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Multicarrier Transport: Coupled Transport of Electrons and Metal Cations Mediated by an Electron Carrier and a Selective Cation Carrier[1]

Sir:

Coupled flow of different substrates across membranes plays a fundamental role in biology[2] and may have important practical applications. The realization of artificial systems displaying such properties should allow one to isolate a given component of a complex natural process and thus provide models for detailed mechanistic studies as well as for the evaluation of practical uses.

We report here an artificial system which performs selective transport of alkali cations coupled to the simultaneous flow of electrons in the same direction (symport) across a membrane containing an electron carrier and a cation carrier.[2b]

Several artificial electron transport systems have been reported.[1-5] Electron transfer in phospholipid vesicles occurs when quinone or dibutylferrocene is present and is affected by ionophores or uncouplers such as valinomycin or nigericin.[2] We have previously reported electron transport across supported liquid membranes using menadione and dibutylferrocene as electron carriers, and we have used this system to demonstrate light-driven electron transport by photochemical generation of a reducing agent.[1] It should be possible to couple such electron flow to the symport or antiport of another species, just as amino acid transport may be pumped by a pH gradient or an ion gradient.[6] This has been shown to occur in the counterflow of electrons and picrate anions.[5,7] The use of a carrier for the coupled species would allow control of the selectivity of the transport.

In the artificial systems mentioned above, the nature of the electron carrier determines the species which is coupled to electron transport in order to maintain charge neutrality in the membrane phase. Quinone type carriers couple to proton transport ($2e^- + 2H^+$) since the reduced form is hydroquinone. Ferrocene is typical of carriers which are neutral when reduced and positive when oxidized and thus can be coupled to anion transport.[7] In order to demonstrate coupled cation transport, it is necessary to choose a carrier which is negative when reduced and neutral when oxidized.

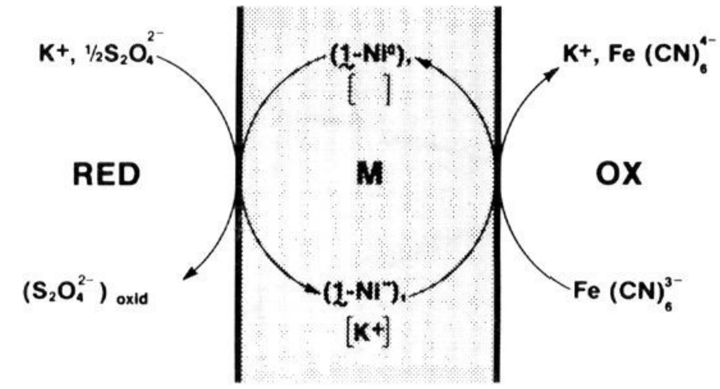
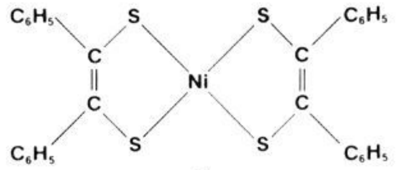


Figure 1. Representation of the mechanism of redox driven potassium cation transport using an electron and a cation carrier. ($\mathbf{1}$-Ni^0) and ($\mathbf{1}$-N$_i^-$) are the oxidized and reduced form of the electron carrier, the nickel bisdithiolene complex **1;** [ ] and [K^+] are the macrocyclic ligand, **2,** and its K^+ complex.



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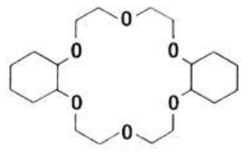
The present system performs *electron/cation symport* mediated by a nickel bisdithiolene electron carrier, **1,** and a selective carrier for alkali cations, dicyclohexyl-18-crown-6, **2,** dissolved in a diphenyl ether membrane, M, separating two



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aqueous phases. The nickel bisdithiolene complex may undergo redox reactions at the interfaces with suitable redox reagents, ($\mathbf{1}$-Ni^0)/($\mathbf{1}$-Ni$^-$) = 0.134 V vs. Ag/AgCl.[8] A number of macrocyclic ligands of different types have been shown to transport alkali metal cations[9-11] by solubilizing inorganic salts in apolar media via formation of macrocyclic cation inclusion complexes;[12] macrocycle **2** is a selective carrier for potassium ions.[10] One of the aqueous phases, RED, contains a reducing agent, sodium dithionite ($E_0 = -1.13$ V[13]) and the other, OX, an oxidizing species, potassium ferricyanide ($E_0 = 0.36$ V[13]) (Figure 1[14]).

The processes occurring in the present system are represented in Figure 1. Figure 2 and Table I display results ob-

Table I. Experimental Parameters and Rates of K^+ and e^- Transport[a]

	aqueous phases, initial concn (10^{-3} M)				M phase, μmol		rate (μmol/h·μmol of **1**)[b]		
	RED		OX				RED,	OX	
expt	$Na_2S_2O_4$	K^+	$Na_3Fe(CN)_6$	K^+	**1**	**2**	K^+	K^+	e^-
1	50	160	1.1	0	0.24	3.1		9.3	7.9
2	9.9	0.53	1.0	0.67	0.31	3.6	3.7	4.7	4.3
3	9.8	2.1	1.1	2.5	0.35	3.6	5.8	4.0	5.4
4	50	160	1.1	0	0	3.5		0	0
5	9.7	0.5	1.0	0.64	0	3.4	0	0	0
6	50	160	1.1	0	0.27	0		0	0
7	9.8	1.2	1.1	1.4	0.32	0	0	0	<0.46
8	50	0	1.1	0	0.31	3.9			1.3
9	9.9	0	1.1	0	0.29	3.5			1.3

[a] Buffer conditions: RED phase, expt 1, 4, and 6, 0.1 M K_2HPO_4/KH_2PO_4, expt 8, 0.1 M Li_2HPO_4/LiH_2PO_4, expt 2, 3, 5, 7, and 9, 0.05 M Li_2HPO_4/LiH_2PO_4; OX Phase, same as corresponding RED phase except expt 1, 4, and 6 were 0.1 M Li_2HPO_4/LiH_2PO_4. [b] K^+ and e^- transport rates are the rates of change of K^+ and K^+ and $Fe(CN)_6^{3-}$ concentrations in RED and OX phases, respectively; rates are normalized to the quantity of **1** in the membrane.

