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# The Semiquinone Cycle. A Hypothesis of Electron Transfer and Proton Translocation in Cytochrome *bc*-Type Complexes[1]

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## Abstract

The Q cycle and the *b* cycle are the main current models of action of the cytochrome *bc*-type complexes of mitochondria, bacteria, and chloroplasts. Both are based on the concept, proposed in 1972, of two sequential one-electron oxidations of (ubi)quinol along two discrete pathways which operate at different redox potentials, and with bound semiubiquinone as an intermediate. The models differ in two respects, viz. in the pathway of electron transfer and the principle of linkage of electron transfer to proton translocation. In this article we outline a new model, called the semiquinone or, simply, SQ cycle, which is based on the electron transfer principles of the *b* cycle but which incorporates the Q cycle concept of direct coupling between electron transfer and proton translocation through action of ubiquinone.


**Key Words:** Cytochrome *b*; energy conservation; cytochrome *b* cycle; ubiquinone; Q cycle.

## Introduction

The cytochrome *bc*-type electron transfer complexes of mitochondrial respiration and photosynthetic electron transfer in bacteria and chloroplasts are analogous both structurally and functionally (Hauska *et al.*, 1983; Crofts, 1985; Crofts and Wraight, 1983). They apparently all contain cytochrome *b* with two hemes in one polypeptide, an iron-sulfur protein of the

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type first described by Rieske and a *c*-type cytochrome (cytochrome $c_1$ in mitochondria and photosynthetic bacteria and cytochrome *f* in chloroplasts). They function as quinol (ubiquinol, plastoquinol)-ferricytochrome *c* (cytochrome $c_2$, plastocyanin) oxidoreductases. In addition, they catalyze proton translocation across the respective energy-transducing membrane.

It is generally agreed that the mechanistic stoichiometry of proton translocation is such that for each electron transferred from quinol to cytochrome *c* (or its analogue) there is release of two $H^+$ on the O (output or electrically positive) side of the membrane, uptake of one $H^+$ from the I (input or electrically negative) side, and translocation of a single electrical charge equivalent across the membrane.[5] The imbalance between proton release and uptake is due to the overall oxidation of the hydrogen-donating quinol by the electron-accepting *c*-type cytochrome.

We are here specifically concerned with the question of what the electron transfer and proton translocation mechanisms are in the cytochrome *bc* complexes. Wikström and Berden (1972) suggested that (ubi)quinol is oxidized in two discrete one-electron steps by different electron acceptors at different redox potentials, and with semiquinone as a protein-associated intermediate. This model, which suggests a branch in the electron transfer sequence, was initially not favorably received because it was thought that the semiquinone would be too unstable to have such a function. Subsequently Mitchell (1976) developed this idea further by suggesting that one of the two electron transferring branches bends back upon the system, giving rise to a cyclic electron transfer path involving the *b*-type hemes. Mitchell's proposal has the further virtue of explaining how electron transfer may be directly linked to proton translocation in a way that is consistent with the observed $H^+/e^-$ stoichiometry. In the following years this so-called Q cycle model has received much experimental support. There are, however, some difficulties with the Q cycle that have led to various modifications of the model.

Outgoing from a thorough revision of the original Wikström-Berden model (Wikström and Berden, 1972), Wikström and Krab (1980) suggested an alternative hypothesis for the pathway of electron transfer in *bc*-type complexes which they called the (cytochrome) *b* cycle. They also suggested that the mechanism of proton translocation may be an indirectly coupled one

[5]Abbreviations: AA, antimycin; I, (input) aqueous side of membrane from which protons are translocated; i (input) antimycin-sensitive center or domain of ubiquinol-cytochrome *c* oxidoreductase, catalyzing oxidation of cytochrome *b*-562 by ubisemiquinone; MX, myxothiazol; O, (output) aqueous side of membrane into which protons are translocated; o, (output) myxothiazol-sensitive center or domain or ubiquinol-cytochrome *c* oxidoreductase, catalyzing oxidation of quinol by the Rieske FeS center; Q, ubiquinone (oxidized, reduced, or semiquinone), or specifically the oxidized quinone; $QH_2$ ubiquinol; SQ, semiubiquinone (irrespective of protonation state); SQ(i), SQ(o), semiquinone interacting with domains i and o, respectively.

where the *b*-type cytochromes would function as proton pumps (Wikström and Krab, 1980; Wikström *et al.*, 1981).

