Diffusive–Convective Transport into a Porous Membrane. A Comparison of Theory and Experiment Using Scanning Electrochemical Microscopy Operated in Reverse Imaging Mode

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Molecule transfer at the interface between a single ion-selective micropore and aqueous solutions is quantitatively investigated using scanning electrochemical microscopy operated in reverse imaging mode (SECM-RIM). Accumulation of two electroactive solute molecules, acetaminophen and ferrocenylmethyltrimethylammonium, at the pore/solution interface is observed when an electrical current is passed through the pore. Slow interfacial transfer of solute relative to the solvent as the solution is driven across the membrane by electroosmosis is responsible for solute accumulation. A theoretical expression for the concentration distribution of solute molecules above an individual pore opening is obtained by analytical solution of the convective–diffusive flux equation. The fluid velocity through the pore at constant electroosmotic force is determined by fitting the theoretical expression to SECM-RIM concentration profiles and is found, as anticipated, to be independent of the solute species and the bulk solute concentration. The results provide a theoretical basis for the SECM-RIM imaging of biological membranes as well as a general method for characterizing interfacial molecule/ion transfer kinetics.

These processes occur sequentially; i.e., the overall process may be expressed as “bulk transport/interfacial transfer/porous phase transport”; thus, any one of these steps may limit the overall molecular flux across a micro- or mesoporous phase.

In previous reports, we and others have demonstrated that scanning electrochemical microscopy (SECM) is particularly well-suited for measuring transport parameters in both synthetic and biological membranes, especially in situations where spatially resolved visualization and quantification of molecular transport is required. Recently, Hupp and co-workers used SECM to quantify the size-selective transport in membranes and quantifying the individual contributions of diffusional, migration, and convection to pore transport. These processes occur sequentially; i.e., the overall process may be expressed as “bulk transport/interfacial transfer/porous phase transport”; thus, any one of these steps may limit the overall molecular flux across a micro- or mesoporous phase.
partitioning of molecules into thin polymer films deposited on electrode surfaces.\textsuperscript{22} In related studies, SECM has also been used to probe charge transfer between immiscible liquid phases\textsuperscript{23–25} and across bilayer lipid membranes,\textsuperscript{26} as well as to measure lateral diffusion of redox-active amphiphiles in Langmuir monolayers.\textsuperscript{27}

Measurement of the net solute flux across porous membranes is readily accomplished by conventional analytical measurement of the solute concentration in the solutions contacting the membranes as a function of time.\textsuperscript{3} However, identification and kinetic characterization of the rate limiting step(s) is considerably more difficult because of the sequential multistep nature of the process. Recently, we described a preliminary SECM study in which we demonstrated that pore transport could be visualized by observing the depletion or accumulation of molecules at the entrance side of the membrane.\textsuperscript{28} Qualitatively, the shape of the concentration profile above the pore reflects the rate of solute transfer into the pore. From a practical point of view, this mode of imaging, referred hereafter as reverse imaging mode (SECM-RIM), is attractive in that it alleviates the need to place the solute species and the SECM tip on opposite sides of the membrane (as required in order to observe the exit of molecules from the membrane pores). In the present report, a quantitative theoretical treatment of the SECM-RIM response corresponding to diffusive–convective transport of solute species into a pore is described. We show that the shape of the concentration profile above the pore entrance directly reflects the rate of solute transfer into the membrane and, thus, can be employed to extract kinetic information about interfacial transfer, for example, solute flux, interfacial transfer rate, or flow velocity.

\textbf{EXPERIMENTAL SECTION}

\textbf{Chemicals.} Acetaminophen (99.9\% Aldrich) was used as received. Ferrocenylmethyltrimethylammonium hexafluorophosphate, FeCp\textsubscript{2}TMA\textsuperscript{+}, was prepared by metathesis of the corresponding iodide salt with ammonium hexafluorophosphate (99.9\% Aldrich) in H\textsubscript{2}O. The precipitate was recrystallized in acetone/ether.

