b) FEBS Lett. 90, 361-365.
Nicholls, P. (1963) in *The Enzymes* (Boyer, P. D. et al., eds) vol. 8, part B, pp. 3-40, Academic Press, New York.
Njus, D. and Radda, G. K. (1978) Biochim. Biophys. Acta 463, 219-244.
Nordenbrand, K., Hundal, T., Carlsson, C., Sandri, G. and Ernster, L. (1977) in *Bioenergetics of Membranes* (Packer, L. et al., eds) pp 435-446, Elsevier/North-Holland, Amsterdam.
Ochoa, S. (1940) Nature 146, 267.
Ohnishi, T. (1979) in *Membrane Proteins in Energy* Transduction (Capaldi, R. A., ed.), l-87, Marcel Dekker, New York.
Painter, A. A. and Hunter, F. E. (1970) Biochem. Biophys. Res. Commun. 40, 360-395.
Papa, S. (1976) Biochim. Biophys. Acta 456, 39-84.
Papa, S., Guerrieri, F., Lorusso, M., Izzo, G., Boffoli, D. and Stefanelli, R. (1978) FEBS Symp. 45, 37-48.
Pauling, L. (1950) *Ann. Rep. Smithsonian Inst.* 225-241.
Planck, M. (1928) *Wissenschaftliche Autobiographic* **,** Leipzig. Planck's remark, as presented in my paper, is a paraphrase of the following passage on p. 22: "Eine neue wissenschaftliche Wahrheit pflegt sich nicht in der Weise durchzusetzen, dass ihre Gegner iiberzeugt werden und sich als belehrt erkllren, sondern vielmehr dadurch, dass die Gegner allmihlich aussterben und dass die heranwachsende Generation von vornherein mit der Wahrheit vertraut gemacht ist." But I have partly followed a later variant of this passage, given in Planck (1933). where he substituted the word Idee for Wahrheit.
Planck, M. (1933) *Ursprung und Auswirkung wissenschaftlicher Ideen.* A lecture reproduced in Planck's *Vortriige und Erinnerungen,* Darmstadt, 1975.
Racker, E. (1961) Adv. Enzymol. 23, 323-399.
Racker, E. (1965) *Mechanisms in Bioenergetics,* Academic Press, New York.
Racker, E. (1967) Fed. Proc. 26, 1335-1340.
Racker, E. (1976) *A New Look at Mechanisms in Bioenergetics,* Academic Press, New York.
Racker, E. (I 977) Ann. Rev. Biochem. 46, 1006-1014.
Ragan, C. I. (1976) Biochim. Biophys. Acta 456, 249-290.
Ragan, C. I. and Heron, C. (1978) Biochem. J. 174, 783-790.
Reynafarje, B. and Lehninger, A. L. (1978) J. Biol. Chem. 253, 633l-6334.
Rich, P. R. and Moore, A. L. (1976) FEBS Lett. 65, 339-344.
Rich, P. R. and Bonner, W. D. (1978) FEBS Symp. 49, 149-158.
Rieske, J. S. (1976) Biochim. Biophys. Acta 456, 195-247.
Robertson, R. N. and Wilkins, M. J. (1948) Aust. J. Sci. Res. ***1,*** 17-37.
Robertson, R. N. (1960) Biol. Rev. 35, 23 1-264.
Robertson, R. N. (1968) *Protons, Electrons, Phosphorylation and Active Transport,* Cambridge University Press, Cambridge.
Rosen, B. P. and Kashket, E. R. (1978) in *Bacterial Transport* (Rosen, B. P., ed.) pp. 559-620, Marcel Dekker, New York.

Rosenberg, T. (1948) Acta Chem. Scand. 2, 14-33.
Sanadi, D. R. (1965) Ann. Rev. Biochem. 34, 21-48.
Sands, R. H. and Beinert, H. (1960) Biochem. Biophys. Res. Commun. 3, 47-52.
Schreckenbach, T. and Oesterhelt, D. (1978) FEBS Symp. 45, 105-119.
Schulten, K. and Tavan, P. (1978) Nature 272, 85-86.