The *b* cycle has been rather cursorily presented in the past, which has led to some misunderstandings. One purpose of the present paper is to give a brief but more explicit account of the electron transfer mechanism of the *b* cycle. Another is to develop and present a new model, called the semiquinone or SQ cycle, in which the electron transfer principles of the *b* cycle are retained, but which incorporates the basic principle of linkage to proton translocation from the Q cycle. We will also discuss certain experimental findings that may be relevant for the evaluation of the different models.

## The *b* Cycle

Figure 1A is a redrawing of the original electron transfer scheme of the *b* cycle (Wikström and Krab, 1980; Wikström *et al.*, 1981). A major feature is that quinol is oxidized in two discrete one-electron steps with different electron acceptors, and at different redox potentials, as suggested by Wikström and Berden (1972), and as also adopted in the Q cycle. The arrangement of the cytochrome *b*-type hemes renders electron transfer in one of the branches cyclic, as in the Q cycle. The evidence for such a cyclic function of the *b*-type cytochromes is strong (see reviews in Hauska *et al.*, 1983; Crofts 1985; Crofts and Wraight, 1983). The most essential difference from the Q cycle lies in the proposal that the acceptor of electrons from *b*-562 is semiquinone that is formed as the immediate product of the initial electron transfer from quinol to Fe/S.

Although the original presentation of the *b* cycle was somewhat abbreviated, it was specifically stressed that the reactions of the $QH_2$/SQ couple with Fe/S and *b*-562, respectively, are sensitive to different specific inhibitors (see Fig. 1A). This implies that they must be catalyzed by different reaction domains in the complex. To emphasize this, the *b* cycle may be drawn more explicitly as shown in Fig. 1B with clearer distinction between the two separate inhibitor-sensitive reaction domains (i and o for input and output domain, respectively, using a terminology analogous to that of the Q cycle). From Fig. 1B it is obvious that the finding of two forms of semiquinone by EPR spectroscopy (Konstantinov and Ruuge, 1977; De Vries *et al.*, 1981) does not contradict the *b* cycle model. The distinction from the Q cycle is also clear in that a central reaction step of the *b* cycle is the direct communication of SQ between the two reaction domains o and i, a step that was specifically excluded from the Q cycle [see, e.g., Mitchell (1976), p. 342].

Another important feature is that in the *b* cycle electron donation from the dehydrogenases is considered to be purely through the ubiquinone/ubiquinol

