AC Research

Anal. Chem. **2000,** *72,* 433−442

Accelerated Articles

Electrically Facilitated Molecular Transport. Analysis of the Relative Contributions of Diffusion, Migration, and Electroosmosis to Solute Transport in an Ion-Exchange Membrane

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Electrically facilitated molecular transport in an ion-exchange membrane (Nafion, 1100 equiv wt) has been studied using a scanning electrochemical microscope. The transport rates of ferrocenylmethyltrimethylammonium (a cation), acetaminophen (a neutral molecule), and ascorbate (an anion) through ∼120-μm-thick membranes were measured as a function of the iontophoretic current passed across the membrane (−1.0 to +1.0 A/cm^2). Transport rates were analyzed by employing the Nernst−Planck equation, modified to account for electric field-driven convective transport. Excellent agreement between experimental and theoretical values of the molecular flux was obtained using a single fitting parameter for each molecule (electroosmotic drag coefficient). The electroosmotic velocity of the neutral molecule, acetaminophen, was shown to be a factor of ∼500 larger than that of the cation ferrocenylmethyltrimethylammonium, a consequence of the electrostatic interaction of the cation with the negatively charged pore walls of the ion-exchange membrane. Electroosmotic transport of ascorbate occurred at a negligible rate due to repulsion of the anion by the cation-selective membrane. These results suggest that electroosmotic velocities of solute molecules are determined by specific chemical interactions of the permeant and membrane and may be very different from the average solution velocity. The efficiency of electroosmotic transport was also shown to be a function of the membrane thickness, in addition to membrane/solute interactions.

Driving molecular transport with an electric force is of great practical significance in chemical analysis,[1] membrane separation technology,[2] and biomedicine.[3] In addition to driving the migration of ions, electric forces often induce an electroosmotic flow of the solution.[4] The undesired "crossover" of organic molecules (e.g., methanol) in fuel cells,[5−8] and the high-efficiency separation of complex mixtures of molecules by capillary electrophoresis (CE),[1,9,10] are well-known examples where electrically facilitated transport, and specifically, electroosmosis, play a key role. Electroosmosis is also employed to pump solution in narrow capillaries in "lab-on-a-chip" technologies[11−16] and to drive drug molecules

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10.1021/ac9910637 CCC: $19.00
Published on Web 01/04/2000

across skin for medicinal applications.[17]

In chemical systems involving electric field-driven transport, the flux of the solute molecule, $N(x)$, can be described by the Nernst−Planck equation, eq 1, modified by a convective term to

$$N(x) = -D\frac{\partial C(x)}{\partial x} - \frac{zF}{RT}DC(x)\frac{\partial \phi(x)}{\partial x} + C(x)v_{eo}(x) \quad (1)$$

account for electroosmotic transport.[18−20] In eq 1, $\phi(x)$ and $v_{eo}(x)$ are respectively the electric potential and solute velocity at position x. D, $C(x)$, and z are the diffusivity, local concentration, and charge of the solute, respectively, F is the Faraday constant, R is the gas constant, and T is temperature. The first, second, and third terms on the right-hand side of eq 1 represent the diffusive, migrational, and convective components, respectively, of the flux. The electric force that drives ion migration is explicitly expressed in the second term. When electroosmosis is operative, the electric force is also implicit in the velocity term, $v_{eo}(x)$.[4] Convective transport driven by pressure, mechanical stirring, and other external fields (i.e., magnetic[21,22]) is also possible but is not considered in the present study.

Electroosmotic flow arises from the viscous drag force exerted on solvent molecules by the charge-carrying counterions that migrate, in response to an electric field, relative to a stationary charged surface.[4,18] Thus, electroosmotic transport tends to be more important in materials and structures that have charged surfaces, e.g., glass capillaries employed in CE,[1,9] ion-exchange membranes,[23] etched channels on glass surfaces,[24,25] and hair follicles in skin.[26] From eq 1, it is clear that the diffusion, migration, and convection of a molecule are highly coupled processes and depend largely on the charge and diffusivity of the molecule as well as the physical characteristics of the medium or structure in which the molecule is being transported. For instance, in CE, diffusion of a charged molecule along the length of a long narrow capillary is negligible in comparison with electroosmosis and migration.[1,27] In contrast, diffusive and electroosmotic transport of a neutral molecule across a thin membrane can occur at comparable rates.

Although an analytical solution of eq 1 is readily obtained (vide infra),[18,26] there are very few quantitative studies in which the contributions of diffusion, migration, and electroosmotic transport have been evaluated for dilute solute molecules without making simplifying assumptions about the transport mechanisms.[19,28] A key limitation of models employed for calculating the electroosmotic flow velocity, v_{eo}, is that they generally require a priori knowledge of the surface charge density, which is typically unknown.[29−33] In addition, even in situations where solution velocities can be estimated from theoretical models, there is no assurance that the solute molecule of interest moves with the same velocity as other components of the solution. Indeed, strong specific chemical interactions of the solute molecule with the stationary surface (e.g., pore wall) may lead to significant differences in the solution and solute velocities.[34]

In the present report, we employed a scanning electrochemical microscope (SECM)[35−38] to investigate the electric field-driven transport of several molecules, possessing different charges, across a model ion-exchange membrane (Nafion,[39] 1100 equiv wt). Previous reports from our laboratories[26,34,40−43] and others[44−47] have demonstrated that SECM is a useful tool for quantitative studies of molecular transport in porous membranes.[48] The goal of the current work is to experimentally evaluate the relative contributions of diffusion, migration, and electroosmotic convection (occurring simultaneously) to the electrically facilitated transport of solute molecules, in a situation where strong specific chemical interactions between the solute and the medium are anticipated. SECM measurements allow the direct determination of electroosmotic solute velocities, which, when coupled with the analytical solution to eq 1, provide a rigorous means to compute the individual fluxes associated with diffusion, migration, and elec-