\textbf{Mica/Nafion Membrane.} Membranes were prepared by cutting 0.75-in. \times 0.75-in. square samples from an \textasciitilde 100 \mu m thick sheet of mica. A single circularly shaped pore in the center of the mica membrane was created by laser ablation using the 355-nm line (five 90-mJ pulses of 10-ns duration) of a Nd:YAG pulsed laser (Spectra Physics). Two \textasciitilde40 \mu L drops of a 5 wt\% solution of Nafion 117 in alcohol/water (Aldrich, 1100 equiv wt) was placed over the pore and drawn into the pore by capillary action.

\textbf{Scanning Electrochemical Microscopy and the Iontophoresis Cell.} The mica/Nafion membrane separated the solutions of a two-compartment iontophoresis cell. Both the donor and the receptor compartments were filled with an aqueous electrolyte. The electroactive species (either acetaminophen or FeCp\textsubscript{2}TMA\textsuperscript{+}) were dissolved only in the donor compartment. As illustrated in Figure 1, the SECM tip was placed in either the donor or the receptor compartment, depending on whether measurements are made in reverse imaging mode (RIM) or forward imaging mode (FIM), respectively. In RIM, the tip and solute are located on the same side of the membrane, whereas in FIM, the tip and solute are on opposite sides. In either mode, the tip is poised at a constant potential to oxidize the electroactive species at the mass transport limited rate.

Applying a current across the membrane controls convective fluid flow through the pore. Nafion has a net negative charge associated with pendant sulfonate groups and is selective to cation transport. The flow of a constant current through the pore results in a steady electroosmotic flow. The iontophoresis cell, electrodes, and circuitry used to pass current across the membrane were described in previous reports.\textsuperscript{12,14}

Carbon fiber SECM tips were fabricated as previously described.\textsuperscript{28} Briefly, the tips were constructed by partial insertion of a 4-\mu m-radius carbon fiber into a 5-mm-diameter glass capillary and sealing this junction with epoxy. A tungsten wire was inserted into the other end of the glass capillary, and silver-conducting epoxy was used to make electrical contact between the carbon fiber and the tungsten wire. The end of the carbon fiber was flame-etched using a butane/O\textsubscript{2} torch to reduce the tip radius. The carbon fiber SECM tips were then insulated by electropolymerization of a thin film of poly(oxyphenylene) oxide following the procedure of Kamloth et al.\textsuperscript{29} The end of the fiber was cut with a razor blade to expose the active electrode. The radius of the SECM tip was determined from the limiting voltammetric current measured in a solution containing 5 m\textsuperscript{m} acetaminophen in 0.2 M NaCl using the reported diffusivity of 9.1 \times 10\textsuperscript{-6} cm\textsuperscript{2}/s.\textsuperscript{15} Tip radii ranged from 0.9 to 3.2 \mu m.

\textbf{RESULTS AND DISCUSSION}

\textbf{Theoretical Description of Ultrafiltration at a Microscopic Pore.} In RIM imaging, the SECM tip is used to measure the local concentration of a solute species above the pore opening (Figure 1). A first step in interpreting SECM-RIM images is to develop a theoretical description of the solute distribution above the pore under the various possible conditions that might be encountered.

![Figure 1. Position of the tip and solute relative to the membrane in SECM-FIM and SECM-RIM. The arrows depict the direction of the solute flux from the donor to the receptor compartment in both imaging modes.](Image)
Figure 2. Pore model used to develop the expression for the ultrafiltration solute distribution, eq 9. Both \( J(r) \) and \( w(r) \) are position-dependent as a result of the convergent flux and fluid flow into the pore.

during imaging. Giddings initially reported a description of ultrafiltration profiles developed at large-area planar membranes without explicit consideration of the microscopic pore structure.\(^{30}\)

In the absence of fluid flow, solute diffusion from the donor compartment into the pore results in the depletion of the solute at the pore entrance. When fluid flows through the pore as a consequence of either a mechanical or electroosmotic pressure gradient, the solute is transported into the pore by both diffusion and convection; however, the solute species may be partially rejected by the pore, resulting in accumulation of the solute in the solution adjacent to the pore entrance. In the following paragraphs, we derive a general theoretical expression for the concentration profile above the pore as a function of the convective flow velocity and the flux of the solute molecule.