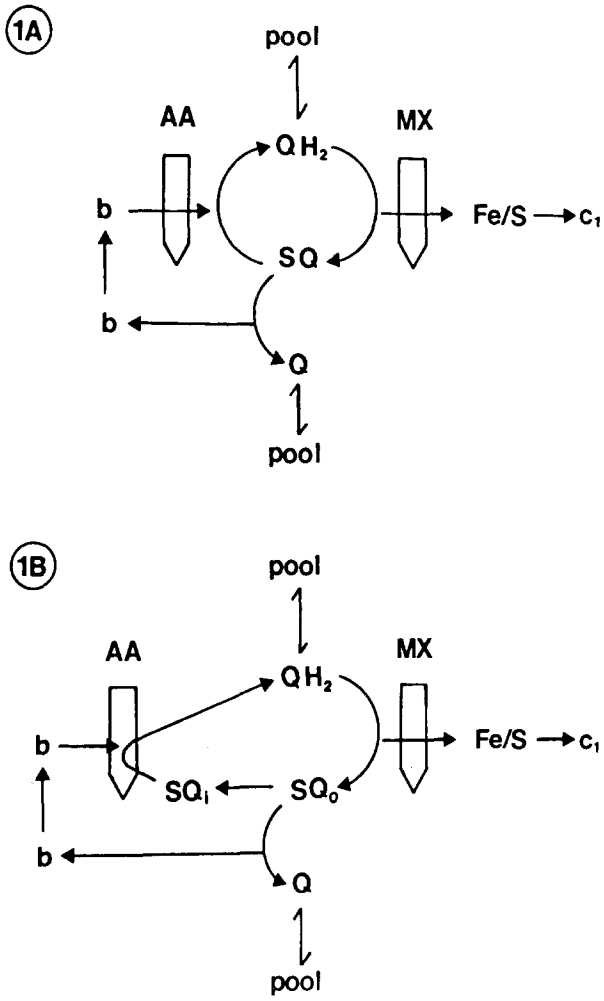


**Fig. 1.** A: The electron transfer scheme of the *b* cycle (slightly modified from Fig. 4 in Wikström and Krab, 1980). AA, antimycin; MX, myxothiazol; SQ, semiquinone. The *b*-type hemes are both indicated with a "*b*", of which the lower and the upper one correspond to *b*-566 and *b*-562, respectively. "Pool" indicates the membranous pool of ubiquinone. Black-headed arrows denote one-electron transfer reactions. B: Electron transfer scheme of the *b*-cycle with explicit separation of o and i domains, and showing the corresponding interaction of SQ with these domains. Such separation has not been drawn for Q or $QH_2$ for simplicity, and due to the postulated rapid equilibration of these protein-associated species with the membranous pool. Black-headed arrows (except the transition of $SQ_o$ to $SQ_i$) denote one-electron transfer steps.

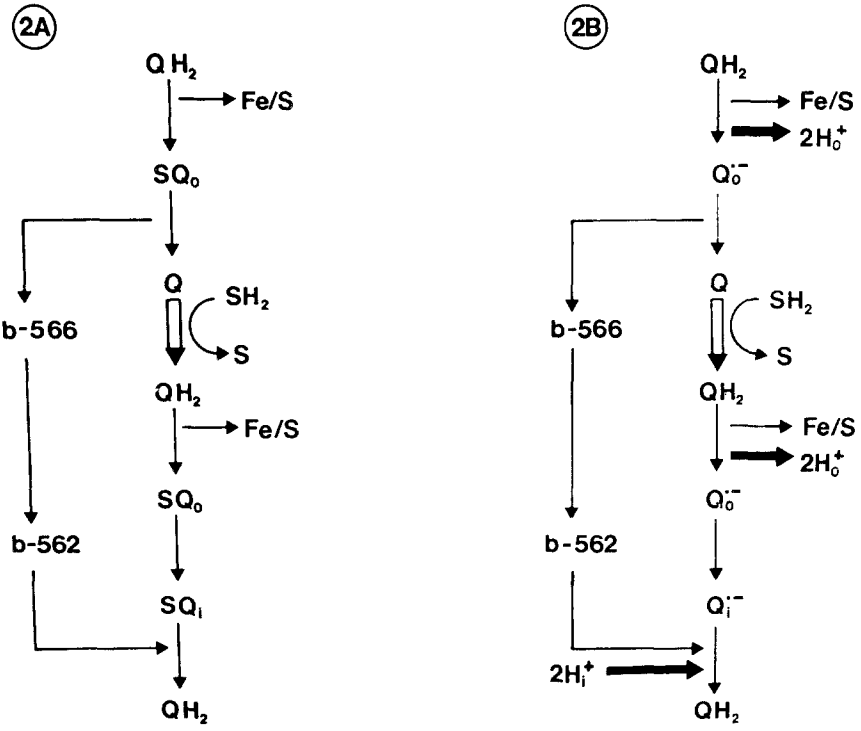


**Fig. 2.** A: Alternative drawing of electron transfer in the *b* cycle. All reactions shown (except those between $SH_2$ and Q, and the transition of $SQ_o$ to $SQ_i$) are one-electron transfers. The reaction between Q and $SH_2$ symbolizes hydrogen transfer from hydrogenated substrates to the membranous pool of ubiquinone. B: The semiquinone or SQ cycle. The scheme is identical to that in A, except for the addition of steps of proton release into the O phase ($H_o^+$) and uptake from the I phase ($H_i^+$), denoted by black arrows, and the specification of the SQ's as semiquinone anions.

"pool". Also, there is no requirement for reversed dismutation of quinol and quinone to produce SQ at domain i, as suggested in the modified Q-cycle of Slater (1981).

An important property of the *b* cycle, not immediately obvious from schemes such as Figs. 1A, B, is the fact that a complete turnover requires oxidation of two molecules of $QH_2$ by Fe/S (cf. Crofts, 1985). To make this clear, the *b* cycle (Fig. 1B) may also be drawn as shown in Fig. 2A.

