Transport Parameters in a Porous Cellulose Acetate Membrane

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ABSTRACT The transport parameters of a cellulose acetate membrane prepared from a mixture of cellulose acetate, formamide, and acetone, 25:25:50 by weight, were studied. The membrane consists of a thin, porous layer, the skin, in series with a thick, highly porous layer, the coarse support. In the skin the diffusional permeability coefficient, \( \omega \), of a number of small amides and alcohols depends critically upon the partition coefficient, \( K_s \), the size of the molecule, and the apparent hydrogen-bonding ability, \( N_s \), of the solute. These observations are in general agreement with our earlier conclusions on the properties of nonporous membranes. On the other hand, the corrected reflection coefficient, \( \alpha' \), is not a very sensitive function of either \( N_s \) or \( K_s \) taken separately. The correlation between \( \alpha' \) and molecular diameter is reasonably good; however, it is much improved when both \( N_s \) and \( K_s \) are taken into consideration. Isotope interaction was also studied in the present preparation and was found to provide only a small (5–8%) contribution to the diffusional permeability coefficient of ethylene glycol. The contribution of solute-water friction was found to be less than 24% of the total solute friction.

In a previous paper we studied the effects of various parameters on the permeability coefficients of nonelectrolytes in a dense cellulose acetate membrane (1). In addition to steric factors and relative solubility, the chemical nature of the solute, as indicated by its hydrogen-bonding ability, was found to be an important factor in controlling permeation through the membrane. Further studies were deemed necessary in order to dissect the total friction, \( f \), experienced by the solute while permeating the membrane into its various components: the solute-water friction, \( f_{sw} \); the solute-matrix friction, \( f_{sm} \); and the solute-solute interaction, \( f_{ss} \). The present work was undertaken in order to determine the contribution of the solute-water friction to the overall solute friction in a more porous membrane by measuring the reflection coefficient and isotope interaction. Special attention was paid to the pa-
rameters that control the reflection coefficient, in particular, its relation with the partition coefficient between the membrane and the bathing solution, \( K_\chi \), and with the hydrogen-bonding ability of the solute, \( N_\iota \).

The membrane studied in the present work is of particular interest from the biological point of view, since it behaves as a porous structure for hydrophilic solutes and as a lipophilic phase for those solutes with high partition coefficients, a behavior resembling that found for the membranes of living cells. The Renkin equation has been used extensively to calculate equivalent pore radii in biological and artificial membranes (2-4) from measurements of the reflection coefficient. Goldstein and Solomon (2) assumed the reflection coefficient of a hydrophilic molecule to be governed entirely by its molecular radius, the radius of the water molecule, and that of the pore. In the present study we have investigated the importance of additional factors: in particular, the specific roles of hydrogen-bonding and the partition coefficient on the correlation between the reflection coefficient and the molecular radius of the probing solute in a porous membrane.

MATERIALS AND METHODS

Membranes were prepared from a mixture of cellulose acetate (Eastman 4644, Rochester, N. Y.; acetyl, 39.8%), formamide, and acetone, 25:25:50 by weight. The casting procedure in the present study differed from that described earlier by Gary-Bobo et al. (1) only in the length of the time used for evaporation and heating. The present membranes were evaporated for 30 sec and heated for 3 min at 80°C, as compared to 60 sec and 5 min, respectively, in the previous studies. In experiments designed to study the coarse component alone, the skin was removed by sandpapering under water.

Measurements of Hydraulic Conductivity, \( L_p \)

Measurements were carried out in a Lucite chamber consisting of two asymmetrical compartments. The membrane which partitioned the two compartments had an effective area of 12 cm² and was supported by a stainless steel screen. A nitrogen tank was connected to the small compartment (volume, 24 cm³) via a mercury manometer to provide hydrostatic pressure. The volume flow, \( J_c \) (ml cm⁻² sec⁻¹), was measured by means of a micro-liter pipette connected to the large compartment (volume, 48 cm³). The membrane was bathed on both sides with distilled water.