Figure 2 illustrates the model pore geometry. The donor solution is assumed to contain the solute species of interest at a bulk concentration equal to \( C^* \). The solute concentration in the receptor solution, in contact with the pore exit, is assumed to be 0. Although the solute concentration in the receptor solution gradually increases during the experiment, its value is assumed to remain sufficiently small that back-diffusion of the solute is insignificant.

For the sake of simplifying the analysis, we assume a hemispherical pore opening of radius \( r_0 \). Although pore openings at real membrane surfaces are generally flush with the surface, the convective–diffusive flux of molecules into a microscopic pore of arbitrary shape follows a quasiradial path that is approximated by the flux lines expected above a true hemispherical pore opening. Consequently, the concentration distribution above a hemispherical pore opening can be used to approximate the distribution above pores of other shapes. This approximation is reasonably accurate at distances into solution from the pore opening that are comparable to or greater than the characteristic dimension of the pore.\(^{12}\)

The general convective–diffusive equation, eq 1, is assumed to govern the flux of the solute through the pore. Here, \( J(r) \) is

\[
J(r) = w(r) - D \frac{dC(r)}{dr}
\]

(1)

the solute flux, \( w(r) \) is the solution velocity, and \( D \) is the diffusion coefficient of the solute (assumed to be constant). Although eq 1 describes the flux both inside and outside of the pore, our concern here is to determine the distribution of the solute in the solution above the pore opening; thus, \( r \) corresponds to the radial distance measured from the center of the pore opening (see Figure 2).

The radially inward directed solute transport and fluid flow require that both the flux and fluid velocity are a function of the position \( r \).

Equation 1 is a linear first-order differential equation that has a general solution expressing \( C \) as a function of \( r, J(r) \) and \( w(r) \). An explicit expression for \( J(r) \) is obtained by integration of the continuity equation,

\[
0 = \frac{1}{r^2} \frac{d}{dr} \left( r^2 J(r) \right)
\]

(2)

using the boundary condition, \( J(r) = J_0 \) at \( r = r_0 \), where \( J_0 \) is the flux at the surface of the pore. The result is

\[
J(r) = \frac{J_0 r^2}{r^2}
\]

(3)

Similarly, for an incompressible solution (i.e., constant fluid density), \( w(r) \) may be written in terms of the fluid velocity at the pore opening, \( w_0 \).

\[
w(r) = \frac{w_0 r^2}{r^2}
\]

(4)

Substitution of eqs 3 and 4 into eq 1 yields

\[
J_0 = w_0 C(r) - \frac{D r^2 dC(r)}{r_0^2 dr}
\]

(5)

Using the change of the variable, \( y(r) = C(r) - J_0 / w_0 \), eq 5 is rewritten as

\[
\frac{D}{w_0 r^2} \frac{dy(r)}{dr} = \frac{dr}{r^2}
\]

(6)

which, upon integration, yields

\[
\frac{D}{w_0 r^2} \ln y(r) = -\frac{1}{r} + A
\]

(7)

The constant, \( A \), is evaluated by noting that the solute concentration approaches \( C^* \) at distances far from the pore opening. Thus, \( y(r) = C^* - J_0 / w_0 \) as \( r \rightarrow \infty \), and

\[
A = \left( \frac{D}{w_0 r^2} \right) \ln \left( \frac{C^* - J_0}{w_0} \right)
\]

(8)

Substitution of \( A \) into eq 7 yields

\[
C(r) = \frac{J_0}{w_0} + \left( \frac{C^* - J_0}{w_0} \right) \exp \left( -\frac{w_0 r^2}{Dr} \right)
\]

(9)

which describes the solute distribution above the pore opening.

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as a function of any combination of the solute surface flux, \( J_0 \), and fluid velocity, \( w_0 \). For instance, Figure 3 shows a series of concentration profiles above the pore as the fluid velocity is increased from \( w_0 = 0 \) (corresponding to pure diffusive transport) to increasingly larger values. In this example calculation, the solute flux \( J_0 \) is assumed to be constant. As the results demonstrate, increasing \( w_0 \) into the pore while maintaining a constant \( J_0 \) requires a separation of solvent and solute molecules at the interface between the pore and donor solution.

