Chapter 3

Mechanistic Studies of Carrier-Mediated Transport Through Supported Liquid Membranes

Lysander A. J. Chrisstoffels, Feike de Jong,
and David N. Reinhoudt

Department of Organic Chemistry, University of Twente,
P.O. Box 217, 7500 AE Enschede, Netherlands

Carrier-assisted transport through supported liquid membranes is one of the important applications of supramolecular chemistry. Carriers for the selective transport of neutral molecules, anions, cations or zwitter ionic species have been developed. The transport can be described by subsequent partitioning, complexation and diffusion. Mechanistic studies are mainly focussed on diffusion limited transport, in which diffusion of the complex through the membrane phase is the rate-limiting step of the transport. Recently, kinetic aspects in membrane transport have been elucidated with new carriers for which the rate of decomplexation determines the rate of transport. In this chapter, recent mechanistic aspects for carrier-assisted transport through supported liquid membranes are reviewed.

Membrane separation is a relatively new and fast growing field in supramolecular chemistry. It is not only an important process in biological systems, but may become a large-scale industrial activity. For industrial applications, many synthetic membranes have been developed. Important conventional membrane technologies are microfiltration, ultrafiltration, electro- and hemodialysis, reverse osmosis and gas separations (1). The main advantages are the high separation factors that can be achieved under mild conditions and the low energy requirements.

In living matter, biological membranes provide a barrier between an intracellular and extracellular aqueous environment. The membranes are bilayers of amphiphilic phospholipids and glycolipids which support the membrane proteins that can induce selective transport through the cell membrane (2). These proteins complex certain species and carry these through the membrane to the other compartment where they are released. The first antibiotic recognized to facilitate selective transport is valinomycin (3). It binds K^+ a thousand times more strongly than Na^+ , and it induces the selective uptake of K^+ in mitochondria.

An artificial membrane set-up that mimics carrier-facilitated transport is the liquid membrane. It consists of two aqueous phases that are separated by a water-immiscible organic phase to which receptors (carriers) are added to facilitate selective transport.

Natural receptors, such as valinomycin or beauverin, can be used as carriers. Also synthetic receptors have been developed. The first generation of synthetic carriers were the crown ether macrocycles, which selectively bind alkali metal ions (4). Since their discovery in 1967, many other types of macrocycles have been synthesized and used for the selective recognition of neutral, charged, or zwitter-ionic species. Many have been used as carriers in liquid membranes (5).

Liquid membrane separations can be achieved by different configurations (Figure 1). The main types will be discussed briefly. Bulk liquid membranes (BLM) have often been used to investigate novel carriers and transport mechanisms, because of their relative simplicity (Figure 1a). They consist of an aqueous source and receiving phase separated by a water-immiscible organic solution in a U-tube. Both aqueous phases and the membrane phase are stirred in order to achieve homogeneous solute concentrations and to minimize the thickness of the unstirred boundary layers. Disadvantages of the BLM are the relative instability and the large amounts of organic solvent and carrier needed.

In an emulsion liquid membrane (ELM), a dispersion of water containing oil droplets is stirred in a bulk aqueous source phase (Figure 1b) (6). Separation occurs very rapidly, because the organic layer is very thin while the surface area is large. Furthermore, the source phase volume is at least ten times larger than that of the receiving phase. A disadvantage is the instability of the emulsions. This is due to pH changes, ionic strength and physical forces. Furthermore, it is difficult to separate the oil droplets from the source phase and to break up the oil droplets to recover the receiving phase.

A supported liquid membrane consists of an organic carrier solution immobilized in a porous hydrophobic polymeric support. Two frequently used configurations are shown in Figure 1. The flat sheet supported liquid membrane is clamped between two cells that are filled with either an aqueous source or a receiving phase (Figure 1c). Because of its simplicity, the small amounts of solvent and carrier required, and its well defined diffusion layer (membrane thickness), this is a suitable system for mechanistic studies. The hollow fiber supported liquid membrane which is shown in Figure 1d has a cylindrical geometry. It consists of a few hundred hollow fibres in which the organic carrier solution is immobilized (7). The hollow fiber configuration is the most suitable for industrial application due to its large exchanging surface and long-term stability.

Carrier-Assisted Membrane Transport of Salts

Assisted transport through a liquid membrane takes place via the following consecutive steps: partitioning of a species from the aqueous source phase into the membrane phase, complexation by the carrier inside the membrane phase, and transport of the complex through the membrane. At the receiving side of the membrane, decomplexation and partitioning of the species into the aqueous receiving phase takes place. The performance of a liquid membrane is strongly related to the characteristics of the carrier, hence it is important to describe its properties with the

Figure 1. Schematic Representation of Different Liquid Membrane Configurations: (a) Bulk Liquid Membrane, (b) emulsion liquid membrane, (c) flat-sheet supported liquid membrane, (d) hollow fiber supported liquid membrane.

Figure 2. Concentration Profile for the Transport of Substrate S Assisted by Ligand L Through a BLM. (Adapted from ref. 5).

physical parameters D_m and K_{ex} . D_m is the apparent diffusion coefficient of the complex, which is a measure of the diffusion velocity of the complex through the membrane. The extraction constant K_{ex} is a measure of the ability of a carrier to extract a certain species from the aqueous phase into the membrane phase. Both parameters are described more fundamentally in the next section.

To determine D_m and K_{ex} , various models have been applied in mechanistic studies of cation-assisted transport. Accurate mechanistic studies are carried out with a SLM, because of its known diffusional layer and negligible external transport resistances. A detailed description of its configuration is given in the section on Transport Through a Supported Liquid Membrane. Models for assisted transport are differentiated by their rate-limiting step for transport, which is dependent on the rate of decomplexation at the receiving phase-membrane interface. Two types of transport mechanisms are distinguished. First, diffusion-limited transport, in which the diffusion process of the complex through the membrane phase is the rate-limiting step (see the section on Diffusion-Limited Transport of Salts). Second is kinetically limited transport in which the rate of decomplexation at the receiving side of the membrane phase is the rate-limiting step (see the section on Reaction-Rate Limited Transport of Monovalent Ions). To distinguish both mechanisms, a dimensionless number α is introduced as is described in the section on Kinetically Limited Transport: Determination of α .

Optimization of the flux is investigated through the variation of external parameters which affect transport, such as the membrane polarity, viscosity, anion used and operating temperature (see the section on Optimization of the Flux: External Influences on Transport). The influence on the transport kinetics has been investigated as well. Until recently, the transport of salts has only been facilitated through the use of a cation carrier. The cation is complexed by the carrier while the anion accompanies the complex as a free ion, hence a lipophilic anion is used to accompany the complex.

Another situation arises when the transport of the anion is assisted. In a later section, the transport of salts using an anion carrier, a mixture of a cation and anion carrier, or a ditopic carrier is discussed. Finally, the transport of neutral molecules will be described in the section on Diffusion-Limited Transport of Neutral Molecules. This is illustrated with our recent investigations on the transport of urea.

Transport Through a Bulk Liquid Membrane. All theoretical models concerning carrier-assisted transport through SLMs are based on the theoretical work for carrier-assisted transport through BLM systems reported by Reusch and Cussler (8). They described the transport of different alkali salt mediated by dibenzo-18-crown-6 through a BLM.

For the simplest case, *i.e.* the transport of a species (S) assisted by a ligand (L), the concentration profile may be visualized as shown in Figure 2. A BLM contains three bulk phases, *viz.* an aqueous source phase, a bulk liquid membrane, and an aqueous receiving phase. In these phases, transport takes place by convection and there are no concentration gradients. There are unstirred aqueous and organic layers at the source and receiving phase interfaces with the bulk liquid membrane. Processes which play a role in these interfacial regions are partitioning, complexation, and diffusion. The function of a carrier can be illustrated by comparison of the "blank"

transport with carrier-assisted transport. For the diffusional processes at the interface, Fick's first law (Equation 1) is used to describe the flux through a stagnant layer with thickness l .

$$J_s = \frac{D_s}{l} \Delta c_s \quad (1)$$

The fluxes through the aqueous interfaces at the source phase (J_{as}) and the receiving phase (J_{ar}) are described according to Equation 2.

$$J_{ar} = \frac{D_a}{l_a} ([S]_{ri} - [S]_{rb}) \quad ; \quad J_{as} = \frac{D_a}{l_a} ([S]_{sb} - [S]_{si}) \quad (2)$$

In case of "blank" transport, only partitioning at both interfaces takes place according to Equation 3.

$$S_{si} \rightleftharpoons S_{mi,s} \quad ; \quad S_{ri} \rightleftharpoons S_{mi,r} \quad ; \quad K_p = \frac{[S]_{mi,s}}{[S]_{si}} = \frac{[S]_{mi,r}}{[S]_{ri}} \quad (3)$$

The fluxes of species "S" through the membrane interface layers at the source side (J_{ms}) and the receiving side (J_{mr}) are written according to Equation 4.

$$J_{mr} = \frac{D_m}{l_m} ([S]_{mi} - [S]_{mb}) \quad ; \quad J_{ms} = \frac{D_m}{l_m} ([S]_{mb} - [S]_{mi}) \quad (4)$$

In the steady state situation, all fluxes are equal and can be summarized to obtain a relation which is expressed in terms of a resistance = (chemical potential/flux).

$$\frac{([S]_s - [S]_r)}{J} = \frac{2l_a}{D_a} + \frac{2l_m}{D_m K_p} \quad (5)$$