The quinone molecule shown in Fig. 1 was suggested to be "a particular protein-bound species of (ubi)quinone" (Wikström and Krab, 1980), or different forms of "only one species of specifically bound (ubi)quinone, called Z" (Wikström *et al.*, 1981). This does not imply that it is a nonexchangeable molecule or a "prosthetic group." It rather means that there is in the

cytochrome $bc_1$ monomer a single unique site for binding or association of ubiquinone, while involved in catalysis (cf. Q cycle). Wikström and Krab (1980) suggested that Q and $QH_2$ associated in this way with the enzyme "equilibrate with the bulk free ubiquinone pool, which is an obligatory intermediate between the dehydrogenases and Complex III." Recent kinetic analyses by Crofts (1985) and Rich (1981) have shown that there must be rapid exchange of Q and $QH_2$ between enzyme-bound and free (pool) forms. In the *b* cycle it is postulated that there can be only one uniquely bound or associated molecule of ubiquinone (whether reduced, oxidized, or semiquinone) in the cytochrome *bc* monomer at any time. This leads to the concept of a ubiquinone "pocket" in the enzyme.

## The Ubiquinone "Pocket"

Recent surface pressure, calorimetric, and NMR studies (Quinn and Esfahani, 1980; Katsikas and Quinn, 1982; Kingsley and Feigenson, 1981) have led to the conclusion that the molecules of Q in the membrane may occupy the central region of the hydrocarbon, with an orientation such that the long isoprenoid side chain lies parallel to the membrane plane. Based on these notions we suggest that the postulated single unique site of ubiquinone association with the *bc* monomer may be described as a ubiquinone "pocket" that is located close to the center of the membrane, and into which Q may be bound with its benzoquinone head first (Wikström and Saraste, 1984).

When inserted in the pocket, the benzoquinone head of ubiquinone may interact with either of two catalytic domains, which are located toward the two sides of the membrane and constitute the o and i domains discussed above. These interactions may be stabilized by proteinaceous positive charges that may attract a negative charge on the quinol ($QH^-$) or semiquinone ($Q\cdot^-$) anion (Rich, 1981, 1984). Uncharged forms of ubiquinone, such as the oxidized Q, may therefore be less strongly associated with the pocket (cf. below).

According to the *b* cycle model, the SQ in the pocket must be able to reorientate itself between the o and the i domains. In particular, when SQ has been formed by oxidation of $QH_2$ in the o domain, it may subsequently be reorientated to become SQ of the i domain (Figs. 1 and 2). This essential and unique step of the *b* cycle is suggested to occur simply by a rotation of the ubiquinone molecule around the axis through the isoprenoid side chain in the plane of the membrane (Wikström and Saraste, 1984).

While Q or $QH_2$ in the pocket must be in rapid equilibrium with the membranous "pool" of ubiquinone (cf. above), for SQ such equilibration would destroy the specific functionality of the *b* cycle. If released into the

membrane, SQ would be expected to rapidly dismutate to Q and $QH_2$. Thus, SQ in the pocket must either be strongly bound or, perhaps more likely, have a kinetic (catalytic) lifetime sufficiently short to effectively prevent its release.

## Cytochrome *b*

Predictions of the folding of apocytochrome *b* in the membrane (Saraste and Wikström, 1983; Saraste, 1984; Widger *et al.*, 1984) have suggested that the two heme groups may lie each with its center about 10 Å from the two membrane/water interphases. Since the side of the porphyrin is approximately 8.5 Å, this yields a distance of approximately 12 Å between the heme edges (about 20 Å between heme irons). The hemes may be "sandwiched" between helical columns that run perpendicular to the membrane plane, and to which they may be associated through axial histidine ligands to heme iron. Functionally, this model suggests that electron transfer between the hemes is transmembranous and hence electrogenic [cf. Mitchell (1972) and Wikström (1973)].

Since the catalytic domains o and i are known to be closely associated with the respective heme groups (*b*-566 and *b*-562), the approximate positioning of the former would also be defined by this structural model. Clearly, this brings the *b*-cycle closer to the Q cycle, in which these domains have been defined to lie near the O and I side of the membrane, respectively.