Fig. 1 shows the variation of \( J_c \) with the applied hydrostatic pressure in centimeters of mercury. \( L_p \) (cm³ dyne⁻¹ sec⁻¹) was calculated from the relation \( J_c = L_p \Delta P \). The observed linear correlation shows \( L_p \) to be constant in the range of pressure used (10-40 cm Hg). The equation (5) relating the hydraulic conductivity of the skin, \( L_{ps} \), to that of the total membrane, \( L_{pt} \), and of the coarse component, \( L_{pc} \), is

\[
\frac{1}{L_{pt}} = \frac{1}{L_{pc}} + \frac{1}{L_{ps}}
\]  

(1)
Measurement of Permeability Coefficient and Partition Coefficient  The diffusional permeability coefficient, $\omega$ (mole dyne$^{-1}$ sec$^{-1}$), and the partition coefficient, $K$, were measured using radioactive tracers. The details of the procedure were described in the previous paper (1). THO and $^{14}$C-labeled solutes were counted in a liquid scintillation counter (Nuclear-Chicago Corporation, Des Plaines, Ill., model 6801). The labeled solutes were obtained from New England Nuclear Corporation (Boston, Mass.), except for butyramide and isobutyramide, which were obtained from International Chemical and Nuclear Corporation (City of Industry, Calif.). All these measurements were carried out at a total concentration of 0.2 M on each side of the membrane.
Measurements of Reflection Coefficient, $\sigma$

The reflection coefficient was measured using the same chamber used for $L_p$. A known concentration (0.1 or 0.2 M) of the solute under study was introduced into the small compartment, and at the same time a known hydrostatic pressure, $\Delta P$, was applied to this compartment and the resulting steady-state volume flow was measured. This procedure was carried out for several values of hydrostatic pressure. The solution in each compartment was changed for each value of $\Delta P$. Each compartment was stirred by magnetic bars driven by external motors; the stirring was particularly efficient in the small compartment, owing to the short distance between the bar and the membrane. The osmolarity was measured by freezing point depression (Fiske osmometer G-62, Fiske Associates, Inc., Bethel, Conn.).

Fig. 2 shows the result of a typical experiment. $\sigma$ was calculated from the $x$-axis intercept, where there is no volume flow ($J_x = 0$) according to the relation

$$
\sigma = \frac{\Delta P}{\Delta x} \bigg|_{J_x = 0}
$$

(2)

No effect of the unstirred layer on the reflection coefficient should be expected in these experiments, owing to the low permeability coefficient for all the solutes studied ($\omega < 10^{-14}$ mole dyne$^{-1}$ sec$^{-1}$ for the total membrane). The reflection coefficient of the skin, $\sigma^t$, is related to that of the total membrane, $\sigma_t$, and of the coarse component, $\sigma_c$, by the following equation (5).
Here \( \omega_t \) is the diffusional permeability coefficient of the total membrane, and \( \omega_s \) and \( \omega_c \) are those of the skin and coarse component. All the coefficients \((L_p, \omega, \sigma)\) were measured using the same piece of total and coarse membrane, and at a temperature of 22 ± 0.5°C.

**RESULTS AND DISCUSSION**

The membranes used in this study were designed to increase the amount of water that is geometrically arranged in the skin component of the membrane (6), as compared with the more random distribution in the nonporous membranes used in the earlier study. Meares\(^1\) has shown that the short period of heating results in an increase in the amount of water clusters in the skin portion of the membranes; these may be arranged in continuous or discontinuous paths, depending on circumstances. Table I gives the main characteristics of the total membrane and its two components. These include the water content, \( \Phi_w \); the hydraulic conductivity, \( L_p \); the THO diffusion coefficient, \( \omega_{THO} \); and the ratio \( g = L_p / \omega_{THO} \Phi_w \). It is clear from the table that \( L_p \) is controlled mainly by the skin, whereas \( \omega \) is controlled by the coarse component. The value of \( L_p \) for the skin in the present study was about twice that found previously for the skin of the nonporous membrane \((L_p = 0.5 \times 10^{-11} \text{ cm}^2 \text{ dyne}^{-1} \text{ sec}^{-1})\), whereas \( \omega_{THO} \) remained nearly the same \((\omega_{THO} = 30 \times 10^{-14} \text{ mole dyne}^{-1} \text{ sec}^{-1})\), as did \( \Phi_w \) \((0.135 \text{ g/g wet membrane})\). The constancy of \( \omega_{THO} \) and \( \Phi_w \) suggests that there was no appreciable increase in the thickness, \( \Delta \), of the skin prepared by the two methods. On the other hand, the 2-fold increase in \( L_p \) suggests that this skin behaves as a porous structure as compared to the dense membrane used earlier \((1)\). In the present membrane, \( g \) had a value of 2 compared with \( g = 1 \) in the membranes used earlier. This is consonant with the presence of porous channels through the

\^1\ P. Meares. Personal communication.
matrix of the membrane, though it may not be accepted as positive proof of
the existence of porous paths, since Thau, Bloch, and Kedem (7) have found
$g = 2.1$ for a liquid membrane, in which no channels are presumed to exist.
Consequently other criteria must also be used to establish the porous behavior
of the present membrane.