Comparison of Theory to Concentration Profiles Above Nafion Membranes. To test the validity of eq 9, SECM-RIM was used to measure the concentration profiles of solute molecules above a single micropore in an otherwise impervious membrane. The single-pore membrane consisted of a ~100-\( \mu \)m-thick sheet of mica in which a single ~20-\( \mu \)m-radius pore was introduced by laser ablation. The pore was filled with a solution containing 1100 equiv wt Nafion and allowed to dry. The purpose of the Nafion was to introduce ion-selective properties to the pore, resulting in electroosmotic flow across the pore when a electrical current was passed across it. Hereafter, we refer to the single pore membrane as a "mica/Nafion" membrane.

The single pore in the mica/Nafion membrane had a disk-shaped opening that was flush with the surrounding surface. Thus, to compare the experimental data to the theoretical predictions, we made use of the fact that the mass transport rate into a disk-shaped pore of radius \( a \) is equivalent to that of a hemisphere with an effective radius, \( r_0^{\text{eff}} \), given by the expression

\[
r_0^{\text{eff}} = \frac{2a}{\pi}
\]  

(10)

Measured values of the true pore radius, \( a \), were thus converted to \( r_0^{\text{eff}} \) for the purpose of comparing eq 9 to the experimental results (vide infra). An analysis of the error resulting from using the hemispherical approximation for estimating the radii of disk-shaped pore openings has been previously reported.\(^{12,13}\)

Figures 4 and 5 show RIM-measured concentration profiles, of acetaminophen and FeCp2TMA\(^+\), respectively, directly above the center of the pore opening (i.e., along the hypothetical centerline axis extending into the solution directly above the center of the pore). The profiles were obtained by measuring the SECM tip limiting current, \( i_t \) (eq 11), at various heights above the center of the pore and converting these values to \( C(r) \).

In eq 11, \( n \) is the number of electrons transferred (\( n = 1 \) for the oxidation of acetaminophen or FeCp2TMA\(^+\)), \( r_i \) is the radius of the SECM tip, and \( F \) is Faraday’s constant. For all experiments reported here, both the donor and the receptor solutions contained 0.2 M NaCl, and a current of 50 \( \mu \)A was passed across the pore to induce electroosmotic solution flow from the donor compartment to the receptor compartment. The profiles presented in Figures 4 and 5 were measured in donor solutions containing 1, 5, 25, and 50 mM solutions of the solute species.

Consistent with previous SECM-RIM images,\(^{17}\) the data in Figures 4 and 5 clearly show an accumulation of acetaminophen and FeCp2TMA\(^+\) at the interface between the mica/Nafion pore and the donor solution, indicating that the pore partially rejects

\[
i_t = 4nFD\frac{C(r)}{r_i}
\]  

(11)
Experimental data require knowledge of the expression describing the solute accumulation, eq 9, to the Figure 3. However, quantitative comparisons of the theoretical data are similar in shape to the theoretical curves present in these solutes as the solution flows through the pore. Qualitatively, the data and eq 12 are fit to the experimental solute concentration profile at the pore exit, measured by SECM-RIM.

Table 1. Transport Parameters for Acetaminophen and FeCp2TMA+$^a$

<table>
<thead>
<tr>
<th>concn of solute in donor, mM</th>
<th>1</th>
<th>5</th>
<th>25</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>acetaminophen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$a$ (μm)$^a$</td>
<td>20.9</td>
<td>20.8</td>
<td>20.7</td>
<td>20.8</td>
</tr>
<tr>
<td>$j_0$ (mol/cm$^2$s)$^a$</td>
<td>$1.72 \times 10^{-9}$</td>
<td>$5.2 \times 10^{-9}$</td>
<td>$1.96 \times 10^{-8}$</td>
<td>$2.78 \times 10^{-8}$</td>
</tr>
<tr>
<td>$w_0$ (cm/s)$^b$</td>
<td>$3.2 \times 10^{-3}$</td>
<td>$1.9 \times 10^{-3}$</td>
<td>$2.9 \times 10^{-3}$</td>
<td>$3.3 \times 10^{-3}$</td>
</tr>
<tr>
<td>$a v w_0 = 2.8 \pm 0.6$ cm/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FeCp2TMA$^+$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$a$ (μm)$^a$</td>
<td>20.2</td>
<td>20.2</td>
<td>20.1</td>
<td>20.0</td>
</tr>
<tr>
<td>$j_0$ (mol/cm$^2$s)$^a$</td>
<td>$2.18 \times 10^{-9}$</td>
<td>$2.92 \times 10^{-9}$</td>
<td>$4.99 \times 10^{-9}$</td>
<td>$5.97 \times 10^{-9}$</td>
</tr>
<tr>
<td>$w_0$ (cm/s)$^b$</td>
<td>$5.9 \times 10^{-3}$</td>
<td>$1.8 \times 10^{-3}$</td>
<td>$4.0 \times 10^{-3}$</td>
<td>$8.0 \times 10^{-3}$</td>
</tr>
<tr>
<td>$a v w_0 = 4.9 \pm 2.6$ cm/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ The pore radius, $a$, and solute flux, $j_0$, were determined by fitting eq 12 to the experimental solute concentration profile at the pore exit, measured by SECM-FIM. $^b$ The solution velocity in the pore, $w_0$, was determined by fitting eq 9 to the experimental solute concentration profile at the pore entrance, measured by SECM-RIM.