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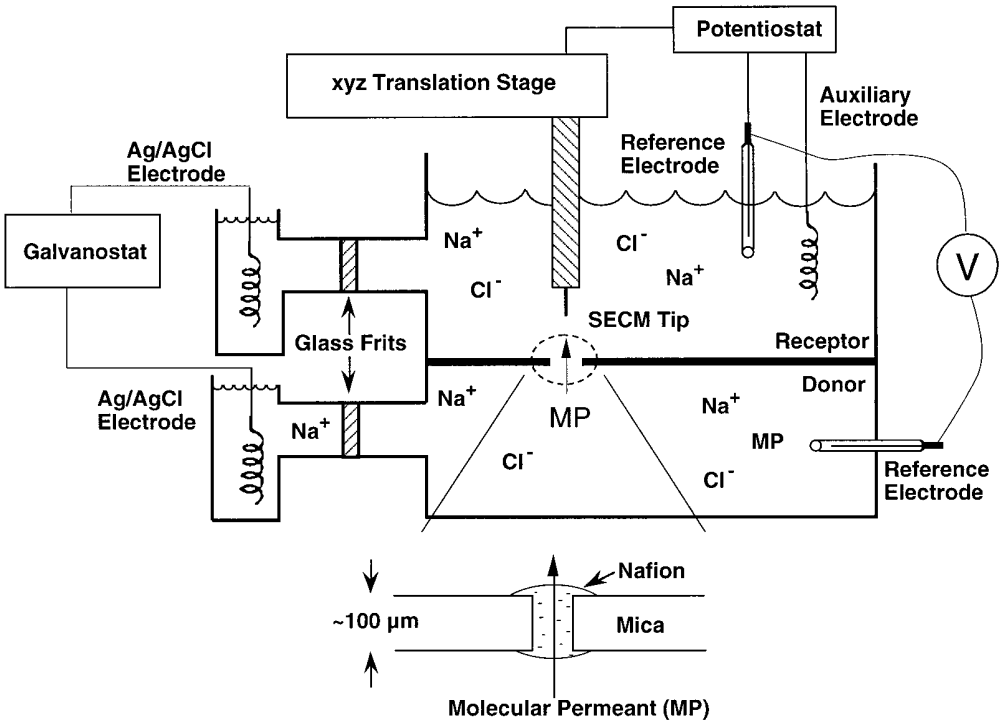

Figure 1. Schematic diagram of the scanning electrochemical microscope and iontophoresis cell. The donor and receptor compartments are separated by an ~100-μm-thick sheet of mica membrane containing a small-area Nafion membrane. A redox-active molecular permeant (MP) is transported across the membrane by diffusion, electroosmotic flow, and migration. The SECM tip is employed to detect the molecular permeant as it emerges from the membrane and enters into the receptor compartment. The translation stage controls the position of the SECM tip in the *x, y,* and *z* dimensions with an accuracy of 0.1 μm. The two Ag/AgCl electrodes and galvanostat are used to apply an iontophoretic current (i_{app}) across the membrane. The two reference electrodes are used to measure the potential drop ($\Delta\phi$) across the membrane.

troosmosis. Factors that influence the efficiency of electroosmotic transport in different chemical applications are also discussed.

EXPERIMENTAL SECTION

Chemicals. Ascorbic acid and acetaminophen (Aldrich Chemical Co.) were used as received. Ferrocenylmethyltrimethylammonium iodide (Strem Chemicals) was converted to the corresponding trifluoromethanesulfonate salt by metathesis with CH_3SO_3Ag. Deionized water was obtained from a Barnstead E-Pure water purifier (resistivity 18 MΩ cm).

Membrane Preparation. Small-area Nafion membranes in a mica support were constructed from 2-cm × 2-cm samples of mica, cleaved using Scotch tape (3M) to a thickness of ~100 μm. The cleaved samples were mounted in the waist of the 355-nm beam of a Nd:YAG pulsed laser (Spectra Physics). Five 90-mJ pulses of 10-ns duration were used to create a single 35−50-μm-radius circular pore in the mica samples. Three ~40-μL drops of a 5 wt % solution of Nafion 117 in alcohol/water (Aldrich Chemical Co., 1100 equiv wt) were then placed over both sides of the pore. On evaporation of the solvent, a small-area Nafion membrane was formed (Figure 1). The mica/Nafion membranes were allowed to dry at room temperature for 12−36 h before use. The polymer protruded ~10 μm out of the pore opening on each side (Figure 1), yielding membrane thicknesses of ~120 μm. The dimensions of individual membranes were characterized by optical microscopy and micrometer measurements.

Scanning Electrochemical Microscopy. The SECM instrumentation and iontophoresis cell used in these studies have been previously described.[34,42] Briefly, a mica/Nafion membrane is sandwiched between the top (receptor) and bottom (donor) compartments of the custom-built iontophoresis cell depicted in Figure 1. The top compartment is open to allow the tip to access the sample. The donor compartment contains an electroactive molecular permeant (MP) and the supporting electrolyte. The receptor compartment contains the supporting electrolyte at a concentration equal to that in the donor compartment.

The SECM tip is an electrochemically etched Pt microelectrode (described below). A custom-built potentiostat controls the tip potential with respect to a Ag/AgCl electrode. Tip current was measured with a precision of ±2 pA. Positioning of the tip along the *x, y, and z* axes, with a repeatability of 0.1 μm, was accomplished with piezoelectric inchworm microtranslation stages (model TSE-75, Burleigh Instruments, Fisher, New York). The tip was positioned directly over the center of the mica/Nafion membrane with the aid of a video camera equipped with a zoom lens. The *x* axis origin ($x = 0$) was defined by lowering the tip until it visibly made contact with the mica surface.

During iontophoresis, a constant current, i_{app}, was driven through the small-area Nafion membrane using two large Ag/AgCl electrodes and a galvanostat (model RDE-4, Pine Instruments, Grove City, PA). Two Ag/AgCl reference electrodes were used to measure the corresponding potential drop across the membrane ($\Delta\phi = i_{app}R$, where R is the total resistance between the two reference electrodes). The sign convention used in this report is as follows: A positive i_{app} refers to the anode of the galvanic circuit being in the donor compartment. *Thus, a positive*