The diffusional permeability coefficients, $\omega$, of various nonelectrolytes
were measured in order to calculate the frictional coefficients and also to
determine the importance of dissolution in the membrane in contributing
to the observed values of the reflection coefficient, $\sigma$. Table II gives the values
of $\omega$ for the total membrane and its two separate components. The partition
coefficients, $K_s$, for the skin are also included in the table. Each value of $\omega$

| Solute          | No. | Total membrane, $\omega_t \times 10^{14}$ | Coarse component, $\omega_c \times 10^{14}$ | Skin component, $\omega_s \times 10^{14}$ | Partition component, $K_s$ |
|-----------------|-----|------------------------------------------|------------------------------------------|------------------------------------------|---------------------------|
| Acetamide       | 1   | 1.03                                     | 1.46                                     | 3.49                                     | 0.31                      |
| Propionamide    | 2   | 0.82                                     | 1.23                                     | 2.49                                     | 0.38                      |
| Butyramide      | 3   | 0.66                                     | 1.05                                     | 1.75                                     | 0.51                      |
| Isobutyramide   | 4   | 0.38                                     | 0.71                                     | 0.81                                     | 0.42                      |
| Malonamide      | 5   | 0.45                                     | 0.92                                     | 0.88                                     | 0.29                      |
| Ethylene glycol | 6   | 0.82                                     | 1.28                                     | 2.38                                     | 0.19                      |
| Glycerol        | 7   | 0.20                                     | 0.32                                     | 0.32                                     | 0.17                      |
| 1-Propanol      | 8   | 1.23                                     | 1.57                                     | 5.65                                     | 0.65                      |
| 1-Butanol       | 9   | 1.18                                     | 1.43                                     | 6.75                                     | 0.95                      |

* $K_s$ was measured as described earlier (1) within ±5%.

in the table is the average of at least 10 measurements. $K_s$ values are the
results of two experiments. The error in $\omega_s$ calculated from the relation
$1/\omega_s = (1/\omega_c) + (1/\omega_t)$ varied from about 5% for the fastest solute (1-
propanol) to less than 1% for the slowest (glycerol). The general behavior of
$\omega$ with respect to molecular size, hydrogen bonding, and partition coefficient
in Table II is in accord with the conclusions reported earlier (1).

To investigate the porous behavior of the skin further, the reflection co-
efficients, $\sigma$, of the same solutes were measured. Table III gives the reflection
coefficients of the total membrane and its two components. At least two ex-
periments were carried out for each molecule. The table shows clearly that
the semipermeability of the total membrane was controlled mainly by the
skin component. For the hydrophilic solutes, $\sigma$, tended to increase with in-
creasing size of the probing molecule. However, in the case of 1-propanol and
1-butanol, molecules with values of $K_s$ greater than 0.6, $\sigma$, was determined
mainly by this parameter, and the dependence on molecular size was less pronounced.

The dependence of $\sigma_i$ on solute concentration (0.1 and 0.2 M) was studied, and the results are given in Table IV. There appeared to be no significant difference except for the two alcohols, 1-propanol and 1-butanol, in which the effect of the concentration on $\sigma_i$ was more pronounced (25%) than for the other solutes (<11%).

In 1961, Kedem and Katchalsky (8) derived the following relation, which relates $\sigma$ to the Spiegler frictional coefficients and the various transport parameters:

$$\sigma = 1 - \frac{\omega \bar{V}_s}{L_p} - \frac{K_{1w}}{\Phi_w (f_{sw} + f_{aw})}$$

(4)
in which \( V_s \) is the solute partial molar volume, \( f_{sw} \) and \( f_{sm} \) are solute-water and solute-matrix frictions, and \( L_p, \omega, \) and \( \Phi_o \) have their usual meanings.

