N_A = molar flux of A with respect to a stationary frame, g.-mole/(sq.cm.)(sec.)
P = pressure
ΔP = pressure drop across the diaphragm
q_1 = inlet flow rate, ml./sec.
q_2 = outlet flow rate, ml./sec.
t = time, sec.
T = absolute temperature, °K.
V_A = molar volume of A at normal boiling point, ml./b.-mole
x = distance coordinate, cm.
x_A = mole fraction of A

Greek Letters

α_{AB} = thermodynamic factor $= 1 + \dfrac{d\ln\gamma_A}{d\ln x_A}$
β' = cell constant, cm.
γ_A = activity coefficient of A
η_A = viscosity of A, centipoise
η_{AB} = viscosity of the mixture of components A and B, centipoise

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Ultrafiltration of Proteins in Stagnation Flow

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The effect of viscosity and diffusivity variations on concentration polarization during the ultrafiltration of protein solutions in two-dimensional stagnation flows is investigated by numerical integration of the equations of continuity and motion. It is found that these effects are surprisingly small and insensitive to the forms of concentration dependence postulated. The high Schmidt numbers and low permeation rates characteristic of these systems result in considerable simplification of the analysis and permit use of a modified Chilton-Colburn relation for predicting the onset of sludge formation at the membrane-solution interface. The predicted dependence on Schmidt number agrees with published experimental data for other boundary-layer flows and suggests the possibility of improved prediction of equipment performance.

Ultrafiltration of proteinaceous solutions is of current interest in the purification of proteins, the processing of fluid food products, and a number of biomedical applications. Ultrafiltration is formally similar to reverse osmosis but is normally characterized by much smaller osmotic pressures, more efficient solute rejection, and much larger changes in transport properties. The high viscosity and low diffusivity of concentrated protein solutions are particularly troublesome and frequently result in the formation of thick sludge layers on the upstream faces of ultrafiltration membranes.

These sludges can be very complex in nature, but they appear to consist basically of protein gels. They tend to thicken with time, and they can reduce ultrafiltration rates so markedly that they provide the chief obstacle to higher productivity of presently available ultrafiltration equipment. At the same time they have interesting permeability characteristics of their own which on occasion can dominate membrane behavior and which suggest the possibility of self-renewing permselective membranes. They are therefore doubly interesting to process engineers.

Protein sludges have their origin in concentration polarization which has already been described for constant-property mixtures in a number of flow systems. These analyses include both papers in the reverse-osmosis literature (*2, 4, 8, 12, 13*) and more general treatments of boundary-layer flows (*5, 6, 9* to *11*). It is our purpose here to assess the importance of viscosity and diffusivity variations on concentration polarization of protein solutions by boundary-layer analysis of a simple flow system suitable for experimental study.

In this preliminary paper we consider only two-dimensional stagnation flow and rather simple expressions for

the concentration dependence of viscosity and diffusivity. This system is particularly convenient in permitting a similarity transformation for boundary conditions realizable in ultrafiltration experiments. Our analysis can however be extended readily to other laminar boundary flows, particularly wedge flows and the flow about spinning discs.

PROBLEM STATEMENT

The system analyzed is the two-dimensional stagnation flow shown in Figure 1. We limit consideration to steady laminar flows of incompressible Newtonian fluids but allow variations in viscosity and diffusivity. The momentum boundary-layer description is of the form

$$\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} = 0 \tag{1}$$

$$u\frac{\partial u}{\partial x} + v\frac{\partial u}{\partial y} = -\frac{1}{\rho_P}\frac{\partial P}{\partial x} + \frac{1}{\rho_P}\frac{\partial}{\partial y}\left(\mu_P \frac{\partial u}{\partial y}\right) \tag{2}$$

$$v\frac{\partial C_P}{\partial y} + u\frac{\partial C_P}{\partial x} = \frac{\partial}{\partial y}\left(\mathcal{D}_P \frac{\partial C_P}{\partial y}\right) \tag{3}$$

With boundary conditions

$$y = 0 \quad u = 0 \tag{4a}$$

$$v = -v_W = \text{constant} \tag{4b}$$

$$C_P = C_{PW} \tag{4c}$$

$$-C_{PW}v_W = +\mathcal{D}_{PW}\frac{\partial C_P}{\partial y} \tag{4d}$$

$$y = \infty \quad u = ax \tag{4e}$$

The solution of this problem for constant properties has been given by Stewart and Prober (*6, 11*) as a special case of their analysis of wedge flows. A more limited analysis has been developed by Zeh and Gill (*12*) for the particular case of desalination by reverse osmosis. This problem may be further simplified by recognizing that the concentration boundary layers are confined to a region in which the y dependence of the shear stress is negligible for the high Schmidt numbers characteristic of protein solutions. Changes in solution density also are very small relative to viscosity changes and therefore may be neglected. Equation (2) may then be replaced in the concentration boundary layer by