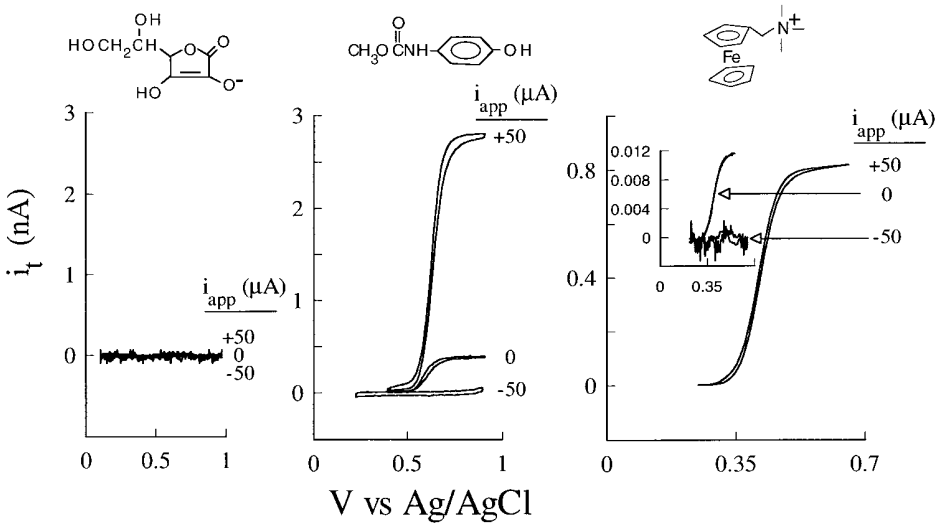

Figure 2. Voltammetric response at an SECM tip (i_t) positioned above a Nafion membrane as a function of applied iontophoretic current (i_{app}) and molecular permeant. The magnitude of the SECM tip current is proportional to the rate of transport of the molecules within the membrane (see text). Positive values of i_{app} indicate the migration of cations (Na^+) from the donor to the receptor compartments; negative values correspond to transport of Na^+ in the opposite direction. Electroosmotic solution flow occurs in the same direction as Na^+ migration. The tip was placed directly ($x = 0$) at the membrane/receptor solution interface to detect molecules as they exit the membrane. Experimental conditions for acetaminophen transport: 0.2 M NaCl as the supporting electrolyte, 0.05 M acetaminophen in the donor compartment; $r_t = 2$ μm. Experimental conditions for ascorbate transport: 0.05 M NaCl, 0.05 M Na_2HPO_4, and 0.05 M NaH_2PO_4 as the supporting electrolyte; 0.04 M ascorbate in the donor compartment; $r_t = 6$ μm. Experimental conditions for $FeCp_2TMA^+$ transport: 0.05 M NaCl, 0.05 M Na_2HPO_4, and 0.05 M NaH_2PO_4 as the supporting electrolyte; 0.5 mM $FeCp_2TMA^+$ in the donor compartment; $r_t = 6$ μm.

i_{app} corresponds to migrational transport of cations from the donor to the receptor compartment. Conversely, a negative i_{app} corresponds to the cathode being in the donor compartment. The iontophoretic current was varied between +50 and −50 μA, resulting in a maximum potential drop across the membrane of ~±3 V. The corresponding current density in the membrane ranged from about −1.0 to +1.0 A/cm^2, the exact value depending on the radius of the pore in the mica sheet.

SECM Tip. Pt SECM tips were constructed using a previously described procedure.[34,49] Tip radii, r_t, were determined by measuring the steady-state limiting voltammetric current in a 2.00 mM acetaminophen solution containing 0.2 M NaCl. Assuming a hemispherical-shaped tip geometry, r_t is related to the limiting current (i_t) by the expression $i_t = 2\pi nFD_sC_sr_t$,[50] where C_s and D_s are the solution concentration and diffusivity [$(9.1 \pm 0.1) \times 10^{-6}$ cm^2/s] of acetaminophen, respectively, and F is Faraday's constant. Tip radii ranged from 1.0 to 10 μm.

RESULTS AND DISCUSSION

Ascorbate, acetaminophen, and ferrocenylmethyltrimethylammonium ($FeCp_2TMA^+$) were used as probe molecules to investigate molecular transport across the Nafion membrane. The rate of transport of each redox-active molecule was determined by electrochemical detection at the SECM tip as the molecule emerged from the membrane. Before describing the transport analysis, we briefly review the redox chemistry of each molecule. The molecular structures are shown in Figure 2.

(1) Ascorbate. Ascorbic acid ($pK_a = 4.2$)[51] solutions were buffered with 0.05 M Na_2HPO_4 and 0.05 M NaH_2PO_4 to maintain a pH of 7, solution conditions in which the molecule exists as the monovalent anion (ascorbate). Ascorbate is detected at the SECM tip by a chemically irreversible two-electron oxidation ($E^{\circ\prime} = 0.31$ V vs Ag/AgCl):[52]

$$[\text{ascorbate}]^- \rightarrow \text{dehydroascorbic acid} + H^+ + 2e^-$$

(2) Acetaminophen. The neutral molecule, acetaminophen, is detected by a chemically irreversible two-electron oxidation ($E^{\circ\prime} = 0.60$ V vs Ag/AgCl):[53,54]

$$\text{acetaminophen} \rightarrow [\text{phenoxonium ion}]^+ + H^+ + 2e^-$$

Oxidation is accompanied by electrophilic attack on the aromatic ring, resulting in the formation of a phenoxonium ion.[53,54]

(3) $FeCp_2TMA^+$. The monovalent cation, $FeCp_2TMA^+$, is detected by a reversible one-electron oxidation ($E^{\circ\prime} = 0.40$ V vs Ag/AgCl):[55,56]

$$FeCp_2TMA^+ \rightarrow FeCp_2TMA^{2+} + e^-$$

Influence of Iontophoretic Current on Molecular Transport. The rates of molecular transport of the above molecules

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Table 1. Diffusion Coefficients of the Molecular Permeants in Aqueous Solution[a]

	$D_s \times 10^6$ (cm^2/s)	electrolyte
ascorbate	7.6 ± 0.2	0.05 M NaCl, 0.05 M Na_2HPO_4, 0.05 M NaH_2PO_4
acetaminophen	9.1 ± 0.1	0.2 M NaCl
$FeCp_2TMA^+$	9.6 ± 0.2	0.05 M NaCl, 0.05 M Na_2HPO_4, 0.05 M NaH_2PO_4

[a] Diffusion coefficients were computed from voltammetric limiting currents ($i_{lim} = 4nFD_sCr_t$) measured at a calibrated Pt microdisk electrode (r_t = 12.5 μm) immersed in 0.0010 M solutions of each species.

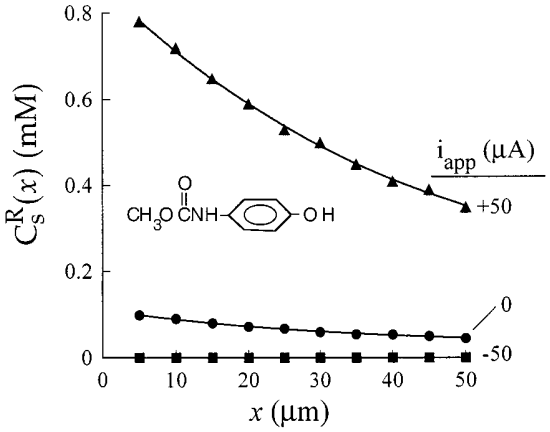

Figure 3. SECM-measured concentration profiles for acetaminophen in the receptor solution above a Nafion membrane as a function of the iontophoretic current. The lines represent the best fit of eq 5 to the experimental data obtained by varying the membrane radius, *a*, and the surface concentration of acetaminophen, $C_s^R(x = 0)$. The donor compartment contained 40 mM acetaminophen in 0.2 M NaCl; the receptor compartment contained 0.2 M NaCl.