The first term of Equation 5 refers to the resistance due to presence of an external interface layer. The internal resistance is described by the second term ($2l_m/D_m K_p$). In the presence of a carrier, both diffusion of uncomplexed and complexed species through the membrane phase takes place. The latter involves the extraction of a species S from the aqueous phase to form a complex "LS" in the membrane phase. In this process both the stability of the complex (K_a) and the partition (K_p) play a role.

$$S_{ai} + L_{mi} \rightleftharpoons LS_{mi} \quad ; \quad K_{ex} = \frac{[LS]_{mi}}{[S]_{ai}[L]_{mi}} \quad (6)$$

The extraction constant K_{ex} is defined as $K_{ex} = K_a K_p$. The association constant K_a is defined as the equilibrium constant for the complexation of species S by ligand L in the membrane phase. Combination of the extraction Equation with the mass-balance for the carrier gives Equation 7, which shows that the flux of species S increases upon the addition of ligand L_0 via the term $(K_{ex} L_0) / ((1 + K_{ex} [S]_s)(1 + K_{ex} [S]_r))$. If no carrier is present, Equation 7 reduces to Equation 5. The rate-limiting step of the process is the diffusion of the complex through the organic layer.

$$\frac{([S]_s - [S]_r)}{J} = \frac{2l_a}{D_a} + \frac{2l_m}{D_m} \frac{1}{\left(K_p + \frac{K_{ex}L_0}{(1 + K_{ex}[S]_s)(1 + K_{ex}[S]_r)}\right)} \quad (7)$$

The thicknesses of both the interfacial layers (l_a and l_m) are unknown. Therefore a quantitative description of the transport is difficult. This is the main disadvantage of the BLM for mechanistic studies.

Transport Through a Supported Liquid Membrane. Mechanistic studies of carrier-assisted membrane transport have been carried out in our group using the supported liquid membrane (SLM) configuration. In comparison with the configuration of a BLM, the SLM has a few differences which favor its use for mechanistic studies. Usually we have conducted transport experiments through SLMs in a permeation cell as shown in Figure 3. The source phase (SP) and the receiving phase (RP) consist of an identical cylindrical compartment with a half-cell volume of 50 mL and an effective membrane area of about 13 cm². Both compartments are double-walled and thermostated at $T = 25^\circ\text{C}$. A flat-bladed turbine positioned in the center is driven by a magnet outside the compartment at a stirring rate of 750 rpm. Compared to BLM transport, stirring of the aqueous phases can take place more vigorously, due to the use of a solid support. For mechanistic studies this implies that the influence of an external transport resistance can be neglected (9). Baffles, which are set radially along the wall of the compartments provide a large top-to-bottom circulation, creating well-mixed solutions without significant concentration gradients.

Hydrophobic polymers as polyethylene, polypropylene, or polysulfone are often used as supports. For fast transport-rates, the exchanging surface between the aqueous phases and the membrane phase should be large. Therefore thin films with high porosity are used (10). The dimensions of the support are known, which is an advantage of the SLM in mechanistic studies. The stagnant diffusional layer of the complex is defined as the length of the polymeric support ($2l_m = d_m$). Commonly used commercial supports are Celgard and Accurel. The membrane thickness of Celgard 2500 is 25 μm with a porosity $\Theta = 0.45$ and a tortuosity $\tau = 2.35$. Accurel has a thickness of 100 μm with a porosity $\Theta = 0.64$ and a tortuosity $\tau = 2.1$.

Solvent characteristics that influence the stability of the membrane are surface tension and water solubility (12). Processes that destabilize liquid membranes are the loss of membrane material due to osmotic (11) or hydrostatic (12) pressure differences over the membrane, formation of emulsions, or formation of inverted micelles. A frequently used organic membrane solvent is *o*-nitrophenyl octyl ether (NPOE). It has a low viscosity, high lipophilicity and a high polarity. Other solvents used are phenylcyclohexane, decanol, and diphenylether.

In order to measure the salt transport, the receiving phase contains a conductivity cell. A typical experiment lasts 24 hours in which the conductivity is

monitored with a time-interval of 60 seconds. The activities are calculated according to the Debye-Hückel theory (13). Fluxes are determined as the first derivative of the activity vs. time according to Equation 8. When competitive transport experiments are carried out, the receiving phase is analysed by atomic absorption spectrometry.

$$J(t) = \frac{V_r}{A_m} \frac{da_r(t)}{dt} \quad (8)$$

where V_r = volume of receiving phase; A_m = membrane surface.

Membrane instability due to leaching of the carrier into the aqueous phases has been studied in our laboratory. This phenomenon is strongly related to the lipophilicity of the carrier. Enhancement of the lipophilicity has been achieved by attachment of carriers to a polymeric backbone (14) or covalent linkage of aliphatic chains to carriers (15, 16). Recently, both the stability of the membrane phase and the solubility of the carrier have been improved by attachment of one or more solvent molecules to the carrier (17). Long-term membrane stability was demonstrated for a period of 5 weeks, while carrier concentrations up to 50 wt% could be used.

Diffusion-Limited Transport of Salts. In the case of fast extraction equilibria for salts at the interfaces, the rate of transport is determined by diffusion of the complex through the membrane and the flux for steady state transport through an SLM is given by Equation 9.

$$J = \frac{D_m}{d_m} ([LS]_{ms} - [LS]_{mr}) \quad (9)$$

where J = flux through the membrane; D_m = apparant membrane diffusion coefficient; d_m = membrane thickness; $[LS]_{mr}$ = internal complex concentration at the receiving side of the membrane; $[LS]_{ms}$ = internal complex concentration at the source side of the membrane.

Two limiting situations can be distinguished based on the presence of complex at the receiving side of the membrane. In the case that $[LS]_{mr}$ is zero, the situation of initial transport is studied and Equation 9 reduces to the so-called "initial flux equation" $J_0 = (D_m/d_m)[LS]_{ms}$. In practice, this assumption is valid when the measured flux remains constant with time. Using this assumption, many transport studies have been carried out in which the flux is related to the initial salt concentration in the aqueous source phase, D_m and K_{ex} . The initial flux model for the transport of ion-pairs is described in the next section. The initial flux model for assisted transport of free-ions is described in the section after that.

When the flux decreases with time, the concentration of complex $[LS]_{mr}$ is no longer zero. This situation arises when the salt in the aqueous receiving phase is significantly extracted. Hence, the concentration of complex at the receiving side of

the membrane deviates from zero. This situation is described later for the diffusion limited transport of salts as free-ions.

Co-Transport of Monovalent Ions as Ion-Pairs. Ion-pair formation is a process which occurs when solvents are of low polarity (dielectric constant ϵ is low). Consequently, transport through non-polar solvents occurs via ion-pairs, whereas in polar solvents ions are solvent separated and transport takes place as free ions. Hence, the polarity of the solvent determines the extraction equilibrium.

In BLM transport, the most common solvents are chlorinated hydrocarbons. These have low dielectric constants and, as a consequence, the transport is described by ion-pairs. Izatt *et al.* have extensively studied ion-pair transport through BLMs (18). In SLM transport, cyclohexyl phenyl ether is an important non-polar membrane solvent (19). The extraction equilibrium at the interface in a non-polar membrane

solvent is written as Equation 10.

Reusch and Cussler were the first to describe crown ether-mediated transport of alkali metal cations through supported liquid membranes as ion pairs and derived for the initial flux Equation 11.

$$J = \frac{D_m K_{ex} L_0}{d_m} \left[\frac{[M^+]_s^2 - [M^+]_r^2}{(1 + K_{ex} [M^+]_s^2) (1 + K_{ex} [M^+]_r^2)} \right] \quad (11)$$

where L_0 = initial carrier concentration in the membrane; $[M^+]_s$ = initial salt activity in the source phase; $[M^+]_r$ = initial salt activity in the receiving phase.

Izatt *et al.* also presented transport studies in which ion-pair formation in the aqueous phase was taken into account (20). The extraction equilibrium was adjusted to Equation 12.

Equation 13 is the resulting initial flux equation.

$$J_0 = \frac{D_m K_{ex} L_0}{d_m} \left[\frac{[MA]_s}{(1 + K_{ex} [MA]_s^2)} \right] \quad (13)$$

In fact, this equation is similar to the flux equation for neutral molecules (see section on Diffusion-Limited Transport of Neutral Molecules).

Figure 3. Representation of the Transport Cell and a Flat Sheet Supported Liquid Membrane.

Chart 1. Structures of Carriers 1-4.

Co-transport of Monovalent Ions as Free Ions. Frequently used polar solvents in supported liquid membranes are *o*-nitrophenyl octyl ether (NPOE, $\epsilon_r=24$), *o*-nitrodiphenyl ether (NDPE, $\epsilon_r=30$) and 2-fluorodiphenyl ether (FNDPE, $\epsilon_r=50$). When the complex concentration in the membrane phase is low, the complex and anion are solvent separated and Equilibrium 14 is obtained.

Besides the mass-balance, an additional assumption concerning the electroneutrality in the membrane phase is included ($[A^-]_m = [ML^+]_m$). The flux (Equation 9) is rewritten to obtain Equation 15.

$$J = \frac{D_m}{2d_m} \left[-A_s + \sqrt{A_s^2 + 4A_s L_0} + A_r - \sqrt{A_r^2 + 4A_r L_0} \right] \quad (15)$$

$$A_s = K_{ex} [M^+]_s^2 \quad A_r = K_{ex} [M^+]_r^2$$

where D_m = apparent membrane diffusion coefficient; L_0 = initial carrier concentration.