## Mechanism of Proton Translocation and the SQ Cycle

Proton translocation in the *b* cycle was originally suggested to occur with the *b*-type cytochromes somehow functioning as proton pumps (Wikström and Krab, 1980; Wikström *et al.*, 1981). This indirectly coupled alternative to the direct kind of coupling in the Q cycle has not received any significant experimental support. On the other hand, distinction between these two types of mechanism is, of course, difficult experimentally. Nevertheless, recent developments seem to make a directly coupled mechanism more attractive. In particular, the structural arrangement of the cytochrome *b* hemes in the membrane (see above), and the likelihood that SQ is usually in the anionic form $Q\cdot^-$ (De Vries *et al.*, 1981; Rich, 1981, 1984; Ohnishi and Trumpower, 1980), make it logical to consider the application of a direct kind of coupling alternative to the *b* cycle model (cf. Wikström and Saraste, 1984).

Figure 2B, which is a direct modification of the *b* cycle in Fig. 2A, describes such an alternative. The basic principle of direct coupling between electron transfer and proton translocation is the same as in the Q cycle, as is

the protonic connection of domains o and i with the aqueous O and I sides of the membrane, respectively. This semiquinone or simply SQ cycle shows some interesting differences from the Q cycle, which obviously stem from the differences in electron-transfer pathway. One difference of this kind relates to the translocation of electrical charge. In the Q cycle this is due to electron translocation across the cytochrome *b* hemes. In the SQ cycle (Fig. 2B; Wikström and Saraste, 1984) it is partially due to this and partially to electrogenic reorientation of the semiquinone anion from its interaction with the o to interaction with the i domain. Since SQ in the i domain is the electron acceptor from *b*-562, it follows that the oxidation phase of *b*-562 may be synchronous with and limited by the electrogenic transpositioning of the SQ anion.

## Comparison between the SQ and Q Cycle Models in the Light of Experimental Data

The main difference between the SQ cycle and various versions of the Q cycle is the way SQ is generated in the i domain, and more generally, the function of this "quinone reductase site" (Crofts, 1985). In Q cycle models, SQ of center i is formed either by reduction of Q by dehydrogenases (Mitchell, 1976), or by reversed dismutation of $QH_2$ and Q (Slater, 1981). Alternatively, it has been suggested that domain i could accept both Q and SQ as electron acceptor, whereby *b*-562 could sequentially reduce Q to $QH_2$ via SQ (Crofts, 1985). In contrast, in the SQ cycle SQ in domain i is formed specifically by (electrogenic) reorientation of the SQ molecule that has been generated in the o domain, or alternatively, in the reverse reaction where $QH_2$ reduces *b*-562. In the SQ cycle Q is not normally reduced to SQ(i) by *b*-562, in contrast with the modified Q cycle advanced by Crofts (1985) and Crofts and Wraight (1983). If this occurred, SQ(i) would occupy the Q pocket by which a further introduction of ubiquinol from the pool may either be prevented, or would lead to expulsion of the SQ from the pocket. Only in the exceptional case where both hemes *b* happen to be reduced simultaneously might Q be reduced to $QH_2$ by two rapid sequential one-electron transfers at domain i. However, during normal operation the interaction of Q with domain i may be improbable due to a higher affinity of association of $QH_2$ than of Q with the pocket. This could be achieved, for example, by stabilization of bound quinol in the deprotonated $QH^-$ form by positive charges in the protein [see Rich (1984) and above].

A typical feature of the SQ cycle is, hence, a compact arrangement of the interaction of ubiquinone with the *bc*-type complex. This leads to some predictions that may be tested experimentally. Oxidation of *b*-562 following

an induced oxidation of cytochrome $c_1$ and Fe/S would be limited only by the rate of oxidation of quinol by Fe/S and the transpositioning of $SQ^-$ from domain o to domain i; the oxidant $SQ(i)^-$ would be produced locally without time for equilibration with the Q pool. Evidence for such local production of the oxidant of *b*-562 as a consequence of turnover at the o site has been published by Rich (1983). It was shown that this oxidant could not be ubiquinone from the pool for kinetic reasons. Rich considered this locally produced oxidant to be ubiquinone. But both Q and $QH_2$ associated with the *bc*-type complex must be in rapid equilibrium with the Q and $QH_2$ in the pool (Crofts, 1985; Rich, 1984). We therefore consider it more likely that the locally produced oxidant is semiquinone, in agreement with the SQ cycle.