through the Nafion membrane were measured by employing the SECM tip to detect the molecules as they emerged from the membrane (Figure 1). A voltammogram (10 mV/s) was recorded with the tip positioned at a tip-to-membrane separation of *x*. The magnitude of the limiting current $i_t(x)$ is proportional to the local concentration of the molecule. For a hemispherical shaped tip, $i_t(x)$ is given by[50]

$$i_t(x) = 2\pi nFD_sC(x)r_t \quad (2)$$

where *n* is the number of electrons transferred per molecule, *F* is the Faraday constant, D_s is the solution diffusivity of the molecule (see Table 1), r_t is the SECM tip radius, and $C(x)$ is the concentration of the molecule. Typically, the SECM tip radius is a few micrometers in diameter (~1 order of magnitude smaller than the diameter of the Nafion membrane).

The diffusional flux of the molecule across the membrane ($x = 0$) is given by eq 3.[48,57]Here, *a* is the radius of the membrane

$$N = 4D_sC_s^R(x = 0)/\pi a \quad (3)$$

and $C_s^R(x = 0)$ is the concentration of the molecule in the solution phase directly next to the membrane/receptor solution interface. $C_s^R(x = 0)$ is determined by measuring the voltammetric limiting current at $x = 0$. (Throughout this report, the subscripts s and *p* are used to indicate the solution and polymer phases, respectively, while the superscripts R and D indicate the side of the membrane [receptor or donor, respectively]). Writing eq 2 for $x = 0$ and combining the result with eq 3 yields[34,48]

$$i_t(x = 0) = (\pi^2 nFr_t a/2)\cdot N \quad (4)$$

Equation 4 demonstrates that the SECM tip current, $i_t(x = 0)$, is directly proportional to the molecular flux, *N*, within the membrane. This relationship holds regardless of the mechanism of transport in the membrane.

Figure 2 shows the voltammetric response of the SECM tip when employed to detect ascorbate, acetaminophen, and $FeCp_2TMA^+$ as these molecules exit the membrane. The voltammetric data were recorded for each molecule at iontophoretic currents of −50, 0, and +50 μA. Na^+ is the predominant charge-carrying ion in the Nafion membrane (vide infra); its concentration was fixed at a constant value (0.2 M) in both the donor and receptor compartments for all experiments. For measurements of ascorbate and $FeCp_2TMA^+$ transport, a buffered solution containing 0.05 M Na_2HPO_4, 0.05 M NaH_2PO_4, and 0.05 M NaCl was employed. An unbuffered solution (0.2 M NaCl) was necessary for the experiments with acetaminophen in order to obtain a well-defined voltammetric curve.

The concentrations of ascorbate, acetaminophen, and $FeCp_2TMA^+$ in the donor solutions were 40, 50, and 0.5 mM, respectively. The relatively low concentration of $FeCp_2TMA^+$ employed in these studies was a consequence of the tendency of $FeCp_2TMA^+$ to strongly partition into the Nafion phase. For the quantitative flux measurements described below, it was necessary to maintain the concentration of $FeCp_2TMA^+$ in the Nafion membrane below its saturation value (~2.5 M). This point is discussed in greater detail below.

The voltammetric data for acetaminophen (middle panel, Figure 2) illustrate the effect of electroosmotic flow on the transport of a neutral species through the cation-selective membrane. The voltammetric wave at $i_{app} = 0$ μA corresponds to the passive diffusion of acetaminophen from donor to receptor compartments. The increase in the voltammetric current at the SECM tip at $i_{app} = 50$ μA (Figure 2) demonstrates that the flux of acetaminophen through the membrane is increased on application of a positive current. The enhancement in the transport of the neutral molecule is solely due to electroosmotic flow from the donor to the receptor compartment (i.e., in the same direction as Na^+ transport). Inspection of Figure 2 indicates that electroosmotic flow at $i_{app} = 50$ μA increased the flux of acetaminophen through the membrane by a factor of ~7 relative to pure diffusion. Reversal of the iontophoretic current, $i_{app} = -50$ μA, reversed the direction of Na^+ transport and electroosmosis, resulting in a solution flow that opposed the diffusion of acetaminophen through the membrane. The data in Figure 2 indicate that the reverse flow of

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solution at $i_{app} = -50\ \mu$A was sufficiently large to reduce the acetaminophen flux to background levels. Quantitatively similar results were previously reported for the iontophoretic transport of the neutral molecule hydroquinone through Nafion.[34]

The transport of ascorbate across ~120-μm-thick Nafion membranes was too small to be detected using SECM under all iontophoresis conditions explored (Figure 2). This finding emphasizes the fact that essentially all of the current across the Nafion membrane is carried by Na^+ and that anions are repelled by the cation-selective membrane. Our results are qualitatively in agreement with those found by Anson and colleagues, who reported on transport of ascorbate across Nafion-coated graphite electrodes.[58] These researchers found that the current at Nafion-coated electrodes due to ascorbate oxidation (in solutions containing 8.2 mM ascorbate) was reduced to near-background levels for Nafion film thicknesses of only ~3 μm.

Transport of $FeCp_2TMA^+$ in Nafion is representative of the case where diffusion, migration, and electroosmosis operate simultaneously (right panel, Figure 2). The tip current for $FeCp_2TMA^+$ oxidation under diffusive conditions ($i_{app} = 0\ \mu$A) is significantly less than that of acetaminophen due, in part, to the much lower concentration of $FeCp_2TMA^+$ and, in part, to the lower diffusivity of $FeCp_2TMA^+$ (vide infra). However, relatively large migrational and electroosmotic fluxes from donor to receptor compartments occur at $i_{app} = 50\ \mu$A. Comparison of the voltammogram with that of diffusion indicates an ~70-fold increase in the flux. Reversal of the iontophoretic current ($i_{app} = -50\ \mu$A) reduced the transport of $FeCp_2TMA^+$ to negligible levels. In the latter case, cation migration and electroosmotic flow from the receptor to the donor compartment prevent $FeCp_2TMA^+$ from diffusing across the membrane.