As Dainty (9) has pointed out, if the solute and solvent permeate the membrane through entirely independent pathways, there is no interaction between solute and water, so that \( f_{sw} = 0 \) and therefore \( \sigma = 1 - \omega V_s/L_p; \) on the other hand, \( \sigma \) will be less than this quantity if the solutes share a common pathway. This criterion, \( \sigma < 1 - \omega V_s/L_p, \) has been used in the present study to test the degree of solute-solvent interaction.

In order to calculate the quantity \( 1 - \omega V_s/L_p \) and compare it with \( \sigma, \) it is necessary to determine \( L_p \) under the same conditions as those for \( \sigma \) and \( \omega, \) and also to know the degree of isotope interaction. \( L_p \) for the skin was therefore measured in the presence of 0.2 \( \text{m} \) ethylene glycol on both sides of the chamber and found to be \( 1.1 \times 10^{-11} \text{ cm}^2 \text{ dyne}^{-1} \text{ sec}^{-1}, \) which is about 10\% less than when no solute was present. We assume that the dependence of \( L_p \) on the nature of the solute present is negligible, and have used the same value for all the hydrophilic solutes. In the present study, the diffusional permeability coefficient of the labeled solute, \( \omega^*, \) measured in the skin component of the membrane, may differ considerably from that of the unlabeled solute because of solute-solute interaction (10, 11). The following equation (see ref. 1) gives the relation between \( \omega^* \) and the various frictional coefficients.

\[
\omega^* = \frac{K_s}{\Delta x(f_{sm} + f_{sw} + 2f_{sw})}
\]

in which \( f_{sw} \) represents the contribution of isotope interaction to the over-all friction and \( \Delta x \) is the thickness of the membrane. For a more detailed analysis, see Essig (12).

To measure the magnitude of the isotope interaction in the membrane used in the present study, a series of experiments were carried out for the solute ethylene glycol under a variety of conditions. There was no net water flow in these experiments, to avoid any contribution from solvent drag. In one case the tracer diffusional permeability coefficient was measured when there was a net flow of the unlabeled species in the same direction as for the tracer, whereas in the other case the net flow of the unlabeled species was in the opposite direction. As the last column of Table V shows, the two permeabilities did not differ significantly from that seen when no net flow was occurring for the unlabeled species (\( \omega_t = 0.82 \pm 0.015 \times 10^{-14} \text{ mole dyne}^{-1} \text{ sec}^{-1} \)).

Osmotic equilibrium was attained by adding sodium chloride, an impermeable solute (\( \sigma = 1 \)), in an amount sufficient to balance the system osmotically. The value for the diffusional water permeability when only ethylene glycol was present on both sides was identical with that found when
### Table V
Solute-solute interaction for ethylene glycol in the total membrane

| Hot compartment | Cold compartment | Water (THO) \((\text{mole dyn}^{-1} \text{ cm}^{-2}) \times 10^4\) | Ethylene glycol |
|-----------------|-----------------|----------------------|-----------------|
| 0.2 M ethylene glycol | 0.2 M ethylene glycol | 4.01 ± 0.08 | 0.82 ± 0.015 |
| 0.2 M ethylene glycol | 0.1 M ethylene glycol + 0.011 M NaCl | 3.98 ± 0.07 | 0.87 ± 0.015 |
| 0.1 M ethylene glycol + 0.011 M NaCl | 0.2 M ethylene glycol | 0.79 ± 0.016 | 0.83 ± 0.02 |
| 0.1 M ethylene glycol + 0.011 M NaCl | 0.1 M ethylene glycol + 0.011 M NaCl | 0.83 ± 0.02 | 0.83 ± 0.02 |
NaCl was substituted for part of the ethylene glycol on one side, as shown in Table V. The effect of NaCl on the permeability of ethylene glycol was also checked in order to avoid any cancellation of effects due to the presence of salt. As shown in the last line of the table, no significant effect was observed when 0.011 M NaCl was present on both sides of the membrane. Comparison of \( \omega \) for ethylene glycol in the top line in Table V with the second and third lines shows clearly that, in the present study, isotope interaction, if present at all, was small (5-8\%). Therefore the permeability coefficient of the membrane measured when tracers are used in the absence of net flow of the un-

![Figure 3](https://i.imgur.com/345.jpg)

**Figure 3.** Reflection coefficient for the skin component as a function of \( 1 - \omega \nu_s/L_p \).

labeled solute is a true measure of the resistance experienced by a solute when crossing the membrane.