In case of initial transport ($\lim t \rightarrow 0$; $A_r=0$) an expression for the initial flux is obtained (Equation 16).

$$J_0 = \frac{D_{ML}}{2d_m} \left[-K_{ex} a_s^2 + \sqrt{K_{ex} a_s^2 + 4L_0 K_{ex} a_s^2} \right] \quad (16)$$

where a_s = activity of salt in the source phase.

The model has been verified experimentally for the transport of alkali metal cations (21) mediated by valinomycin (1), dibenzo-18-crown-6 (2) and calix[4]crown-5 derivative 3 and calix[4]arene tetraester derivative 4 (Chart 1). D_m and K_{ex} for the transport of guanidinium ion (22, 23) mediated by calix[6]arene derivatives have been obtained as well.

The transport parameters of carrier 1-4 are summarized in Table 1. Transport parameters D_m and K_{ex} (Table 1) are determined by describing the initial fluxes obtained from transport experiments as a function of the initial salt activity with the initial flux model (Equation 16) according to the best fit of the model to the experimental data.

The results presented in Table 1 indicate that diffusion coefficients show little variation ($\sim 1 \times 10^{-11} \text{ m}^2 \text{ s}^{-1}$), while the extraction constants are strongly dependent on the carrier.

Table 1. Transport Parameters Based on Diffusion-Limited Free-Ion Transport Through Supported Liquid Membranes (Adapted from ref. 14)

Carrier	Salt	$10^{12} D_m$ [m ² .s ⁻¹]	K_{ex} [l.mol ⁻¹]
1	KClO ₄	9.4	2300
2	KClO ₄	19	1.3
3	KClO ₄	12.5	2.6
4	NaClO ₄	12.6	10.6

The characteristics of membrane transport are illustrated in Figure 4. The curve represents the calculated relation between the initial flux and the initial activity of the salt in the source phase. Based on the shape of the curve, two conclusions can be drawn. The steepness of the initial slope is a measure for the extraction coefficient, K_{ex} . The height of the plateau-value is a measure of the diffusion coefficient, D_m . When the flux reaches the plateau value, the carrier at the source phase interface is saturated. Hence, the diffusion coefficient is calculated from the corresponding flux (J_{max}) according to $J_{max} = (D_m/d) L_0$.

Time Dependency of the Flux. In the above discussions, only initial transport is examined. The flux equation is a simplified version, because conditions are chosen in such a way that the salt concentration in the receiving phase can be neglected. When time-dependency of transport is examined, the concentration of salt in the receiving phase can no longer be neglected and the influence on transport has to be taken into account.

Lehn *et al.* addressed the time dependency in BLM counter-transport. They performed numerical simulations to describe the competitive transport of two species as a function of time (24). Ibáñez *et al.* investigated time-dependent transport through a BLM system and used a model to obtain the membrane permeability. An analytical equation was derived which describes the concentration of salt in the aqueous receiving phase as a function of time (25). Recently, measurements of time-dependent, single-ion transport using carriers with a high K_{ex} ($K_{ex} > 1000$ l mol⁻¹) indicated that fluxes decrease even in an early stage of transport ($a_r < 10\%$ a_s). Using the law of conservation for the receiving phase (Equation 17), time dependency was introduced into the model equation for cation-assisted transport (Equation 15).

$$V_r \frac{da_r}{dt} = A_m \times J_M \quad (17)$$

The flux equation J_m (Equation 15) is rewritten as a function of $a_r(t)$ by using the mass-balance for the total amount of salt: $a_s(t) = a_{s,0} - V_r/V_s a_r(t)$. Subsequent introduction in Equation 17 leads to a differential equation which can be integrated by numerical integration to obtain the salt concentration in the receiving phase as a function of time (26).

The influence of the transport characteristics D_m and K_{ex} has been investigated by simulation of the transport as a function of time as a function of D_m and K_{ex} . From Equation 15, it is evident that the transport rate $J_m(t)$ linearly increases with the diffusion coefficient. The influence of K_{ex} on the transport rate is more difficult to predict. In Figure 5, the flux is depicted as a function of time. Figure 6 shows the resulting time-dependent activity in the receiving phase. The decrease of flux with time is explained by complex formation at the receiving side of the membrane. When a carrier has a high affinity for a salt (*i.e.*, K_{ex} is high), even at low salt activities in the receiving phase, complexation at the receiving phase interface takes place which lowers the transport rate, because the driving force is reduced.

We have used the time-dependent model to develop a system (Cursim) which determines the transport parameters by curve-fitting of a single-ion transport experiment $a_{r,exp}$ as a function of time (24 hrs). From an initial starting point (D_m^i, K_{ex}^i) the parameters are varied in such a way that the model describes the experiment, *i.e.* the deviation between the experimental data and the model is minimized. The deviation is expressed in terms of the least squares σ^2 value. Having obtained the best-fit parameters D_m^* and K_{ex}^* , the optimum is examined by a search for other "best fits" around the best-fit parameter set (D_m^*, K_{ex}^*). This is represented by a 3-dimensional plot of the transport parameters and the inverse least squares value ($1/\sigma^2$). In the case of a precise estimation, a single and sharp peak in D_m^* and K_{ex}^* can be observed.

To illustrate the validity of this approach with respect to the initial flux determination as described in the section on Co-transport of Monovalent Ions as Free Ions, both initial fluxes have been determined and time-dependent measurements have been carried out for $KClO_4$ transport with the 1,3 diethoxy calix[4]crown-5 (5) and the 1,3-bis isopropoxy calix[4]crown-5 (6) in the 1,3 alternate conformation (Chart 2). The results of both methods are presented in Table 2. The parameters obtained by the time-dependent approach and initial flux approach agree well. The 3-dimensional surface plots, which illustrate that the optimum is indeed global, are depicted in Figure 7.

Table 2. The Transport Parameters D_m and K_{ex} Obtained from the Initial Flux Approach and Cursim in the Determination of the Transport Parameters for Carriers 5 and 6

Carrier	$10^{11} D_m^a$ [m ² s ⁻¹]	$10^{-4} K_{ex}^a$ [l mol ⁻¹]	$10^{11} D_m^b$ [m ² s ⁻¹]	$10^{-4} K_{ex}^b$ [l mol ⁻¹]
5	1.1	28	1.0	41
6	1.2	40	1.4	36

^aDetermined by the initial flux approach.

^bDetermined by the Cursim system.

The main advantage of Cursim is that it only requires one experiment, whereas the initial flux approach requires at least six measurements at different salt concentrations.

Figure 4. Transport of $KClO_4$ by Valinomycin [1] at 298 °K. Flux as a Function of the $KClO_4$ Activity. (Adapted from ref. 21).

Figure 5. Simulation of the Flux Through an SLM as a Function of Time and Extraction Constant. (Adapted from ref. 25).

Figure 6. Simulation of the Activity in the Receiving Phase a_r as a Function of Time and Extraction constant. (Adapted from ref. 25).

- R
- 5 CH_2CH_3
 6 $\text{CH}_2(\text{CH}_3)_2$

Chart 2. Structures of Calix[4]crown-5 Carriers 5 and 6.

Figure 7. 3-Dimensional Representations of the Surface Area Around the Optimum Determined by Curve-Fitting of the Down-Hill Transport of KClO_4 ($a_{s,0}=0.1$ [M]) by Carriers 5 and 6. (Adapted from ref. 25).

Figure 8. Lag-Time Experiment for the Transport of NaClO_4 Mediated by Carrier 3. (Adapted from ref. 9).

Independent Determination of Diffusion Coefficients. Independent methods for the determination of diffusion coefficients serve as a reference for the determination of transport parameters. Different methods can be applied to determine diffusion coefficients independently from transport experiments, *e.g.* determination of the lag-time (27), pulsed-field gradient NMR (28), and permeability measurements (9).

The diffusional process through an SLM is affected by the porosity and tortuosity of the polymeric support. Direct comparison of fluxes J and the corresponding diffusion coefficients D_m when using different supports is not possible and D_m has to be corrected for the membrane characteristics in order to obtain the bulk diffusion coefficient D_b (29).

$$D_b = D_m \frac{\theta}{\varepsilon} \quad (18)$$

The bulk diffusion coefficient D_b is described by the Stokes-Einstein equation (Equation 19) and the Wilke-Chang relation (Equation 20) (30).

$$D_b = \frac{kT}{6\pi\eta r} \quad (19)$$

$$D_b = 7.4 \cdot 10^{-8} \left[\frac{(M)^{0.5} T}{\eta V^{0.6}} \right] \quad (20)$$

The bulk diffusion coefficient D_b obtained from membrane transport can differ from the Stokes-Einstein equation and Wilke-Chang relation. Both equations are valid under free-isotropic conditions, whereas the diffusion through the membrane can be reduced by an additional resistance of the pores (31). Significant reduction of the diffusion process takes place when pores are less than 10 times larger than the diffusing species.

A lag-time is defined as the time required for the complex to diffuse across the membrane from the source phase to the receiving phase, assuming dilute conditions.

$$t_{lag} = \frac{d_m^2}{6D_{lag}} \quad (21)$$

Lag-times can be obtained from lag-time experiments of which an example is shown in Figure 8. The resulting diffusion coefficient D_{lag} has to be corrected for the tortuosity τ , to obtain the bulk diffusion coefficient ($D_b = D_{lag}\tau$).