The kinetics of the cytochrome $bc_1$ complex have by far been best studied in bacterial chromatophores. At certain high ambient redox potentials ubiquinone and the *b* cytochromes are initially highly oxidized but the Rieske Fe/S and cytochromes $c_2$ and $c_1$ are highly reduced. In this condition a light flash induces oxidation of the latter, and generation into the Q pool of a single ubiquinol molecule per $bc_1$ complex, on the average (see Crofts, 1985). The reaction of this ubiquinol molecule with the $bc_1$ complex results in reduction of *b*-562, the reoxidation of which is very slow, however. This may be compared with the much faster reoxidation kinetics at a lower ambient $E_h$, when more $QH_2$ is available. If Q was the normal oxidant of *b*-562 it would be curious that *b*-562 ($E_{m,7}$ approximately 50 mV) fails to become rapidly oxidized at high ambient redox potentials (where ubiquinone is abundant), but is rapidly oxidized when there is less Q and more $QH_2$. In our opinion this is further strong evidence against the possibility that Q from the membranous pool would normally rapidly accept electrons from *b*-562 in domain i. The fact that the oxidation phase of *b*-562 is much accelerated when, on the average, several molecules of $QH_2$ are present per $bc_1$ complex, is in good agreement with the postulate that the oxidant of *b*-562 is locally produced following oxidation of ubiquinol in domain o.

Another problem of the Q cycle is how it is initiated, by oxidation of Fe/S, from a state where all components of the complex (and the *b*-type heme in particular) are initially reduced [see also Bowyer and Trumpower (1981) and Mitchell (1982)]. This problem obviously arises from the fact that the Q cycle oxidation of cytochrome *b* necessarily requires prior reduction of cytochrome *b*. In the SQ cycle (or *b* cycle) this is not a problem since SQ generated in domain o can be transpositioned to domain i to oxidize *b*-562. As recently reported by Rich and Wikström (1986), there is no significant difference in the fast velocity by which cytochrome *b* is oxidized whether it is partially or fully reduced initially. This finding strongly favors the electron transfer scheme of the *b* and SQ cycles. Stopped-flow experiments of Papa *et al.* (1981) also show that reduction of cytochrome *b* does not necessarily

occur prior to oxidation, upon initiation of electron flow by oxidation of Fe/S and cytochrome $c_1$. The initial reduction phase was favored when a membrane potential was generated, but was absent when it was rapidly dissipated by valinomycin plus $K^+$ (Papa *et al.*, 1981). This agrees well with the SQ cycle, because the fate of the SQ anion generated at domain o (i.e., either reduction of *b*-566 or reorientation to the i domain to accept an electron from *b*-562) is expected to depend on membrane potential.

Recent work with chloroplasts has also shown that even though plastoquinone and cytochrome *b* are highly reduced before flash-induced oxidation of cytochrome *f*, there is still a normal electrogenic reaction (Girvin and Cramer, 1984; Joliot and Joliot, 1985) and fast oxidation of cytochrome *b* (Joliot and Joliot, 1985). However, the half-time of the overall oxidation phase of cytochrome *b* was approximately five times longer than the electrochromic band-shift indicative of membrane charging (Joliot and Joliot, 1985). But this does not necessarily contradict the *b*-cycle, as suggested (Joliot and Joliot, 1985), because the overall kinetics of oxidation of cytochrome *b* may be composed of both reductive (by plastosemiquinone) and oxidative elements.

Recent experiments with chromatophores have established that both the reduction and the oxidation of *b*-562 is associated with generation of membrane potential (Glaser and Crofts, 1984). This is nicely consistent with the SQ cycle in which both electron transfer between the cytochrome *b* hemes and transpositioning of $SQ^-$ are expected to contribute to the generation of membrane potential. As indicated above, the latter reaction would be expected to limit the oxidation of *b*-562 and thereby be kinetically linked to it.