If a major fraction of the solute were to pass through small equivalent pores in the membrane which occupy a small fraction of the total area, a larger isotope interaction would be expected. Thus, the small isotope interaction is consistent with the view that only a small fraction of the most hydrophilic molecules cross the membrane via the equivalent pores.

In order to estimate this fraction, the quantity \( 1 - \omega \nu_s/L_p \) was calculated and compared with \( \sigma \), as has been done in Fig. 3. As would be expected, 1-butanol (point No. 9), for which \( K_\nu \) is 0.95, lay closest to the line of identity, which shows that the most important pathway for this molecule is by dissolution in the membrane. Since \( \Phi_\nu \) has been measured, as well as \( K_\nu \), for
each molecule, it is possible to calculate the ratio $f_{sw}/(f_{sw} + f_{sm})$ from equation 4, as has been done in Table VI. As already discussed, this ratio gives the fraction of the solute-water friction experienced by the solute as it goes through the membrane, and should be zero if solute and solvent penetrated by entirely separate pathways. However, as Table I shows, $\Phi_w$ in the skin is 0.14, and one would expect random collisions between solute and solvent even in the case of a molecule that permeates almost entirely by dissolution in the matrix. Thus the value of 0.01 for the ratio $f_{sw}/(f_{sw} + f_{sm})$ for 1-butanol is not unexpected and is entirely consistent with the physical picture. Furthermore, this low value shows that the importance of random collisions with the water that is uniformly distributed within the membrane is of negligible importance, since the solute-water frictional ratio is 0.08 or greater for all the rest of the molecules studied.

As Fig. 3 shows, the reflection coefficients of all eight other probing molecules studied lay well below the line of identity. This is true even for 1-propanol (point No. 8), for which $K_s = 0.65$. This clearly indicates that for each of these eight molecules $f_{sw} > 0$. These data suggest that these molecules share a common pathway with water and hence serve as evidence that the skin component of the membrane can be treated operationally as containing an array of equivalent pores with respect to these solutes.

The fraction of solute-water interaction in Table VI gives a more quantitative estimation of the importance of the common pathway. The fact that all the numbers are almost an order of magnitude greater than the figure for 1-butanol shows that the fraction indeed provides a satisfactory measure of the interaction between solute and water within the equivalent pores. Since the largest ratio is 0.24, it is also clear from the table that only a small fraction of the most hydrophilic molecules crosses the membrane via the

| Solute         | $1 - \sigma$ | $f_{sw}/(f_{sw} + f_{sm})$ | $P_s$ |
|----------------|-------------|-----------------------------|------|
| Acetamide      | 0.43        | 0.20                        | 50.9 |
| Propionamide   | 0.34        | 0.13                        | 70.1 |
| Butyramide     | 0.36        | 0.10                        | 84.4 |
| Isobutyramid   | 0.29        | 0.10                        | 86.0 |
| Malonamide     | 0.33        | 0.24                        | 69.3 |
| Ethylene glycol| 0.32        | 0.24                        | 55.6 |
| Glycerol       | 0.24        | 0.21                        | 73.1 |
| 1-Propanol     | 0.25        | 0.08                        | 74.6 |
| 1-Butanol      | 0.06        | 0.01                        | 91.5 |
equivalent pores, which is also consistent with the relative unimportance of the isotope interaction.