Determination of the diffusion coefficient by permeability experiments has been investigated in our group recently (9). In these experiments, a liquid membrane is clamped between a source and receiving phase, which both contain a membrane

solvent. At time $t=0$, a carrier which is substituted with a chromophoric group is added to the source phase ($c_s(0)$). The carrier diffuses through the membrane and the increase of concentration $c_r(t)$ in the receiving phase is monitored by UV/Vis spectroscopy as a function of time. The transport through the pores of the membrane is assumed to be rate-limiting and Equation 22 is derived.

$$\ln \frac{c_s(0) - 2c_r(t)}{c_s(0)} = -2 \frac{A_m D_m}{V_r d_m} t \quad (22)$$

The bulk diffusion coefficient is obtained by correction of D_m for the tortuosity and porosity of the support ($D_b = D_m \tau / \Theta$).

Pulse Field Gradient NMR spectroscopy can be applied to investigate self-diffusion of molecules in solution, through membranes, and through zeolites. PFG NMR is a direct method to measure the mean square distance $\langle r^2(t) \rangle$ which is traveled by a tracer during a time period Δt . Under the conditions of free-isotropic diffusion in three dimensions (dilute solutions), the replacement is related to the self-diffusion coefficient D_{sd} by Equation 23.

$$\langle r^2(t) \rangle = 6D_{sd} \Delta t \quad (23)$$

With PFG NMR the molecular displacements by self-diffusion can be measured to give the microscopic diffusion coefficient D_{sd} in the range of 10^{-6} - 10^{-14} m^2s^{-1} with an optimum between 10^{-9} - 10^{-13} m^2s^{-1} . Geringer and Sterk have determined the diffusion constant of 18-crown-6 and its Cs^+ complex in D_2O (32). The diffusion constant of ovalbumine inside porous particles, such as those used for gel filtration, has been investigated as a function of the protein concentration by Gibbs *et al.* (33). Our group has investigated the self-diffusion of NPOE inside the pores of various membranes (34). Through comparison of D_{sd} in the bulk liquid and in the pores of the membrane, it was found that the diffusion coefficient in Accurel was reduced by a factor of about 2.5, and in the case of Celgard by a factor of about 10. The radial and axial diffusion coefficients in the pores were measured by changing the orientation of the magnetic field compared to the pores of the membrane. For Celgard the radial self-diffusion coefficient was about 4 times lower than the axial self-diffusion coefficient, while for Accurel no significant difference was found. These results indicate that not only the porosity and tortuosity of the support have a large influence on the diffusion process, but the morphology of the support as well.

Reaction-Rate Limited Transport of Monovalent Ions. From ^1H NMR studies it is known that decomplexation rates can be very slow and, as a consequence, complexes can be kinetically stable (35,36). Until recently the role of slow rates of cation release in SLM transport was unclear. Lehn *et al.* (24) and Fyles (37) theoretically raised the question of the influence of slow rates of alkali metal cation release on transport through a BLM. Experimentally, this phenomenon has only been observed by Yoshida *et al.* (38). They showed that cation transport through a BLM mediated by polynactin was limited by the rate of cation release from the membrane. In 1994, Echegoyen stated that in SLM transport the rate of cation release from the membrane could never

be rate limiting due to the large diffusional layer in the membrane (39). However, in cation transport experiments with different calix crown ether derivatives, we have proven recently that the rate of decomplexation can be indeed rate-determining in the transport through SLMs (9, 40).

Mechanism of Kinetically Limited Transport. The flux of KClO_4 for the two very similar calix[4]crown-5 derivatives 6 and 7 (Chart 3) was examined as a function of the initial KClO_4 concentration. As was discussed earlier, the diffusion coefficient D_m can be obtained from the maximum flux, assuming that transport is diffusion limited. Figure 9 shows that the maximum flux and resulting the diffusion coefficient of carrier 7 ($3.7 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$) is almost three times lower than that for carrier 6 ($11.6 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$). Because both carriers are of comparable size, one would expect the diffusion coefficients of both carriers to be almost equal. Also from transport experiments using other calix[4]arene based ligands (Table 1) an average diffusion coefficient of about $10^{-11} \text{ m}^2 \text{ s}^{-1}$ was found.

From a lag-time experiment, the diffusion coefficient D_m of carrier 7 could be obtained independently (Equation 21). D_m is $9.4 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$ which deviates from the diffusion coefficient D_m as obtained by applying the diffusion limited model ($D_m = 3.7 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$). Apparently, the diffusion limited model can not be applied to determine the transport parameters of carrier 7. Hence, kinetics must influence the transport mechanism that lowers the transport rate as an additional resistance.

Kinetically limited transport; determination of α . In this section the influence of decomplexation kinetics in membrane transport will be discussed. An overview will be given of the different methods to distinguish diffusion-limited transport from kinetically limited transport. To illustrate these techniques, they will be applied to a diffusion limited (carrier 7) and a kinetically limited (carrier 6) transport system. A general model, that also includes the rate of cation release, was reported by Reichwein-Buitenhuis *et al.* (9). The flux is described by Equation 24.

$$J = \frac{D_m}{2d_m} \left\{ \frac{-A + \sqrt{A^2 + 4AL_0 \frac{(1+2\alpha)}{(1+\alpha)}}}{1+2\alpha} \right\} \quad (24)$$

where $\alpha = \text{dimensionless number } D_m/kd_m\theta$, k rate of release at the membrane-water interface, $\theta = \text{porosity of the membrane}$, $A = K_{ex}a_s^2$.

The basic transport parameters in the model given above are D_m , K_{ex} , and α . The parameter α is a dimensionless number which relates diffusion limited transport to kinetically limited transport. When the transport is purely limited by diffusion ($\alpha \rightarrow 0$), D_m and K_{ex} can be obtained from measurements of the flux as a function of a_s (21). In principle, all parameters can be derived by measuring the flux

$$J_{\max} = \left(\frac{D_m}{d_m} L_0 \right) \left(\frac{1}{1+\alpha} \right) \quad (25)$$

while varying a_s and d_m . Equation 24 can be simplified in the case when the carrier at the source phase interface of the membrane is fully loaded by cations (large value for A). This situation is achieved when the flux reaches its maximum value ($J_{\max}$). The first term in Equation 25 describes the diffusion-limited flux, while the second term $1/(1+\alpha)$ is a correction factor for slow kinetics of release. Because α is defined as the ratio $D_m/kd_m\theta$, the values of D_m and k have to be determined independently. We have developed two methods to determine the transport regime, viz. (i) independent determination of diffusion constants from lag-time measurements and (ii) direct determination of k and D_m from flux measurements as a function of the membrane thickness. As a result α is obtained. If α is lower than 1, the transport is mainly limited by diffusion of the complex; while the transport is primarily controlled by the cation release in the case that α is larger than 1.

From lag-time experiments, the diffusion coefficient D_{lag} obtained as shown in the section on Independent Determination of Diffusion Coefficients. D_{lag} is related to the membrane diffusion coefficient after correction for the porosity of the support ($D_m = D_{\text{lag}} \theta$). By combining this relationship with Equation 25, α is obtained from D_{lag} and $J_{\max}$ (Equation 26).

$$\alpha = \frac{D_{\text{lag}} \theta L_0}{d_m J_{\max}} - 1 \quad (26)$$

Separation of the diffusional and kinetic terms is achieved by expressing the flux as the ratio of driving force and flux (Equation 27).

$$\frac{L_0}{J_{\max}} = \frac{d_m}{D_m} + \frac{1}{\theta k} \quad (27)$$

Consequently, a plot of $L_0/J_{\max}$ vs. d_m should give a straight line with a slope $1/D_m$ and an intercept of $1/\theta k$. The value of α can be determined directly by calculation of the ratio of the kinetic and diffusional resistances via $\alpha = (1/\theta k)/(d_m/D_m)$. The values for the rate of cation release (k) and the diffusion coefficient D_m are determined by measuring the flux at different membrane thicknesses and consequently α is obtained by application of Equation 31.

The results shown in Table 3 and 4 both indicate that the transport of KClO_4 by carrier 7 is mainly limited by a slow decomplexation rate ($\alpha > 1$), while carrier 6 is mainly diffusion limited ($\alpha < 1$).

Table 3. Calculated α Values from Lag Times and Maximum Fluxes for Carrier 6 and 7 at 298 °K

Carrier	t_{lag} [s]	$10^{11} D_{\text{lag}}$ [m ² s ⁻¹]	$10^{11} D_m$ [m ² s ⁻¹]	$10^7 J_{\max}$ [mol m ⁻² s ⁻¹]	α
6	260	2.6	1.6	10.6	0.56
7	452	1.5	9.5	3.2	2.0

Figure 10. Influence of the Membrane Thickness ($n \cdot 100 \mu\text{m}$) on L_0/J for Carrier 6 and 7. $[\text{Carrier}]_m = 0.01 \text{ [M]}$, $[\text{KClO}_4] = 0.1 \text{ [M]}$, $T = 298 \text{ }^\circ\text{K}$.

Figure 11. Eyring plots for KClO_4 Transport by Carrier 6 and 7 Across a NPOE-Accurel Membrane.

Table 4. D_m , K and α -Values Calculated from L_0/J vs. d_m for Carriers 6 and 7 at $T=298$ °K (Figure 10)

Carrier	$10^{11} D_m$ [m ² s ⁻¹]	$10^7 k$ [m.s ⁻¹]	α
6	1.1	61	<0.1
7	0.9	0.8	1.8

Activation energy, E_a , for transport. Apart from the calculation of α as discussed above, determination of the apparent activation energy of transport gives information about the rate-limiting step in the transport process. Lazarova *et. al.* varied the temperature in order to determine the activation energy E_a from an Eyring plot (41). They indicated that E_a values below ca. 20 kJ mol⁻¹ are generally accepted as indicative of pure diffusion limited transport. Generally, activation energies are above 40 kJ mol⁻¹ when chemical reactions do play a role in the transport (42).