## Some Notes on the Thermodynamics of the Model

A much discussed point in this context is the question of the midpoint redox potentials of the $QH_2/SQ$ and SQ/Q couples, and the stability constant of SQ in domain o (see, e.g., Hauska *et al.*, 1983; Crofts and Wraight, 1983; Mitchell, 1976; Wikström and Saraste, 1984; Hendler *et al.*, 1985). The Q cycle was recently criticized by Hendler *et al.* (1985) based on these thermodynamic parameters. However, such discussions are often of limited practical value, because usually they require the assumption of redox equilibrium among the different forms of ubiquinone while functionally it is an induced disequilibrium (i.e., an operation at different redox potentials) between them that is essential. The "stability constant" of SQ is also of little functional relevance, at least in the context of the SQ cycle, because the dismutative reaction between two molecules of SQ would not be expected to occur to any

significant extent, since the enzyme pocket can accommodate only one molecule at the time. We therefore find it functionally more instructive to look upon the oxidative reaction path of ubiquinol as a "dismutation" of the potential energy of its two (energetically equivalent) electrons.

With two consecutive redox reactions (cf. Figs. 1 and 2), i.e.,

$$QH_2 \xrightarrow[-e]{E_h(1)} SQ \xrightarrow[-e]{E_h(2)} Q \tag{1}$$

occurring at the redox potentials $E_h(1)$ and $E_h(2)$, and where the $E_h$ of the $Q/QH_2$ couple is defined as $E_h(0)$, it can easily be shown that

$$E_h(1) + E_h(2) = \text{const} \tag{2}$$

for the cases where $E_h(0)$ and the involved midpoint potentials are constant. Thus a sudden increase of $E_h(1)$, e.g., by oxidizing the Fe/S center and cytochrome $c_1$, will impose a corresponding symmetric decrease of $E_h(2)$. This will make reduction of cytochrome *b*-566 more favorable than before the pulse of oxidant. As a reasonable numerical example $E_h(1)$ may be 110 mV before the pulse (cytochrome $c_1$ 99% reduced) and 290 mV after addition of the oxidant (90% oxidized), a positive shift of 180 mV. The term $E_h(2)$ may be 50 mV prior to the pulse (*b*-562 50% reduced and *b*-566 highly oxidized). With essentially unchanged $E_h(0)$ and midpoint potentials the upward shift in $E_h(1)$ would induce a 180-mV downward shift in $E_h(2)$, i.e., to a value of $-130$ mV. This is more than sufficient for effective reduction of *b*-566, which has an apparent $E_{m,7}$ of about $-30$ mV. Notice that this description of oxidant-induced reduction of cytochrome *b* (or the redox "see-saw" effect; Mitchell, 1976) in terms of a "dismutative" energy gain of one of the quinol electrons at the expense of the other does not require any assumptions about the midpoint potentials of the redox couples involving ubiquinone, nor of the stability constant of SQ.

Due to the electrogenicity of the transition of SQ(o) to SQ(i), this event may be expected to become unfavorable at high membrane potentials and hence kinetically improbable. It may therefore be necessary to postulate that the rotational equilibrium lies relatively far toward SQ(i) in the absence of membrane potential, i.e., that the SQ is less tightly associated with the o than with the i domain. Interestingly, this postulate has corollaries which are in good agreement with what is known about the system, such as the apparently higher stability of $SQ_i$ (De Vries *et al.*, 1980, 1981).

A problem common to the SQ and Q cycle schemes is to understand why the $Q\cdot^-$ formed by oxidation of $QH_2$ in domain o does not deliver its electron to the Fe/S center, a reaction that would be thermodynamically more favorable than the reduction of the low-potential heme *b*-566 (see, e.g., Hendler *et al.*, 1985). If the former reaction did occur, there would be uncoupling of

"site 2" electron transfer from proton translocation, and consequent rapid antimycin-insensitive respiration. We suggest that electron transfer from ubiquinone to Fe/S in the o domain may be catalyzed by protons so that the activation barrier for electron transfer from an unprotonated quinone (e.g., $Q\cdot^{-}$) is sufficiently high to prevent the reaction in practice, but drastically lowered when the reaction is associated with a local release of protons (see Malmström, 1985).

## Concluding Remarks

The above has been a general outline of a new model, called the SQ cycle, which has its origins in the Wikström–Berden model and incorporates central features from both the *b* cycle and the Q cycle. Whether this new model is a modified Q or *b* cycle is not important in our opinion. What may be more important is that the new model appears to provide a sensible explanation for a number of experimental findings that are difficult to explain on the basis of the old models. It may therefore be worth considering in future experimental evaluations of the intriguing chemistry of cytochrome *bc*-type complexes.

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