Table VI also gives values for \(1 - \sigma' = 1 - \sigma - \omega \tilde{V}_s/L_p\). This corrected reflection coefficient depends on each of the parameters—the partition coefficient, \(K_s\); the molecular diameter, \(d\); and the number of possible hydrogen bonds, \(N_s\), which the solute is able to form [\(N_s\) is taken as 4 and \(N_s\) is taken as 3 for the monoamides, 4 for ethylene glycol, and 6 for glycerol and malonamide, as discussed previously (1)]. Various combinations of these parameters and \(1 - \sigma'\) have been plotted on a logarithmic scale against the molecular diameter (Fig. 4). The points for propanol and butanol have been omitted from Fig. 4 because their very high partition coefficients, as shown in Table II, indicate that the major permeation pathway is by dissolution in the skin. The best correlation was obtained when both the partition coefficient and the number of hydrogen bonds were taken into consideration, as shown in the bottom section of the figure (line d). The correlation was not good when either \(N_s\) or \(K_s\) was taken alone (lines b and c), whereas the correlation was reasonable when neither of these two parameters was considered (line a), as in the procedure originally used by Goldstein and Solomon (2). It is clear that in these specific compounds there is a relation between \(K_s\) and \(N_s\), in that an increase in ability to form hydrogen bonds tended to be associated with a decrease in the partition coefficient, presumably because hydrogen bonds can readily be formed with water. Nonetheless, there is a considerable increase in the goodness of fit when both parameters are taken into account simultaneously. A quantitative measure of the correlation can be obtained from the standard error in the slope of the line relating the reflection coefficient to the diameter of the solute. When \(1 - \sigma'\) is not corrected with respect to either \(K_s\) or \(N_s\) (line a), the slope is \(-1.55 \pm 0.65\), whereas when it is corrected for both parameters the slope is \(-3.12 \pm 0.46\). In the first instance the error is 42\% of the slope, whereas in line d it is 15\%, clearly a much better correlation. This behavior of \(1 - \sigma'\) contrasts with that of the diffusional permeability coefficient, \(\omega\), which has been shown to be highly sensitive to both \(N_s\) and \(K_s\) (1).

Accordingly, it is not surprising to find two molecules with the same \(\sigma'\) and entirely different \(\omega\). For example, in the present study, ethylene glycol \((K_s = 0.19, N_s = 4)\) has about the same value of \(\sigma'\) in the skin as malonamide \((K_s = 0.2, N_s = 6)\); yet it penetrates the skin about 3 times faster. In

\[\text{The data in either line a or line d of Fig. 4 fall quite nicely on the usual form of Goldstein and Solomon's plot (2) of } 1 - \sigma. \text{ However, the skin membrane is a composite membrane, and as Dainty and Ginzburg (13) have pointed out, a number of corrections are required for a quantitative treatment of a mosaic membrane in which both pathways are important. It is possible, nevertheless, to use our standard computer program to compute an apparent equivalent pore radius from the slope of the line d in Fig. 4. This comes out to be 5.6 } \text{Å, and is in reasonable physical agreement with the radii of the probing molecules given in Table III.}\]
other words, it is entirely possible for a hydrophilic molecule to be characterized by a value of \( \sigma' \) which is predictable from its molecular radius and

\[
(1 - \sigma') = C - \frac{d}{K}
\]

\[
(1 - \sigma') \frac{N}{N_s} = C - \frac{d}{K}
\]

\[
(1 - \sigma') \frac{K_w}{K_s} = C - \frac{d}{K}
\]

\[
(1 - \sigma') \frac{N_w K_w}{N_s K_s} = C - \frac{d}{K}
\]

\[
\ln(d) = \text{constant} - \frac{1.55 K}{K_w}
\]

**Figure 4.** Correlation between the corrected reflection coefficient, \( \sigma' \); and the molecular diameter, \( d \); solubility, \( K_s \); and hydrogen-bonding ability, \( N_s \). In the case of water, \( K_w = \Phi_w \), and \( N_w \) is the hydrogen-bonding ability. As described in the text, lines \( a \) and \( d \) were drawn by the method of least squares.

at the same time be characterized by a value for \( \omega \) which lies much below that predicted by its radius. Such a conclusion can be extended to biological membranes. This finding may well be related to the fact that the reflection coefficient is a physical measure of discrimination of the equivalent pore
between solute and solvent, whereas \( \omega \) is a measure primarily of solute flux. As seen from equations 4 and 5 (neglecting isotope interaction), an important difference between \( \sigma' \) and \( \omega \) is the presence of \( f_{sw} \) in the numerator of the frictional expression of \( \sigma' \). This means that if \( f_{sw} \gg f_{sm} \), \( \omega \) will be relatively very much smaller than \( 1 - \sigma' \), if the relations among \( K_{sw}, \Phi_{sw} \), and \( \Delta x \) are similar to those in present study. Thus the correlation between \( \omega \) and the equivalent pore radius is particularly sensitive to evaluation of all the controlling parameters, whereas the conclusions drawn from the \( (1 - \sigma) \) treatment of Goldstein and Solomon (2) are less dependent upon hydrogen bonding and the partition coefficient. In both cases, however, it is clear that increased knowledge of all the parameters leads to increased understanding of the basic physical and chemical principles governing passive transport through biological membranes.

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