Seaston, A., Carr, G. and Eddy, A. A. (1976) Biochem. J. ***154, 669-676.***
Senior, A. E. (1979) in *Membrane Proteins in Energy Transduction* (Capaldi, R. A., ed.) in press, Marcel Dekker, New York.
Singer, S. J. and Nicholson, G. L. (1971) Science ***175,*** 720-731.
Skulachev, V. P. (1970) FEBS Lett. 11, 301-308.
Skulachev, V. P. (1974) Ann. N. Y. Acad. Sci. 227, 188-202.
Skulachev, V. P. (1977) FEBS Lett. 74, l-9.
Slater, E. C. (1953) Nature 172, 975-978.
Slater, E. C. and Cleland, K. W. (1953) Biochem. J. 53, 557-567.
Slater, E. C. (1958) Rev. Pure Appl. Chem. 8, 22 l-264.
Slater, E. C. and Hulsmann, W. C. (1959) in *Ciba Foundation Symp., Regulation of Cell Metabolism* (Wolstenholme, G. E. W. and O'Connor, C. M., eds) pp. 58-83, Churchill, London.
Slater, E. C. (1966) Compr. Biochem. 14, 327-396.
Slater, E. C. (1971) Quart. Rev. Biophys. 4, 35-71.
Slater, E. C. (1974) Biochem. Soc. Trans. 2, 39-1163.
Slater, E. C. (1975) in *Electron Transfer Chains and Oxidative Phospholylution* (Quagliariello, E. et al., eds) pp. 3-14, North-Holland, Amsterdam.
Slater, E. C. (1976) in *Reflections on Biochemistry* (Kornberg, A. et al., eds) pp. 45-55, Pergamon Press, Oxford.
Slater, E. C. (1977) in *Living Systems as Energy Converters* (Buvet, R. et al., eds) pp. 22l-227, North-Holland, Amsterdam.
Stoeckenius, W. (1977) Fed. Proc. 36, 1797-1798.
Storey, B. T. (1970) J. Theoret. Biol. 28, 233-259.
Storey, B. T. (1971) J. Theoret. Biol. 31, 533-552.
Takemori, S. and King, T. E. (1962) Biochim. Biophys. Acta 64, 192-194.
Toll, L. and Howard, B. D. (1978) Biochemistry ***17,*** 2517-2523.
Trumpower, B. L. (1976) Biochem. Biophys. Res. Commun. 70, 73-80.
Trumpower, B. L. (1978) Biochem. Biophys. Res. Commun. 83, 528-535.
Trumpower, B. L. and Katki, A. G. (1979) in *M em brane Proteins in Electron Transport* (Capaldi, R. A., ed.) in press, Marcel Dekker, New York.
Ussing, H. H. (1947) Nature ***160, 262-263.***
Ussing, H. H. (1949) Physiol. Rev. 29, 127-155.
Wang, J. H. (1972) J. Bioenerg. 3, 105-114.
Weiner, M. W. and Lardy, H. A. (1974) Archs. Biochem. Biophys. 162, 568-577.
Wikstriim, M. and Krab, K. (1978) FEBS Lett. 91, 8-14.
Williams, R. J. P. (1962) J. Theoret. Biol. 3, 209-229.
Williams, R. J. P. ***(1970)*** in *Electron Transport and Energy Conservation* (Tager, J. M. et al., eds) p. 38 1, Adriatica Editrice, Bari.
Witt, H. T. (1967) in *Fast Reactions and Primary Processes in Chemical Kinetics,* Nobel Symp. 5, (Claesson, S., ed.) pp. 261-316, Interscience, London.
Witt, H. T. (1977) in *Living Systems as Energy Converters* (Buvet, R. et al., eds) pp. 185-197, Elsevier / North-Holland, Amsterdam.
Yu, C. A., Yu, L. and King, T. E. (1977a) Biochem. Biophys. Res. Commun. 78, 259-265.
Yu, C. A., Yu, L. and King, T. E. (1977b) Bïothem. Biophys. Res. Commun. 79, 939-946.
Yu, C. A., Nagaoka, S., Yu, L. and King, T. E. (1978) Biochem. Biophys. Res. Commun. 82, 1070-1078.