To obtain a clearer indication of the activation energy for diffusion-limited transport, the activation energy for the self-diffusion coefficient of NPOE can be measured. The activation energy for self-diffusion of a solvent often correlates well with the activation energy for diffusion of a solute species, since on a molecular level diffusion of a solute can be considered as a process in which either a solute or solvent molecule jumps from solvent cavity to cavity. Since the activation energy for self-diffusion varies with the solvent used, it is important to determine the activation energy E_a for the self-diffusion of NPOE first. The temperature dependency of the viscosity of organic solvents η has an Arrhenius-type behaviour.

$$\eta(T) = \eta_0 \exp(E_a/RT) \quad (28)$$

An activation energy for self-diffusion or viscous flow may be calculated from Equation 28 by measuring the kinematic viscosity as a function of temperature. The activation energy for the self-diffusion through NPOE is 24 kJ mol⁻¹.

The influence of the temperature on the transport rate is related to the Arrhenius equation: $J = J_0 \exp(-E_a/RT)$. In order to obtain activation energies for the transport of KClO₄ by carriers 6 and 7, the maximum flux J_{max} as a function of operating temperature was measured. Figure 11 shows an Eyring plot of $\ln J_{max}$ as a function of $1/T$. Values of the apparent activation energies are obtained from the slopes of the curves: $E_a = 32 \pm 2$ kJ mol⁻¹ and $E_a = 59 \pm 7$ kJ mol⁻¹. Consequently, it can be concluded that the transport of KClO₄ by carrier 7 is diffusion limited and that of carrier 6 is determined by the slow kinetics of release.

Optimization of the Flux; External Influences on Transport. Apart from the properties of the carrier transporting a cation selectively through the membrane phase, external factors can influence the transport. Properties of the membrane phase that

influence transport are solvent polarity and viscosity. The operating temperature has also a large influence on the transport, as well as the anion that accompanies the complex through the membrane. In this section, the external factors which influence transport are summarized.

Parameters that Affect Diffusion-Limited Transport. Brown *et al.* varied the length of the alkyl chain of alkyl *o*-nitrophenyl ether membrane solvents and examined its influence on the proton-coupled transport of alkali metal cations by a crown ether derivative. By comparison of solvent characteristics, such as the dielectric constant, viscosity, and surface tension, they concluded that hexyl *o*-nitrophenyl ether is a better membrane solvent than NPOE (43). The effect of the solvent on the transport of NaClO₄ by carrier 4 has been studied by Visser *et al.* (44). Transport parameters D_m and K_{ex} were determined. A series of octyl phenyl ethers containing an electron withdrawing group (NO₂, CN) of various positions on the phenyl ring were used. Data are presented in Table 5.

Table 5. Influence of the Membrane Solvent on the Transport of NaClO₄ Mediated by Carrier 4 at T = 298 K (Adapted from ref 43)

Membrane solvent ^a	ϵ_r	η [mPa s]	$10^8 J^b$ [mol m ⁻² s ⁻¹]	$10^{12} D_m^c$ [m ² s ⁻¹]	K_{ex}^c [l mol ⁻¹]
<i>o</i> -NPOE	23.1	11.5	121	12.6	10.6
<i>m</i> -NPOE	16.3	13.6	88.6	9.47	0.35
<i>p</i> -NPOE	16.7	19.0	64.2	6.52	1.68
<i>o</i> -CPOE	23.4	14.9	99.6	9.94	8.38
<i>p</i> -CPOE	14.6	15.8	80.3	8.47	0.46
<i>o</i> -NDPE	28.1	18.3	72.5	7.50	40.0
<i>o</i> -CDPE	29.1	22.9	63.1	6.61	24.4
FNDPE	50	25.9	55.8	5.64	220

^a NPOE = nitrophenyl octyl ether; CPOE = cyanophenyl octyl ether;
NDPE = nitrodiphenyl ether; CDPE = cyanodiphenyl ether;
FNDPE = *o*-fluoro *o'*-nitrodiphenyl ether.

^b Flux measured at [NaClO₄]_{s,0} = 1.0 M.

^c Transport parameters obtained by curve-fitting of the initial flux model.

Solvent characteristics that influence the diffusion and extraction are found to be viscosity (η) and polarity (ϵ). For spherical solutes, the diffusion coefficient depends on the solvent according to the Stokes-Einstein relation (Equation 19). From this, it follows that the diffusion coefficient linearly increases with T/η . Hence, the permeability increases linearly with the reciprocal viscosity of the membrane solvent (12). Dozol *et al.* plotted the permeability P vs. $\eta/MW^{0.5}$ and obtained a linear fit

(45). Visser *et al.* related the diffusion coefficient D_m to the solvent viscosity η (Figure 12). The solvent effect on K_{ex} is a combination of the influence on salt partition (K_p) and association (K_a). Both processes are influenced by the polarity of the solvent. An empirical relation, the Kirkwood function, describes the relation between polarity (dielectric constant ϵ_r) and extraction coefficient well. From Figure 13 it follows that a more polar membrane solvent promotes extraction. In general, polar solvents favor salt partition, but the tendency towards complexation diminishes. Since the overall effect of solvent polarity on the extraction is positive, the polarity appears to affect the partition coefficient to a higher degree.

At higher temperatures, both the diffusion and decomplexation processes are accelerated, and transport rates increase. The transport parameters D_m and K_{ex} were determined at elevated temperatures. The diffusion coefficient D_m increases, while the extraction coefficient K_{ex} decreases with increasing temperature. D_m correlates well with T/η as described by the Stokes-Einstein equation and Wilke-Chang relation.

The anion effect on BLM transport of metal salts was examined by Lamb *et al.* (46). From determination of the transport rates for different alkali metal salts by dibenzo-18-crown-6, it became clear that the rate of transport was strongly dependent on the co-transported anion. The relative fluxes of different potassium salts were related to the hydration energy. Cations which are accompanied by a hydrophilic anion ($-\Delta G_{g-w}$ is large) show low fluxes, due to a decrease in the partitioning. A linear relation was obtained by plotting $\ln J$ vs $-\Delta G_{g-w}$ of the anion. For transport through an SLM, a similar relationship was found (47).

Parameters that Affect Kinetically Limited Transport. Both the diffusional process and cation release are influenced by the membrane solvent, support and anion in kinetically limited transport (40, 44). Using the membrane solvents listed in Table 6, the diffusion coefficient D_m and the decomplexation rate constant k were determined for the transport of $KClO_4$ through NPOE/Accurel by 1,3-dimethoxycalix[4]crown-5 (carrier 9). The value for α is 1.9 and the activation energy E_a is 61 kJ mol^{-1} . The transport is therefore considered as a kinetically limited process (9).

From comparison of the transport parameters in *o*-NPOE and *p*-NPOE, it follows that the diffusion coefficient in *p*-NPOE is twice as high as in *o*-NPOE. Since the viscosity of *p*-NPOE is almost twice as high as that of *o*-NPOE, this is in accordance with the Stokes-Einstein equation.

From the α -values, it is clear that the transport regime strongly depends on the solvent. The transport varies from purely diffusion limited to mainly kinetically limited. Both transport parameters D_m and k have been correlated to the viscosity η and polarity ϵ_r (Kirkwood function) of the solvent, respectively.

The diffusion coefficient correlates linearly with the viscosity η as was already shown in the case of a diffusion limited transport system (Figure 14). When using the empirical Kirkwood function, a linear relationship between k and ϵ_r is obtained. Figure 15 shows that the use of a more polar solvent slows down the rate of decomplexation. Hence, the regime of the transport can be influenced by the solvent polarity.

Figure 12. Relationship Between the Diffusion Coefficient and Solvent Viscosity η for the Transport of NaClO_4 by Carrier 3 (Adapted from ref. 43).

Figure 13. Relationship Between the Extraction Constant and Solvent Dielectric Constant ϵ_r for the Transport of NaClO_4 by Carrier 3 (Adapted from ref 43).

Figure 14. Relationship Between the Diffusion Constant and Solvent Viscosity for Transport of KClO_4 by Carrier 9 (Adapted from ref. 43).

Figure 15. Relationship Between the Decomplexation Rate Constant and the Solvent Polarity for the Transport of KClO_4 by Carrier 9 (Adapted from ref. 43).

Table 6. Diffusion and Decomplexation Rate Constants for the Transport of KClO_4 by Carrier 9 as Influenced by Variation of the Membrane Solvent (Adapted from ref 43)

Membrane solvent ^a	$10^8 J_{\text{max}}$ [mol m ⁻² s ⁻¹]	$10^{12} D_m^b$ [m ² s ⁻¹]	$10^8 k^b$ [m s ⁻¹]	α
<i>o</i> -NPOE	34.1	9.85	5.24	1.9
<i>m</i> -NPOE	52.7	8.40	13.8	0.6
<i>p</i> -NPOE	52.8	6.48	33.1	0.2
<i>o</i> -CPOE	35.3	8.12	6.44	1.3
<i>p</i> -CPOE	48.9	7.54	12.8	0.6
<i>o</i> -NDPE	13.4	5.38	1.82	3.0
<i>o</i> -CDPE	17.0	4.04	2.94	1.4
FNDPE	9.1	4.31	1.14	3.8

^a For abbreviations see Table 5.^b Parameters obtained from Equation 27.

Although it is assumed that transport takes place via solvent separated ions, it is seen (Table 7) that the nature of the anion affects the rate of the decomplexation process. The transport of KSCN by carrier 9 is mainly limited by diffusion, while the transport of KClO_4 is primarily kinetically controlled.