Quantitative SECM Analysis of Electrically Assisted Transport. Absolute values of the diffusive and iontophoretic fluxes of acetaminophen and $FeCp_2TMA^+$ through the Nafion membrane were determined using a previously reported procedure that involves mapping concentration profiles of each molecule above the membrane surface.[34,48] For diffusional transport away from membrane, the concentration profile in the receptor solution along the hypothetical center line orthogonal to the membrane surface is given by eq 5.[57] The concentration profile is uniquely determined

$$C_s^R(x) = \frac{2C_s^R(x=0)}{\pi} \tan^{-1}\left(\frac{a}{x}\right) \qquad (5)$$

by two parameters, $C_s^R(x = 0)$ and a. These parameters are determined by measuring the concentration of the molecule, $C(x)$, as a function of the tip-to-membrane separation, x (eq 2) and fitting eq 5 to the data. Substituting the resulting values of $C_s^R(x = 0)$ and a into eq 3 yields the flux in the membrane (N).

Figure 3 shows concentration profiles corresponding to the diffusive ($i_{app} = 0\ \mu$A) and iontophoretic ($i_{app} = +50$ and $-50\ \mu$A) transport of acetaminophen across a Nafion membrane. The lines represent best fits of eq 5 to the experimental data. A membrane radius of 36 μm was obtained from the numerical fits at both $i_{app} = 0$ and 50 μA. The SECM-measured diffusive and iontophoretic fluxes were 3.9×10^{-10} and 2.7×10^{-9} mol/(cm^2 s), respectively. (Note: the SECM-measured concentrations at $i_{app} = -50\ \mu$A were below the background level; therefore, no attempt was made to fit eq 5 to these data.)

Table 2. Diffusional (N_{diff}) and Iontophoretic (N_{iont}) Fluxes, Enhancement Factor (E), Peclet Number (Pe), and Electroosmotic Velocity (v_{eo}) for Acetaminophen and $FeCp_2TMA^+$ Transport in Nafion (1100 equiv wt)

$N_{diff} \times 10^{10}$ (mol/(cm^2 s)) for $i_{app} = 0\ \mu$A	$N_{iont} \times 10^{10}$ (mol/(cm^2 s)) for $i_{app} = 50\ \mu$A	E	Pe	$v_{eo} \times 10^5$ (cm/s)
		acetaminophen		
3.9	27	6.9	7.4	17
16	84	5.3	6.8	16
7.6	51	6.7	7.0	16
9.3	70	7.5	7.5	17
24	168	7.0	7.5	17
		6.7 ± 0.8		17 ± 1
		$FeCp_2TMA^+$		
0.106	6.90	65	8.4	0.013
0.122	8.33	68	30	0.046
0.113	8.13	72	27	0.041
0.105	8.40	80	26	0.040
0.110	7.09	64	22	0.0330
		70 ± 7		0.035 ± 0.013

The diffusive (N_{diff}) and iontophoretic (N_{iont}) fluxes of acetaminophen and $FeCp_2TMA^+$ for several membranes are presented in Table 2. N_{diff} and N_{iont} varied somewhat from sample to sample, most probably due to small differences in the thickness of the membranes. However, the ratio of iontophoretic and diffusive fluxes, defined as the enhancement factor, E (eq 6), shows less

$$E = N_{iont}/N_{diff} \qquad (6)$$

variation. E is a quantitative measure of the effect that the electric field has on the transport of each molecule.[18] The average value of E at $i_{app} = 50\ \mu$A for acetaminophen (five samples) is 6.7 ± 0.8. As discussed above, the enhancement of the acetaminophen flux was solely due to electroosmotic flow. In contrast, the average enhancement for $FeCp_2TMA^+$ is considerably larger, 70 ± 7, due to migration of the cation, in addition to electroosmosis.

While migration is the predominant mechanism by which $FeCp_2TMA^+$ is transported at $i_{app} = 50\ \mu$A, the majority of the current in the membrane is still carried by the electrolyte cation, Na^+. For example, a typical value of the flux of $FeCp_2TMA^+$ through a 40-μm-radius membrane at $i_{app} = 50\ \mu$A is 8×10^{-10} mol/(cm^2 s) (Table 2). The total flux of charge-carrying cations (Na^+ and $FeCp_2TMA^+$) is $i_{app}/zFA = 1.03 \times 10^{-7}$ mol/(cm^2 s). Thus, the $FeCp_2TMA^+$ flux is responsible for less than 1% of the current in the membrane.

Electroosmotic Velocity. The electroosmotic velocities of the solute molecules may be determined from the integrated form of the Nernst−Planck equation (eq 1). Figure 4 shows a schematic depiction of the membrane and a hypothetical concentration profile of a molecular permeant during steady-state iontophoretic transport. Equilibrium partitioning of the molecule between the aqueous solution and Nafion membrane was assumed on both sides of the membrane. The equilibrium constant, κ, can be written

(58) Anson, F. C.; Tsou, Y. M.; Savéant, J. M. *J. Electroanal. Chem.* **1984**, *178*, 113−127.

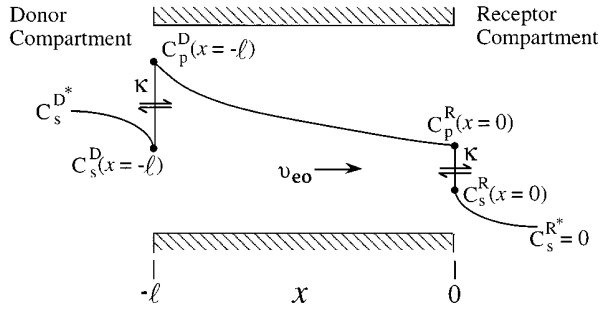

Figure 4. Coordinate system describing molecular transport in the Nafion membrane. κ is the equilibrium partition coefficient. A hypothetical concentration profile across the membrane is shown.

in terms of the concentrations of the molecular permeant at the interfaces:

$$\kappa = C_p^D(x = -l)/C_s^D(x = -l) = C_p^R(x = 0)/C_s^R(x = 0)$$

Following ref 18, integration of eq 1 over the thickness of the membrane, l (Figure 4), using the equilibrium concentrations at the entrance and exit, and employing the assumption of a constant potential gradient in the membrane ($\partial\phi/\partial x = \Delta\phi/l$), yields eq 7,

$$N_{iont} = \left(\frac{\kappa D_p}{l}\right) \times \left\{\frac{\{C_s^D(x = -l)[Pe - Q]\} + \{C_s^R(x = 0)[Q - Pe][\exp(Q - Pe)]\}}{1 - \exp(Q - Pe)}\right\} \quad (7)$$

where Q is the dimensionless potential drop across the membrane ($Q = zF\Delta\phi/RT$) and Pe is the Peclet number ($= \upsilon_{eo}l/D_p$). Equation 7 takes into account the mass-transfer resistance in the solution phase on both sides of the membrane, as discussed below.