Approximate values of $J_0$ and $a$ (and thus, $r_0^{eff}$ from eq 10) were determined by mapping the concentration profile of the solute molecules in the solution adjacent to the pore exit using SECM operated in FIM. The procedure for this measurement has been previously described in detail. Briefly, solute diffusing from the disk-shaped pore results in a concentration profile described by eq 12,

$$ C(z) = \frac{2C_s}{\pi} \tan^{-1}\frac{a}{z} $$  \hspace{1cm} (12)

where $z$ is the axis orthogonal to the center of the pore, and $C_s$ is the concentration at $z = 0$. Equation 12 is fit to the $C(z)$ data to extract $C_s$ and $a$. A simplex algorithm written in MATLAB is used to minimize the squares of the residuals between the experimental data and eq 12. Both $a$ and $C_s$ are determined from the curve-fitting routine. The flux through the pore is then determined using the expression for a disk-shaped source,

$$ J_0 = \frac{4DC_s}{\pi a} $$  \hspace{1cm} (13)

Values of $a$ and $J_0$ for each experiment are summarized in Table 1. (The reader is referred to ref 14 for examples of SECM-FIM-measured $C(z)$ data sets obtained above single mica/Nafion pores.)

Application of eqs 12 and 13 to describe transport at the pore exit into the receptor solution is not precise, since it ignores convective transport of the solute away from the pore. However, a more rigorous analysis of diffusive–convective transport away from small pores (Appendix I) indicates that the diffusion from the pore is the predominant mode of mass transport. (The error incurred in the experimentally determined values of $J_0$ arising from use of the approximate "diffusion only" analysis results in a slight underestimation (<10% error) of the true flux.) In addition, we have found that these expressions yield very accurate values of $a$ (as tested by comparison to optical micrographs) as well as values of $J_0$ that are self-consistent within large sets of data. Thus, although the use of eqs 12 and 13 is approximate and clearly

Figure 5. Comparison of SECM-RIM measured (points) and theoretical (solid line) ultrafiltration profiles for FeCp2TMA$^+$ transport through an ~20-μm-radius mica/Nafion pore. Values of $J_0$ and $w_0$ used to compute the theoretical line are listed in Table 1.
introduces some error into the measurement of \( J_0 \), we believe that this error is small.

The final parameter, \( w_0 \), cannot be obtained directly from the SECM-FIM concentration profiles and is employed as an adjustable parameter in fitting eq 9 to the ultrafiltration profiles shown in Figures 4 and 5. The solid lines show the best fits to each data set after converting values of \( \alpha \) to \( r_0^w \) (eq 9) and using values of \( w_0 \) tabulated in Table 1. Ideally, a single value of \( w_0 \) should be used to fit the data sets for each molecule, independent of the chemical nature or bulk concentration of the solute, since \( w_0 \) is determined only by the ion-selective properties of Nafion, the applied current (50 \( \mu \)A), and the pore geometry, all of which remain constant in our measurements. Inspection of the values of \( w_0 \) in Table 1 demonstrates that \( w_0 \) within error, has the same value for experiments using FeCp\( _2\)TM A\(^+\) (\( w_0 = 4.9 \pm 2.6 \text{ cm/s} \)) and acetaminophen (\( w_0 = 2.8 \pm 0.6 \text{ cm/s} \)) as the solute species and is independent of the bulk solute concentration between 1 and 50 mM. Thus, even though there is significant scatter in the values of \( w_0 \) listed in Table 1, the results indicate that the accumulation of solute above the pore opening is reasonably well-described by eq 9. We note that the calculated C(r) profiles are relatively sensitive to the values of \( J_0 \), suggesting that experimental errors arising in the SECM-FIM determination of \( a \) and \( C_0 \) are likely sources of error in the determination of \( w_0 \). M ore systematic studies examining the influence of applied current, solute properties, and electrolyte concentration are currently in progress.