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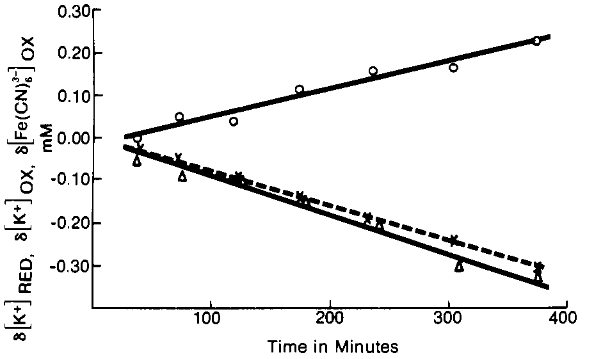

Figure 2. Time dependence of the concentrations of K^+ and $Fe(CN)_6^{3-}$ in RED and OX phases for run 3 (Table I): $\delta[K^+]_{RED}$ (Δ), $\delta[K^+]_{OX}$ (○), $\delta[Fe(CN)_6^{3-}]_{OX}$ (×), are differences in concentration at time t minus concentration at time $t = 0$.

tained under different conditions. The following comments may be made. (1) When neither **1** nor **2** is present in the membrane, the system remains unchanged. (2) With the complete system represented in Figure 1 (Table I, runs 1-3), the K^+ concentration decreases in RED and increases by about the same amount in OX where also the ferricyanide concentration decreases similarly (Figure 2). Thus, the membrane has become permeable to electrons and to K^+ cations which flow simultaneously from RED to OX: compounds **1** and **2** function as *electron* and *cation carriers*, respectively. (3) No transport is observed when *either* **1** (Table I, runs 4, 5) or **2** (Table I, runs 6, 7) are absent in the membrane. (4) The observed *e^-/K^+ symport* may be explained by a four-step reaction sequence: (i) at the RED/M interface, (**1**-Ni^0) is reduced by $S_2O_4^{2-}$ and charge neutrality is maintained by simultaneous transfer of a K^+ cation to the ligand **2** to form the double-complex ion pair $\{(\mathbf{1}\text{-}Ni^-),[K^+]\}$; (ii) the $\{(\mathbf{1}\text{-}Ni^-),[k^+]\}$ species diffuses across the membrane; (iii) it is oxidized by ferricyanide at the M/OX interface regenerating (**1**-Ni^0) and releasing K^+ at the same time; (iv) the oxidized electron carrier and the empty macrocyclic ligand diffuse back to the RED/M interface where the cycle starts again. (5) *Active K^+ transport* against its concentration gradient (uphill) occurs, driven by the redox gradient and the electron flow (see for instance Figure 2). (6) The transport rate is *cation dependent;* it is much slower when only Na^+ cations are present (Table I, runs 8, 9). Indeed **2** and similar ligands are known to complex and to transport K^+ more efficiently than Na^+.[10,12] (7) The total process thus involves a *redox pump*, via the electron carrier, a cation *selection* process, via the macrocyclic ligand, and a *regulation* process since transport rates depend on the carrier efficiency for a given ligand-cation pair.

The model system described in this report (Figure 1) may be considered as a prototype for the design of other multicarrier coupled transport systems. A number of variations and extensions may be envisaged either as biological models[2b] or as potential applications. For instance, employing other carriers for anions as well as for cations will provide different substrate selectivity; coupling with a light-driven process[1] also represents a promising extension.

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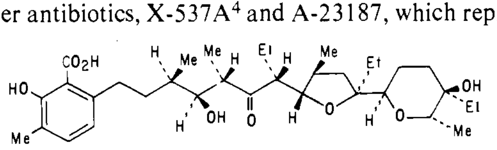
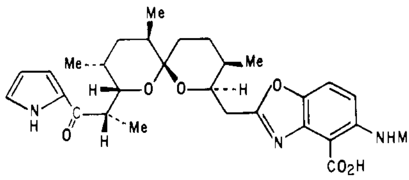
Synthesis of New, Noncyclic Ionophores Exhibiting Efficient Ca^{2+} Transport

Sir:

The phenomenon of ion transport across cell and organelle membranes which mediate numerous cellular events is receiving ever-increasing attention.[1] Although a number of naturally occurring molecules are known which substantially enhance the passive transport of ions across cell membranes (ionophores),[2,3] they are all relatively complex structures requiring multistep procedures for organic synthesis. Two of the more oft-employed ionophores as biochemical tools are the polyether antibiotics, X-537A[4] and A-23187, which represent the class of monobasic, carrier-type ionophores.[1a] We believed that the intriguing possibility of designing and constructing a synthetic ligand system capable of mimicking the transport properties of these complex ionophores merited further attention[5] and report herein our approach to this goal.



X-537A (LASALOCID)



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To fulfill the interrelated criteria for ion selectivity and

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