Table 7. Determination of the Transport Limitation for Potassium Transport by Carrier 9 (Adapted from ref. 43)

Salt	t_{lag} [s]	$10^{11} D_{\text{lag}}$ [m ² s ⁻¹]	$10^7 J_{\text{max}}$ [mol m ⁻² s ⁻¹]	α^a	E_a^b [kJ mol ⁻¹]
KClO_4	395	1.7	3.3	2.3	63
KSCN	415	1.6	6.3	0.6	41

^a α -values obtained from Equation 26.^b E_a -value obtained from an Eyring plot.

No clear explanation was given for the influence of the co-transported counter ion on the kinetics. It can be due to ion-pair formation, influence of size and shape of the anion, or independent partition of the anion.

The effect of the support on the transport kinetics has been examined by normalizing the decomplexation rate constant for the porosity of the membrane: $k_n = k \cdot \theta$ (40, 44). Consequently, α can be calculated from the rate of decomplexation k_n and the diffusion coefficient D_m and compared with other supports. From the

calculation of α for the transport of KClO_4 by carrier **9** through a NPOE/Celgard-2500 ($\alpha = 4.9$) and a NPOE/Accurel membrane ($\alpha = 1.9$), it follows that the support may influence the transport regime (40, 44).

Transport Selectivity. For separation purposes, the selectivity of transport by macrocyclic carriers through supported liquid membranes has been investigated extensively. The transport selectivity of a carrier towards two different cations M_1^+ and M_2^+ is obtained by competition experiments in which both M_1^+ and M_2^+ were present in the receiving phase.

The selectivity not only depends on the relative fluxes, but is related to the relative concentration in the aqueous source phase as well. Therefore, the selectivity is often expressed as ratio of permeabilities $S = P_{M_1}/P_{M_2}$ (48).

In 1973, Cussler related the "selectivity" of dibenzo-18-crown-6 for potassium over other alkali and alkaline earth metal cations to the correlation between the radius of the unsolvated cation and the radius of the internal cavity of the crown ether (8). He obtained the highest flux for potassium, which has the best fit with the cavity of the carrier. However, his observations were based on the results of single-ion transport experiments.

In 1975, Lehn *et al.* reported the selective transport of alkali metal ions by cryptands through BLMs by competitive experiments (49). The cation concentration inside the membrane did increase when the association constant was larger. However, the resulting flux in competitive experiments did not correlate with the association constant and reversed selectivities were found. Strong binding of the substrate has a negative effect on the transport selectivity. Therefore, they concluded that an optimal association constant for transport lies in the range of $\log K_a(\text{methanol}) \approx 5$. Behr *et al.* reported numerical simulations to investigate selective transport theoretically (24).

Lamb *et al.* carried out competitive experiments of monovalent and divalent cations mediated by various crown ethers and cryptands through chloroform BLMs. Relative fluxes from binary mixtures were explained in terms of ring substituents and ring size of the crown ether carriers (50,51). Saito studied the transport of alkali and alkaline earth metal cations as their ClO_4^- salts through SLMs by triphenyl phosphate and observed a selective transport of Li^+ in the presence of Na^+ , K^+ , and Mg^{2+} (52).

When the transport is limited by diffusion, the initial transport selectivity is predicted from the results of single-ion transport experiments (21). The flux ratio can be expressed by Equation 29.

$$\frac{J_{M_1^+}}{J_{M_2^+}} = \frac{D_{m,LM_1^+} K_{ex,M_1^+} a_{M_1^+}}{D_{m,LM_2^+} K_{ex,M_2^+} a_{M_2^+}} \quad (29)$$

Assuming that the sizes of the complexes are nearly the same, the ratio of the diffusion coefficients is 1. The transport ratio and hence the selectivity is dependent on the ratio of the extraction constants. A high extraction selectivity ($K_{ex,M_1}/K_{ex,M_2}$) does not always imply a high transport selectivity. With high extraction constants, the maximum flux is reached at low salt concentrations and the carriers at the source phase side are nearly 100% complexed.

Since transport rates change with time due to the presence of salt in the receiving phase, selectivity may also change in time. In order to investigate the time dependency of selectivity, transport of potassium in the presence of sodium has been investigated using different calix[4]crown-5 carriers and valinomycin. The amount of Na^+ and K^+ in the receiving phase was measured by atomic absorption spectroscopy after 2 and 24 hours of transport. The results are presented in Table 8.

Table 8. Selective Transport of Potassium in the Presence of Sodium. Determination of the Selectivity after 2 and 24 hours of transport^a

Carrier	t_{isp} [hours]	% NaClO_4 transported	% KClO_4 transported	Selectivity
1	2	8.9×10^{-3}	91.5	10300
1	24	0.293	99	338
5	2	4.72×10^{-3}	94.8	20100
5	24	0.232	98.8	426
6	2	4.2×10^{-3}	93.8	22300
6	24	0.252	95.2	378

^a Source phase: 10^{-4} M KClO_4 / 10^{-1} M NaClO_4 , 298 °K.

From the 2-hour transport data, it is clear that both carriers 5 and 6 are extremely selective for potassium in the presence of sodium. However, the selectivity drops dramatically with time. This is rationalized by the fact that after 2 hours virtually all of the KClO_4 has been removed from the source phase and only NaClO_4 remains to be transported. Additional proof for this explanation was obtained from the conductivity in the receiving phase as a function of time. After approximately 2 hours a sharp levelling of in the conductivity increase was observed, indicating that NaClO_4 was being transported instead of KClO_4 (Figure 16).

When kinetics play a role, transport selectivity can not simply be determined by the ratio of the extraction constants. The operating temperature and membrane thickness influence the transport selectivity. Selectivity experiments ($S_{\text{K/Na}}$) have been reported for 1,3-diethoxycalix[4]crown-5 in the partial cone conformation (carrier 7). It is a potassium-selective carrier for which the KClO_4 transport is kinetically limited ($\alpha_{\text{K}} = 3.6$) (9). With a membrane thickness of 100 μm the potassium selectivity over sodium is 160. The selectivity $S_{\text{K/Na}}$ increases when the temperature (at $T = 43^\circ\text{C}$, $S_{\text{K/Na}} = 420$) or membrane thickness (with $d_{\text{m}} = 300 \mu\text{m}$, $S_{\text{K/Na}} = 300$) is increased. Under these conditions, transport of K^+ is determined more by the diffusional resistance in the membrane and to a smaller extent by the complexation kinetics. Apparently, the selectivity drops when a kinetic resistance influences the rate of transport.

Uphill Transport. Cussler *et al.* have shown that common-ion pumping can be used

to transport a salt against its concentration gradient (53). When a secondary salt with the same anion and a low extraction constant is present in large excess, the anion gradient acts as a "pump" for the primary salt. The ideal carrier for uphill transport of M_1^+ by common-ion pumping has a high affinity for M_1^+ , but shows *no* significant transport for M_2^+ .

Nijenhuis *et al.* have derived a model for competitive transport of two cations and a common ion in the case of 1:1 complexation and free ions in the membrane phase (21). When the extraction constant for the secondary salt is negligible, the flux for the primary cation is given by Equation 30.

$$J_{M_1} = \frac{D_m(a_{M_1} + a_{M_2})K_{ex,1}a_{M_1}}{d_m} \left(-1 + \sqrt{1 + \frac{4L_0}{a_{M_1}K_{ex,1}(a_{M_1} + a_{M_2})}} \right) \quad (30)$$

Using the common-ion principle, uphill transport of $KClO_4$ by valinomycin was achieved by adding an excess of $LiClO_4$ or HNO_3 to the aqueous source phase. The common ion effect as described above can be useful for the removal of small amounts of heavy metal ions or radioactive salts from waste water streams.

Uphill transport of silver nitrate was reported by Sirlin *et al.* (54). Plutonium(IV) nitrate was transported completely from a HNO_3 aqueous solution through an SLM containing dicyclohexyl-18-crown-6 in toluene. At the receiving phase side, a stripping agent was added (0.5 M Na_2CO_3). Plutonium selectivity was observed in the presence of Cs^{137} , Ru^{106} , and Sb^{125} (55). Cesium was separated completely ($\geq 99.8\%$) (Figure 17) from a radioactive waste stream within 25 hours (56) using different calix[4]crown-6 carriers (Chart 4). An overall transport selectivity for Cs^+ over Na^+ of about 400 was obtained.

In nature uphill transport is often achieved by proton gradients. In liquid membrane transport studies, counter transport of protons is generated by applying a pH gradient and by using proton-ionizable carriers (azacrown ethers) in the membrane phase.

Carrier-Assisted Transport of Anions. Assisted transport of anions has been investigated less thoroughly than cation transport. The measured transport rates are lower and selectivity mostly follows the Hoffmeister series (57): $ClO_4^- > I^- > SCN^- > NO_3^- > Br^- > Cl^- \gg CO_3^{2-}, H_2PO_4^-, SO_4^{2-}$.

Assisted anion transport through a BLM was first reported by Behr and Lehn, who investigated the transport of amino acids at high pH with a quaternary ammonium salt as carrier (58). Selectivity was based only on the difference in partition coefficients of the amino acids. Since then, many charged carriers have been utilized for the transport of anions via a counter-transport mechanism.

Cussler *et al.* showed that alkyl ammonium cations are suitable for the transport of Cl^- when an opposing OH^- gradient was applied (59). Neplenbroek *et al.* transported NO_3^- with alkyl ammonium cations by an opposing Cl^- gradient (60). Phosphates were transported through a BLM containing a tetraphenylporphyrin-oxomolybdenum(V) complex, when coupled to a counter flow of halide ions (61). Selective counter transport of CN^- was achieved by Sumi *et al.* They reported the

Figure 16. Time-Dependent Na^+/K^+ -Transport by Carrier 5; Conductivity in the Receiving Phase as a Function of Time. Source phase: 10^{-4} M KClO_4 / 10^{-1} M NaClO_4 , 298 °K.