In the absence of an applied current, both Q and Pe are equal to zero, and the flux through the membrane is purely diffusional. In this limit, eq 7 reduces to

$$N_{diff} = \kappa D_p[C_s^D(x = -l) - C_s^R(x = 0)]/l \quad (8)$$

which is the expected diffusional limited response.[59] From SECM measurements of the concentration distribution above the membrane opening, we observe that the value of $C_s^R(x = 0)$ during diffusive transport is always approximately equal to the bulk solution concentration on the receptor side; i.e., $C_s^R(x = 0) \approx C_s^{R*} = 0$. For instance, Figure 3 shows the concentration profiles for acetaminophen at the membrane exit. At $i_{app} = 0$ μA (diffusion), the concentration measured at the surface is ~0.1 mM, sufficiently small to take $C_s^R(x = 0)$ as being equal to 0.0 mM. By similar argument, and because the membrane entrance and exit have identical circular geometries, the concentration at the membrane entrance, $C_s^D(x = -l)$, can be approximated to be equal to the bulk concentration in the donor solution; i.e., $C_s^D(x = -l) = C_s^{D*}$. Substituting these approximations into eq 8 yields

$$N_{diff} = \kappa D_p C_s^{D*}/l \quad (9)$$

Note that the approximations $C_s^R(x = 0) \approx C_s^{R*} = 0$ and $C_s^D(x = -l) \approx C_s^{D*}$ cannot be employed under iontophoretic conditions (eq 7) since migration and/or electroosmosis can greatly decrease the mass-transfer resistance in the membrane, resulting in significant perturbation of the solution concentrations near the membrane entrance and exit.

Taking the ratio of N_{iont} (eq 7) to N_{diff} (eq 9) yields the expression for the enhancement factor:

$$E = \frac{[Pe - Q]\left\{\frac{C_s^D(x = -l)}{C_s^{D*}} - \frac{C_s^R(x = 0)}{C_s^{D*}}[\exp(Q - Pe)]\right\}}{1 - \exp(Q - Pe)} \quad (10)$$

Values of the Peclet number may be evaluated using experimental values of E (e.g., Table 2) and eq 10. Calculation of υ_{eo} requires measurements of the potential drop across the Nafion membrane ($\Delta\phi$), the membrane thickness (l), the entrance and exit concentrations, $C_s^D(x = -l)$ and $C_s^R(x = 0)$, and the solute diffusivity in the Nafion membrane (D_p). $C_s^R(x = 0)$ was determined directly from SECM measurement of the concentration above the membrane exit (vide supra) (Figure 3). $C_s^D(x = -l)$ was computed by assuming that the change in concentration across the membrane entrance (i.e., $C_s^{D*} - C_s^D(x = -l)$) was equal to that across the membrane exit (i.e., $C_s^R(x = 0) - C_s^{R*}$). This assumption seems reasonable given that the membrane entrance and exit have identical geometries.

The diffusivity D_p was determined by measuring κD_p (eq 9) from the diffusive flux (Table 2) and combining this value with the independently measured quantity $\kappa(D_p)^{1/2}$. The latter was obtained from the cyclic voltammetric response of Nafion-coated electrodes immersed in an aqueous solution containing the redox molecule.[34] This procedure yielded values for $FeCp_2TMA^+$ (κ = 1600 and $D_p = 1.9 \times 10^{-10}$ cm^2/s) and acetaminophen ($\kappa = 1.3$ and $D_p = 2.9 \times 10^{-7}$ cm^2/s) that are in good agreement with previously reported values.[55,60]

As a side note, the large value of κ (1600) for $FeCp_2TMA^+$ requires that the solution concentration of $FeCp_2TMA^+$ is no greater than ~1 mM. At higher solution concentrations, the amount of $FeCp_2TMA^+$ in the Nafion approached its saturation concentration (~2.5 M)[55] and the boundary conditions used to obtain the flux expression, eq 7 (i.e., $\kappa = C_p^D(x = -l)/C_s^D(x = -l) = C_p^R(x = 0)/C_s^R(x = 0)$), are no longer applicable. For this reason, the concentration of $FeCp_2TMA^+$ in the solution was maintained at 0.5 mM.

Values of the Peclet number and the corresponding values of υ_{eo} obtained at $i_{app} = 50$ μA are listed in Table 2. Figure 5 shows the dependence of υ_{eo} on i_{app} over a range of i_{app} values. Theoretical

(59) Cussler, E. L. *Diffusion: Mass Transfer in Fluid Systems*; Cambridge University Press: New York, 1997.

(60) The partition coefficient and diffusivity of acetaminophen reported here are similar to that previously reported for hydroquinone ($\kappa = 0.78$ and $D_p = 3.7 \times 10^{-7}$ cm^2/s), a neutral organic molecule of similar size as acetaminophen.[34]

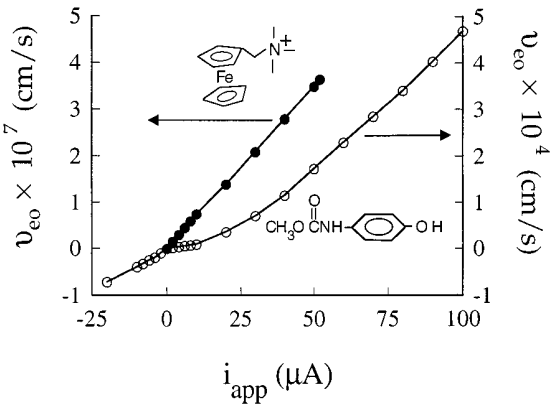

Figure 5. Electroosmotic velocities (v_{eo}) for acetaminophen and $FeCp_2TMA^+$ as a function of applied iontophoretic current (i_{app}). Note the 1000-fold change in scale for acetaminophen and $FeCp_2TMA^+$. Solution conditions are identical to those in Figure 2.

descriptions of electroosmosis suggest that v_{eo} should be proportional to i_{app} if the conductivity of the membrane remains constant.[4,29,30] A linear relationship was indeed observed for $FeCp_2TMA^+$ (Figure 5). (Note that v_{eo} could not be determined at negative i_{app} because of the low flux of $FeCp_2TMA^+$.) However, the plot of v_{eo} versus i_{app} for acetaminophen exhibits significant curvature at small i_{app}. We are not aware of any theoretical description that predicts this behavior.

The data in Table 2 and Figure 5 indicate that the electroosmotic velocity of $FeCp_2TMA^+$ is a factor of ~500 lower than that of acetaminophen. This difference is most likely due to electrostatic interactions between $FeCp_2TMA^+$ and the fixed-site SO_3^- groups of Nafion. It is interesting to note that the ratio of the v_{eo} of acetaminophen to that of $FeCp_2TMA^+$ (~500) is of the same order of magnitude as the ratio of their diffusivities in Nafion (~1500). This finding suggests that similar chemical and physical processes in the polymer determine the rates of both transport mechanisms.