Finally, we note that because the aqueous solutions employed here are essentially incompressible, the value of \( w_0 \) reported above is also equal to the solution velocity within the Nafion filled pore. The previously reported electroosmotic velocities, \( v_0 \), of FeCp\( _2\)TM A\(^+\) and acetaminophen in the Nafion phase,\(^{15}\) measured under identical experimental conditions and applied current, however, are considerably smaller (3.5 \( \times \) 10\(^{-7}\) and 2 \( \times \) 10\(^{-4}\) \text{ cm/s}, respectively) than the value of \( w_0 \) reported here. The finding that \( v_0 < w_0 \) clearly indicates that convective transport of the solute molecules in the Nafion phase is impeded relative to convective transport of the solvent molecules. For instance, the very small value of \( v_0 \) for FeCp\( _2\)TM A\(^+\) is most likely due to electrostatic interactions of this cation with the fixed-site sulfonate groups of Nafion.

**SUMMARY**

A theoretical expression describing the accumulation of solute molecules at the entrance to an individual microscopic pore resulting from diffusive–convective transport has been developed. Comparison of the theory to experimental results obtained using a single mica/Nafion pore indicates that the ultrafiltration of small molecules by the Nafion membrane accounts reasonably well for the accumulation profiles observed using SECM-FIM. By analogy, the previously reported accumulation of solute molecules above pores in mouse skin,\(^ {28}\) a phenomenon similar to that observed the mica Nafion membranes, most likely also results from solute rejection at the pore entrance. The quantitative treatment presented here is useful only when transport can be probed by both SECM-FIM and SECM-RIM and, thus, is not generally useful when only one side of a porous membrane can be interrogated. However, in situations in which the electroosmotic flow rate can be independently measured, the SECM-RIM concentration profiles alone are sufficient to determine the solute flux to the pore and, thus, the rate of interfacial transfer. Regardless of this limitation, our current report provides a theoretical basis for employing SECM-RIM to visualize molecular transport.

**APPENDIX I.**

**Diffusive–Convective Transport from the Pore Exit.** The concentration profile at a hemispherically shaped pore exit for diffusive–convective transport is readily derived using eqs 1–9 in the text, substituting \( y(r) = -J_0/w_0 \) as \( r \rightarrow \infty \) for the boundary condition. The latter corresponds to the absence of solute in the receptor solution. The result is

\[
C(r) = \frac{J_0}{w_0} \left( 1 + \exp\left( -w_0 r^2 / (D r) \right) \right) \quad (AI.1)
\]

Figure AI.1 shows an example comparison of the pore exit concentration profiles for diffusive–convective transport and purely diffusive transport for acetaminophen transport, using the experimental values of \( J_0 \), \( w_0 \) and \( r_0 (= 2/\pi a) \) in Table 1 corresponding to \( C^* = 25 \text{ mM} \). The diffusion profile is obtained from eq. AI.1 in the limit \( w_0 \rightarrow 0 \). The slopes of the two profiles at any position \( r \) differ by a few percent, indicating that diffusion is the dominant transport process for the conditions employed in this work. The agreement is best at moderate distances from the pore exit, which constitutes the region where most of the SECM-FIM values of \( C(r) \) are obtained. A similar level of agreement is obtained for other solution conditions listed in Table 1. (Note: Convective transport becomes significantly more important as the pore radius or fluid velocity is increased. Thus, the use of the “diffusion only” approximation is limited to small pores and low fluid velocities.)

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