Figure 17. Transport Rates of CsNO_3 as a Function of Time for Carriers 10, 11, 12 $[\text{L}_0] = 5$ mM. The source phase was a mixture of 1 mM CsNO_3 , 4 M NaNO_3 , and 1 M HNO_3 (Adapted from ref. 55).

counter-transport of CN^- against OH^- upon the addition of a tetraphenylporphyrinato-manganese(III) complex through a BLM and SLM. Selective transport was achieved in the presence of various anions, Cl^- , F^- , NO_3^- (62).

Co-transport by charged carriers can be achieved by introducing a pH-gradient into the system. The carrier is protonated at the source phase side of the membrane, which is then charged and therefore capable of complexing an anion. At the receiving phase side deprotonation and decomplexation takes place to regain a neutral carrier. Using this concept, Sessler *et al.* enhanced the transport of nucleotide monophosphates (AMP and GMP) by a sapphyrin carrier through a BLM (63). Araki *et al.* obtained selective SCN^- transport through a BLM containing a 6,6'-bis(4-hexylbenzoylamino)-2,2'-bipyridine complex of Cu(II). The metal center serves as a binding site for SCN^- . Via reverse dissociation/association of the amide proton(s), a neutral or charged carrier can be obtained. Hence, the uptake and release of SCN^- can be regulated (64).

Selective co-transport by neutral carriers was reported recently by our group (65). The transport of phosphates through an SLM was achieved by using uranyl salophene carrier **13** which is functionalized with two additional amide groups (Chart 5). The transport rate of KH_2PO_4 was measured. In the membrane phase the anion is complexed, whereas the cation diffuses through the membrane as a free ion. By the addition of the K^+ -selective carrier **9**, both the complexed anion and cation are transported through the membrane as complexes and the transport is further enhanced. By measuring the transport rate while varying the ratio of cation and anion receptor from 100% anion receptor to 100% cation receptor, a bell-shaped curve was obtained with a maximum at a 1:1 ratio. Selectivity ratios of phosphate over chloride of 140 were achieved.

Covalent binding of an anion and a cation receptor to obtain a ditopic receptor and subsequent application in an SLM has been reported by Rudkevich *et al.* (66). They synthesized a receptor (carrier **14**) which is capable of binding a cation and an anion simultaneously. The crown ether part binds Cs^+ , while the salophene moiety can complex Cl^- . For carrier **14** CsNO_3 -fluxes ($J = 0.89 \times 10^{-7} \text{ mol m}^{-2} \text{ s}^{-1}$) and CsCl -fluxes ($J = 1.2 \times 10^{-7} \text{ mol m}^{-2} \text{ s}^{-1}$) were measured. In the case of cation assisted transport, CsNO_3 is expected to give a higher flux than CsCl , due to the higher lipophilicity of the NO_3^- anion. This proves that both the anion and the cation are involved in the complexation of CsCl , and that selective transport of a hydrophilic salt over a lipophilic salt can be obtained with a ditopic receptor.

Diffusion-Limited Transport of Neutral Molecules. Contrary to the transport of charged molecules, only a few receptors that assist the transport of neutral compounds have been reported. Pirkle *et al.* reported the enantioselective transport of different *N*-(3,5-dinitrobenzoyl)amino acid derivatives through supported liquid membranes containing (*S*)-*N*-(1-naphthyl)leucine octadecyl ester carriers in dodecane. The transport of neutral amines assisted by a 4-octadecyloxybenzaldehyde carrier was investigated by Yoshikawa *et al.* (67,68). The transport process is based on the reversible formation of a Schiff base between the amino group and the aldehyde. The assisted transport rate of *D*-glucosamide is about two times the blank transport and the transport is described using Michaelis-Menten kinetics, which in principle describes catalysis in product formation when using an enzyme able to complex the substrate involved in the reaction.

Chart 4. Structures of Calix[4]crown-6 Carriers 10-12.

Chart 5. Structures of Carriers 13 and 14 for Transport of Anions.

Nijenhuis *et al.* were the first to report assisted transport of neutral molecules by macrocyclic receptors (69). They investigated the transport of urea by neutral metallosalophenes through an SLM (Chart 6). A model for diffusion limited transport of neutral molecules has successfully been applied to describe the transport of urea (70). For neutral molecules, the extraction equilibrium (1:1 host-guest complex) at the interface is expressed by Equation 31.

$$U_a + L_m \rightleftharpoons UL_m ; \quad K_{ex} = \frac{[UL]_m}{[U]_w[L]_m} \quad (31)$$

The extraction coefficient K_{ex} is the product of the partition coefficient and the association coefficient $K_{ex} = K_p K_a$. Partitioning of the carrier to the aqueous phases was neglected, because of the high lipophilicity of the carrier. The total carrier concentration is written as Equation 32.

$$[L]_{m,0} = [L]_m + [LU]_m \quad (32)$$

Assuming that all equilibria are fast, the rate-limiting step of transport is the diffusion of the complex through the membrane. The flux is described by Fick's first law. When examining initial transport, the complex concentration at the receiving phase side of

$$J_{ass,0} = \frac{D_m}{d_m} [LU]_{m,0} \quad (33)$$

the membrane is again neglected.

Equation 33 can be rearranged using the mass-balance (Equation 32) and the extraction coefficient K_{ex} (Equation 31) to obtain Equation 34.

$$J_{ass,0} = \frac{D_m}{d_m} \frac{K_{ex}[U]_{w,0}[L]_{m,0}}{1 + K_{ex}[U]_{w,0}} \quad (34)$$

The blank flux of urea can not be neglected ($J_{blank} = 4.4 \times 10^{-8} \text{ mol m}^{-2} \text{ s}^{-1}$), and the assisted flux was obtained by subtraction of the blank flux from the measured flux. The model has been applied for the transport of urea using two types of carriers, *e.g.* lipophilic metallomacrocycles **15** and **16** (69), and polyaza (cleft-type) receptors **17**, **18**, and **19** (71). The transport data are presented in Table 9. Transport experiments were carried out by varying the urea concentration to obtain D_m and K_{ex} . In Figure 18, the assisted flux is plotted vs. the initial urea concentration for carrier **15**. Diffusion constants and extraction constants for macrocycles **15** and **16** are also given in Table 9.

Chart 6. Structures of Carriers 15-19 for Transport of Neutral Molecules.

Figure 18. Influence of the Urea Concentration in the Source Phase on the Assisted (Initial Minus Blank) Flux Through a Supported Liquid Membrane Using Carrier 15 ($[\text{CA}]_{\text{m},0} = 6 \text{ mM}$). The line is drawn according to the model and the symbols are measure values (Adapted from ref. 69).

Table 9. Total Urea Fluxes Carrier-Assisted Urea Transport Through Supported Liquid Membranes, D_m and K_{ex} (Adapted from ref. 69, 70)

Carrier ^a		$J_{initial}^b$ [mol m ⁻² s ⁻¹]		$10^{12}D_m$ [m ² s ⁻¹]	K_{ex} [l mol ⁻¹]
15	61	64	64	9.7	20
16	50	50	50	6.1	22
17	25	23	24	-	-
18	36	36	36	-	-
19	16	14	14	-	-

^a $[U]_{w,0} = 1.0$ M; $[CA]_{m,0} = 6$ mM.^b Initial fluxes after 0, 24, and 48 hrs^c.^c Second replacement of the water phase after 48 h.

The flux strongly increases as the urea concentration is enhanced and reaches a plateau value (J_{max}) at higher urea concentrations. The diffusion coefficient and the extraction constant were obtained by curve-fitting of the flux as a function of the urea concentration. With values for D_m and K_{ex} , the percentage of carrier complexed at the source interface can be calculated. For carrier 15, 67% is complexed using a 0.1 M urea source phase solution and 92 % with a 0.5 M urea solution. This clearly indicates that the maximum flux can be explained by complete loading of the carrier.

Conclusions

Several models have been developed for the transport of different types of species through supported liquid membranes. The transport is described by subsequent partitioning, complexation and diffusion. Mechanistic studies are mainly focussed on diffusion limited transport of cations in which diffusion of the complex through the membrane phase is the rate-limiting step of the transport. Recently, kinetic aspects in membrane transport have been elucidated for new carriers with which the rate of decomplexation determines the rate of transport.

New topics in the field are the assisted transport of anions and transport assisted by ditopic receptors through SLMs. In the future, new studies have to be undertaken to elucidate the corresponding transport mechanisms.

Acknowledgement

The authors like to thank all co-workers and colleagues, the names of whom are given in the literature cited. Financial support of the Netherlands Foundations for Chemical Research (SON) and from the Netherlands Technology Foundation (STW) is gratefully acknowledged.