Relative Contributions of Diffusion, Migration, and Electroosmosis to the Flux. The preceding analysis indicates that the transport of acetaminophen and $FeCp_2TMA^+$ in the Nafion membrane occurs by a mechanism that involves a combination of diffusion, migration, and electroosmosis. The contributions of each process to the net molecular flux may be evaluated by computing the value of each term in the Nernst−Planck equation (eq 1). This calculation requires knowledge of the steady-state concentration profile, $C_p(x)$, inside the membrane. $C_p(x)$ is readily obtained by integration of eq 1 using the boundary condition $C_p^D(x = -l) = \kappa C_s^D(x = -l)$ and combining the result with eq 7 to eliminate N.

$$\frac{C_p(x)}{\kappa C_s^{D*}} = \left[\left[1 - \exp\left((Pe - Q)\frac{x}{l}\right)\right] + \left[(C_s^R(x = 0)/C_s^D(x = -l))\left\{\left(\exp\left((Pe - Q)\frac{x}{l}\right)\right) - \exp(Q - Pe)\right\}\right]\right]/[1 - \exp(Q - Pe)] \quad (11)$$

Concentration profiles for acetaminophen and $FeCp_2TMA^+$ were computed using experimentally determined values for all

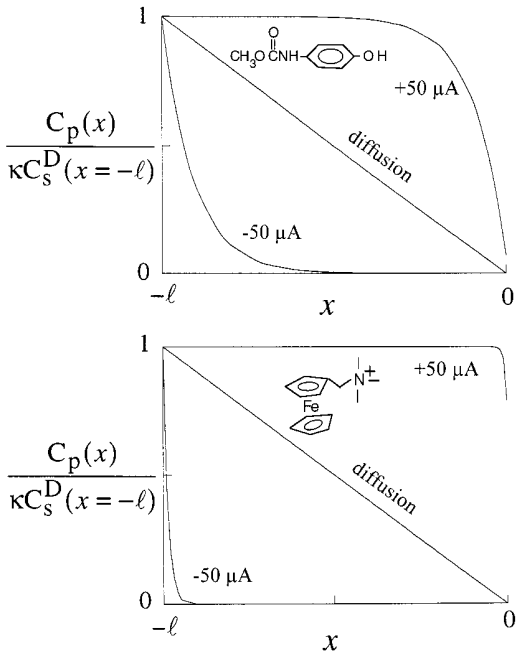

Figure 6. Steady-state concentration profiles of acetaminophen and $FeCp_2TMA^+$ inside a Nafion membrane under diffusive and iontophoretic conditions (+50 and −50 μA). The profiles were computed using eq 11 and the experimental results in Table 2.

quantities in eq 11 (Figure 6). Linear profiles were obtained for $i_{app} = 0$ μA for both molecules, as expected when diffusion is the sole transport mechanism.[34] When a positive current was applied, the concentration profile shifted toward the membrane exit, a consequence of convection and/or migration contributing to the net transport of the molecule. Neither of these mechanisms requires a gradient in the concentration, and thus the steady-state profile is relatively flat near the middle of the membrane.

It is immediately apparent from eq 1 and Figure 6 that *the contributions of diffusion, migration, and electroosmosis are dependent on the spatial position inside the membrane.* For instance, in the case of acetaminophen at $i_{app} = 50$ μA, diffusion is the dominant transport mechanism near the membrane exit ($x = 0$) where the concentration gradient is large. In contrast, electroosmosis is the predominant mechanism near the membrane entrance ($x = -l$) where the concentration gradient is vanishingly small.

Substitution of eq 11 into each term of eq 1 allows the absolute values of diffusion, migration, and electroosmosis to be computed. The results are shown in Figure 7, where the relative percentage of the total iontophoretic flux (at $i_{app} = 50$ μA) attributed to each process is plotted as a function of position in the membrane. This plot is particularly instructive in visualizing the overall mechanism of transport for each molecule in the membrane. For instance, diffusion plays essentially no role in the transport of the cation, $FeCp_2TMA^+$, the flux resulting from migration (~85%) and electroosmosis (~15%).

Electroosmotic Drag Coefficient. Traditionally, the electroosmotic drag coefficient, t_D, is defined as the ratio of the flux of solute (or solvent molecules) transported by electroosmosis relative to the flux of current-carrying ions that induce the flow

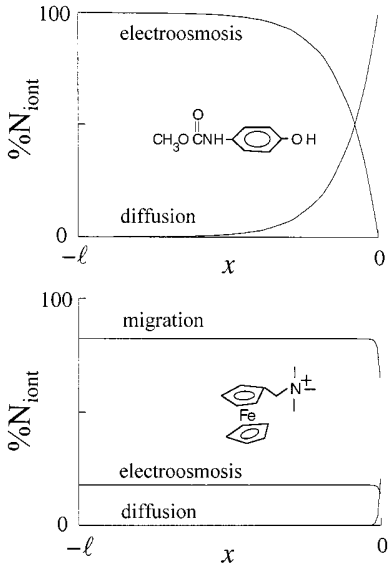

Figure 7. Relative contributions of diffusion, migration, and electroosmosis to the overall iontophoretic flux (N_{iont} at i_{app} = 50 μA) of acetaminophen and $FeCp_2TMA^+$ inside a Nafion membrane. The contribution of each transport mechanism is a function of position in the membrane.

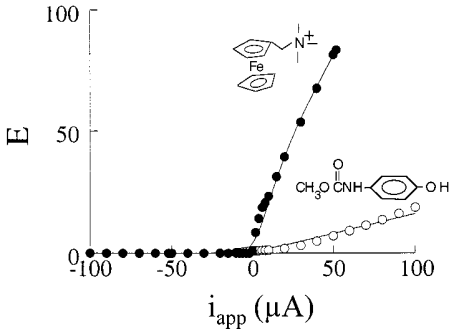

Figure 8. Enhancement factors for acetaminophen and $FeCp_2TMA^+$ transport measured as a function of applied iontophoretic current (i_{app}). The line drawn through the points represents the best fit of eq 10 to the experimental data. Solution conditions are the same as those in Figure 2.

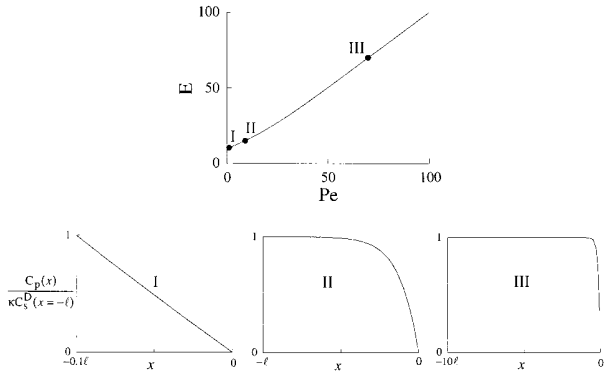

Figure 9. (top) Enhancement factor as a function of the Peclet number ($Pe = v_{eo}l/D$) for a neutral molecule (z = 0), eq 10. Points labeled I, II, and III correspond to Pe = 0.7, 7, and 70, respectively. (bottom) Concentration profiles of the molecule at Pe = 0.7, 7, and 70.

(eq 12).[61] Here, A_p is the area of the membrane and z and t_+ are

$$t_D = v_{eo}C_p(x)/[t_+i_{app}/(zFA_p)] \qquad (12)$$

the charge and transference number of the current-carrying ions. For the experiments reported here, $t_+ \approx 1$ since Na^+ carries ~100% of the current in Nafion.[62] As noted above, the presence of the cationic species $FeCp_2TMA^+$ in the solution does not alter the fact that Na^+ is the predominant charge carrier.

In published analyses of electroosmotic transport, diffusion is frequently assumed to be negligible, and thus, the concentration in the membrane (or other medium) is uniform; i.e., C_p is constant.[29,30,33,61] However, it is evident from the results presented in Figure 6 that C_p varies as a function of the spatial position inside the membrane, x. If one assumes that the electroosmotic velocity, v_{eo}, is independent of the local solute concentration, $C_p(x)$, it follows that the drag coefficient is also a function of x. Rearranging eq 12 to obtain the velocity, and indicating the spatial dependence of the concentration and drag coefficient, yields

$$v_{eo} = [t_D(x)/C_p(x)][t_+i_{app}/zFA_p] \qquad (13)$$

Since v_{eo} is independent of position, the *ratio* $t_D(x)/C_p(x)$ must also be a position-independent value. Hereafter, we will express this ratio as t_D/C_p. The quantity t_D/C_p is the key fundamental parameter that allows the velocity (eq 13), the solute flux (eq 7), and the enhancement factor (eq 10) to be computed. Figure 8 shows a plot of the experimental values of E as a function of i_{app} and the best fit of eq 10 to the data obtained using values of v_{eo} computed from eq 13. The single adjustable parameter in the procedure is t_D/C_p. Values of t_D/C_p equal to 18.5 and 0.038 cm^3/mol for acetaminophen and $FeCp_2TMA^+$, respectively, yield good theoretical fits over the entire range of applied currents.

Influence of Peclet Number on the Rate of Electroosmotic Transport. In the preceding analysis, the solute diffusivities (D_p) and membrane thickness (l) were assumed to be constant valued parameters, and the dependence of the flux on the electroosmotic velocity, v_{eo}, was emphasized. Although well understood by practitioners in the field, it is informative to recall that variations in either l or D_p (while maintaining a constant v_{eo}) may also lead to *qualitative* changes in the transport mechanism. For instance, Figure 9 shows a plot of E versus Pe ($= v_{eo}l/D_p$) calculated using the experimentally determined parameters for acetaminophen at i_{app} = 50 μA. Point II on the plot indicates a Pe of 7, the value corresponding to the acetaminophen experiments using the ~120-μm-thick Nafion membrane. The dimensionless concentration profile for this case is shown at the bottom of Figure 9 and is identical to that previously reported in Figure 6. Decreasing l (or increasing D_p) by a factor of 10 while maintaining a constant v_{eo} results in a decrease in E, as marked by point I. In this case (Pe = 0.7), transport is dominated by diffusion, and electroosmotic flow has an insignificant affect on the net flux. The linear concentration profile across the membrane for this case (bottom of Figure 9) clearly indicates that diffusion is the dominant process. Conversely, increasing l (or decreasing D_p) by 1 order

(61) Breslau, B. R.; Miller, I. F. *Ind. Eng. Chem. Fundam.* **1971**, *10*, 554−565.
(62) Pintauro, P. N.; Bennion, D. N. *Ind. Eng. Chem. Fundam.* **1984**, *23*, 234−243.

of magnitude (point III, $Pe = 70$) results in electroosmosis being the dominant transport process in the membrane. In the latter case, the net solute flux is proportional to the electroosmotic velocity and diffusion is negligible except near the exit membrane. It is clear that the efficiency of electroosmotic transport in a chemical system depends on the rate of electroosmosis relative to diffusion and to migration, which in turn is a function not only of the membrane/solution interactions but also of the membrane geometry.

CONCLUSIONS

The individual components (diffusion, migration, convection) of electrically facilitated transport in a model ion-exchange membrane have been separated and measured, without approximation, using SECM-based methodology. We have demonstrated that the Nernst−Planck equation, with a linear convection term to account for electroosmotic transport, quantitatively captures the dependence of the net molecular flux on the applied iontophoretic current. However, the electroosmotic flow velocity that results from the electrical field is molecule-specific and does not necessarily correspond to the average velocity of solution.

The electroosmotic velocity of acetaminophen in Nafion is ~500 times larger than that of $FeCp_2TMA^+$, reflecting the electrostatic interaction of the cation with the negatively charged membrane. There are two possible causes of this effect. First, an electrical drag force *selectively* acts on the charged molecules as they are transported by the solution flow in the interior pores of the Nafion membrane. This force arises from local interactions between the $FeCp_2TMA^+$ and the negative SO_3^- sites that line the pore walls. This braking effect tends to be most pronounced for cations that strongly associate with the SO_3^- sites. Second, cations tend to reside near the negatively charged pore walls, where the flow velocity is lowest. Thus, in the present experiments, $FeCp_2TMA^+$ is concentrated in a region of the pore where the solvent is moving at its lowest velocity. Both explanations are consistent with the higher convective velocity of the neutral molecule relative to the cation.

ACKNOWLEDGMENT

We thank Mr. Rory Uibel for developing the data analysis computer program and Mr. James Kliemeyer and Prof. Joel Harris for the use of the Nd:YAG laser. This research was supported by ALZA Corp., the American Chemical Society Division of Analytical Chemistry Full-Year Fellowship sponsored by Eli Lilly and Co., the Edward G. Weston Summer Fellowship of the Electrochemical Society, and the Office of Naval Research.

Received for review September 14, 1999. Accepted December 3, 1999.

AC9910637