Literature cited

1. Lonsdale, H. K. *J. Membr. Sci.* **1982**, *10*, 81.
2. Singer, J.; Nicolson, G. L. *Science* **1972**, *175*, 723.
3. Moore, C.; Pressmann, B. C. *Biochem. Biophys. Res. Comm.* **1964**, *15*, 562.
4. Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017.
5. de Jong, F.; Visser, H. C. In *Supramolecular chemistry*; Vol 10, in press.
6. Li, N. N. *U.S. Patent 3 410 794*, **1968**.
7. de Haan, A. B.; Bartels, P. V.; de Graauw, J. *J. Membr. Sci.* **1989**, *45*, 281.
8. Reusch, C. F.; Cussler, E. L. *AIChE J.* **1973**, *19*, 736.
9. Reichwein-Buitenhuis, E. G.; Visser, H. C.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 3913.
10. van Straaten-Nijenhuis, W. F., de Jong, F., Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 317.
11. Fabiani, C.; Merigiola, M.; Scibona, G.; Castagnola, A. M. *J. Membr. Sci.* **1987**, *30*, 97.
12. Deblay, P.; Delepine, S.; Minier, M.; Renon, H. *Sep. Sci. Technol.* **1991**, *35*, 123.
13. Kolthoff, I. M.; Elving, P. J. In *Treatise on Analytical Chemistry*; Part 1, Vol. 1; Eds.; Interscience Publishers, Inc.: New York, NY 1959.
14. Wienk, M. M.; Stolwijk, T. B.; Sudhölter, E. J. R.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1990**, *112*, 797.
15. Stolwijk, T. B.; Sudhölter, E. J. R.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1987**, *109*, 7042.
16. Nijenhuis, W. F.; Walhof, J. J. B.; Sudhölter, E. J. R.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1991**, *110*, 265.
17. Visser, H. C.; Vink, R.; Snellink-Ruel, B. H. M.; Kokhuis, S. B. M.; Harkema, S.; de Jong, F.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 285.
18. Izatt, R. M.; Clark, G. A.; Bradshaw, J. S.; Lamb, J. D.; Christensen, J. J. *Sep. Purif. Methods* **1986**, *15*, 21.
19. Lamb, J. D.; Bruening, R. L.; Izatt, R. M.; Hirashima, Y.; Tse, P.-K.; Christensen, J. J. *J. Membr. Sci.* **1988**, *37*, 13.
20. Izatt, R. M.; Bruening, R. L.; Bruening, M. L.; LindH, G. C.; Christensen, J. J. *Anal. Chem.*, **1989**, *61*, 1140.
21. Nijenhuis, W. F.; Buitenhuis, E. G.; de Jong, F.; Sudhölter, E. J. R.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 7963.
22. Stolwijk, T. B.; Sudhölter, E. J. R.; Reinhoudt, D. N.; *J. Am. Chem. Soc.* **1989**, *111*, 6321.
23. Casnati, A.; Minari, P.; Pochini, A.; Ungaro, R.; Nijenhuis, W. F.; de Jong, F.; Reinhoudt, D. N. *Isr. J. Chem.* **1992**, *32*, 79.
24. Behr, J.-P.; Kirch, M.; Lehn, J.-M. *J. Am. Chem. Soc.* **1985**, *107*, 241.

25. Ibáñez, J.; Victoria, L.; Hernández, A. *Sep. Sci. Technol.* **1990**, *25*, 739.
26. Chrisstoffels L. A. J.; Struijk, W.; de Jong, F.; Reinhoudt, D. N. *J. Chem. Soc., Perkin 2*. accepted for publication.
27. Bromberg, L.; Levin, G.; Kedem, O. *J. Membr. Sci.* **1992**, *71*, 41.
28. Zhu, X. X.; MacDonald, P. M. *Macromolecules* **1992**, *25*, 4345.
29. Kiani, A.; Bhave, R. R.; Sirkar, K. K. *J. Membr. Sci.* **1986**, *26*, 79.
30. Wilke, C. R.; Chang, P. *AIChE J.* **1955**, *1*, 264.
31. Anderson, J. L.; Quinn, J. A. *Biophys. J.* **1974**, *14*, 130.
32. Geringer, M.; Sterk, H. *Magn. Res. Chem.* **1989**, *27*, 1148.
33. Gibbs, S. J.; Lightfoot, E. N.; Root, T. W. *J. Phys. Chem.* **1992**, *96*, 7458.
34. van den Berg, R.; Schulze, D.; Bolt-Westerhoff, J. A.; de Jong, F.; Reinhoudt, D. N.; Velinova, D.; Buitenhuis, L. *J. Phys. Chem.* **1995**, *99*, 7760.
35. Ghidini, E.; Ugozzoli, F.; Ungaro, R.; Harkema, S.; Abu El-Fadl, A.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1990**, *112*, 6979.
36. Reinhoudt, D. N.; Dijkstra, P. J.; in 't Veld, P. J. A.; Bugge, K. E.; Harkema, S.; Ungaro, R.; Ghidini, E. *J. Am. Chem. Soc.* **1987**, *109*, 4761.
37. Fyles, T. M. *J. Membr. Sci.* **1985**, *24*, 229.
38. Yoshida, S.; Hayano, S. *J. Membr. Sci.* **1982**, *11*, 157.
39. Li, Y.; Gokel, G.; Hernández, J.; Echegoyen, L. *J. Am. Chem. Soc.* **1994**, 3087.
40. Casnati, A.; Pochini, A.; Ungaro, R.; Bocchi, C.; Ugozzoli, F.; Egberink, R. J. M.; Struijk, W.; Lugtenberg, R. J. M.; de Jong, F.; Reinhoudt, D. N. *Chem. Eur. J.* accepted for publication.
41. Lazarova, Z.; Boyadzhiev, L. *J. Membr. Sci.* **1993**, *78*, 239.
42. O'Hare P. A.; Bohrer, M. P. *J. Membr. Sci.*, **1989**, *44*, 273.
43. Brown, P. R.; Hallman, J. L.; Whaley, L. W.; Desai, D. H.; Pugia, M. J.; Bartsch, R. A. *J. Membr. Sci.* **1991**, *56*, 195.
44. Visser, H. C.; de Jong, F.; Reinhoudt, D. N. *J. Membr. Sci.* **1995**, accepted for publication.
45. Dozol, J. F.; Casas, J.; Sastre, A. M. *Sep. Sci. Technol.* **1993**, *28*, 2007.
46. Lamb, J. D.; Christensen, J. J.; Izatt, S. R.; Bedke, K.; Astin, M. S.; Izatt, R. M. *J. Am. Chem. Soc.*, **1980**, 3399.
47. Visser, H. C., *Thesis*, University of Twente, Enschede, The Netherlands, **1994**.
48. Deblay, P.; Minier, M.; Renon, H. *Biotech. Bioeng.* **1990**, *35*, 123.
49. Kirch, M.; Lehn, J.-M. *Angew. Chem.* **1975**, *15*, 542.
50. Lamb, J. D.; Izatt, R. M.; Garrick, D. G.; Bradshaw, J. S.; Christensen, J. J. *J. Membr. Sci.* **1981**, *9*, 83.
51. Lamb, J. D.; Brown, P. R.; Christensen, J. J.; Bradshaw, J. S.; Garrick, D. G.; Izatt, R. M. *J. Membr. Sci.* **1983**, *13*, 89.
52. Saito, T. *Sep. Sci. Technol.* **1993**, *28*, 1629.

53. Caracciolo, F.; Cussler, E. L.; Evans, D. F. *AIChE J.* **1975**, *21*, 160.
54. Sirlin, C.; Burgard, M.; Leroy, M. J. F. *J. Membr. Sci.* **1990**, *54*, 299.
55. Shukla, J. P.; Kumar, A.; Singh, R. K. *Sep. Sci. Technol.*, **1992**, *27*, 477.
56. Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767.
57. Wegmann, D.; Weiss, H.; Amman, D.; Morf, W. E.; Pretsch, E.; Sugahara, K.; Simon, W. *Mikrochim. Acta.* **1984**, *3*, 1.
58. Behr, J.-P.; Lehn, J.-M. *J. Am. Chem. Soc.* **1973**, *95*, 6108.
59. Molnar, W. J.; Wang, C. P.; Fennel-Evans, D.; Cussler, E. L. *J. Membr. Sci.* **1978**, *4*, 129.
60. Neplenbroek, A. M.; Bargeman, D.; Smolders, C. A. *J. Membr. Sci.* **1992**, *16*, 107.
61. a)Kukufuta, E.; Nobusawa, M. *Chem. Lett.* **1988**, 425; b) Kokufuta, E.; Nobusawa, M. *J. Membr. Sci.* **1990**, *48*, 141.
62. Sumi, K.; Kimura, M.; Kokufuta, E.; Nakamura, I. *J. Membr. Sci.* **1994**, *86*, 155.
63. Furuta, H.; Cyr, M. J.; Sessler, J. L. *J. Am. Chem. Soc.* **1991**, *113*, 6677.
64. Araki, K.; Lee, S. K.; Otsuki, J.; Seno, M. *Chem. Lett.* **1993**, 493.
65. Visser, H. C.; Rudkevich, D. M.; Verboom, W.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, 11554.
66. Rudkevich, D. M.; Mercer-Chalmers, J. D.; Verboom, W.; Ungaro, R.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 6124.
67. Yoshikawa, M.; Mori, Y.; Tanigaki, M.; Eguchi, W. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 304.
68. Yoshikawa, M.; Kishida, M.; Tanigaki, M.; Eguchi, W. *J. Membr. Sci.* **1989**, *47*, 53.
69. Nijenhuis, W. F.; van Doorn, A. R.; Reichwein, A. M.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 3607.
70. van Straaten-Nijenhuis, W. F.; van Doorn, A. R.; Reichwein A.M.; de Jong, F.; Reinhoudt, D. N. *J. Org. Chem.* **1993**, *58*, 2265.
71. van Straaten-Nijenhuis, W. F.; de Jong, F.; Reinhoudt, D. N.; Thummel, R. P.; Bell, T. W.; Liu, J. *J. Membr. Sci.* **1993**, *82*, 277.