$$-\frac{\mu_P}{x}\frac{du}{dy} = \tau_\infty \tag{5}$$

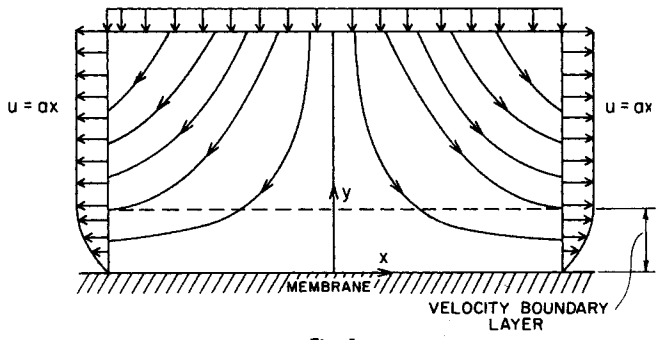

Fig. 1.

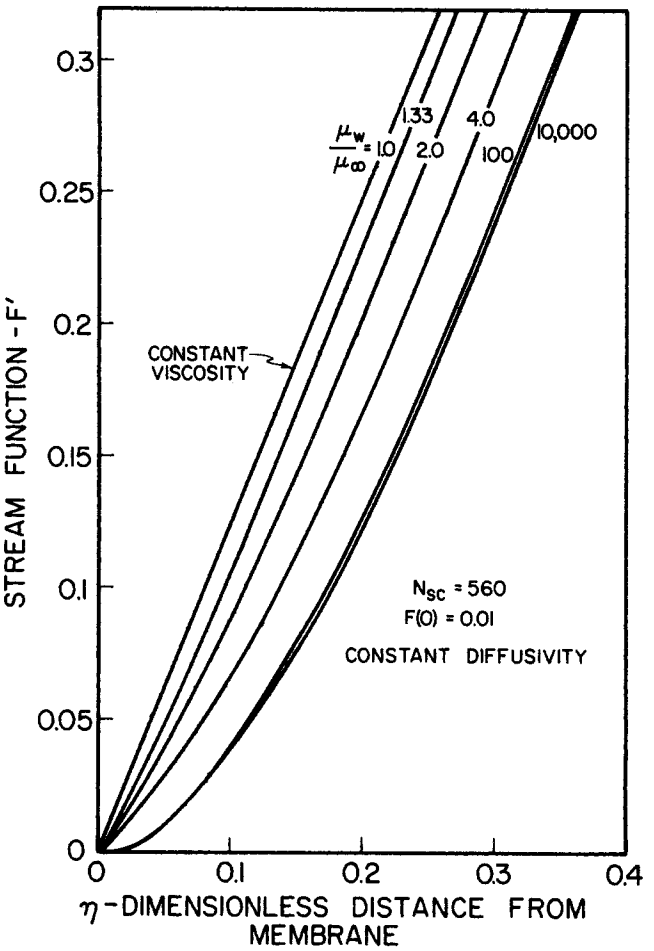

Fig. 2. Stream function; F' with variable viscosity.

The value of τ_∞ is determined by matching with the constant-property shear stress outside the concentration boundary layer.

Reliable expressions for the concentration dependence of viscosity and diffusivity are not presently available for any protein over the whole concentration range of current interest: dilute solution to protein sludge. We must therefore resort to approximate relations.

For viscosity μ_P we use the following semiempirical modification of the Einstein relation

$$\mu \equiv \frac{\mu_P}{\mu_{P\infty}} = 1/(1 - 2.5\,\alpha\phi) \tag{6}$$

This form of viscosity expression has been found reasonable for many suspensions and colloidal sols (*2*). The non-Newtonian behavior of proteins has not been included in this analysis as it is very complex and not at all well understood.*

For diffusivity $\mathcal{D}_P$ we use the Nernst-Einstein relation

$$\mathcal{D}_P\,\mu_P = f(T) \tag{7}$$

or

$$D \equiv \mathcal{D}_P/\mathcal{D}_{P\infty} = 1 - 2.5\,\alpha\phi \tag{8}$$

* In addition, non-Newtonian effects are of second order because the rate of change of effective viscosity with y due to concentration changes is very large compared to the change of effective visosity with x which is largely due to the change in shear rates. Even this qualification is not necessary for the important case of globular proteins which are very nearly Newtonian.

We are not aware of any theoretical justification for this expression for our conditions, but tentative experimental findings from other laboratories suggest it may be reasonable (K. H. Keller, private communication).

It will be seen from the discussion below that the uncertainties inherent in Equations (6) and (8) are not likely to have a major effect on predictions of sludging conditions.

Formulation of our problem is now complete, but the above two-dimensional problem can be made one-dimensional by introducing the well-known similarity transformation:

$$u = axF'(\eta);\ v = -\sqrt{\nu_{P\infty} a}\ F(\eta) \qquad (9)$$

where $\eta = \sqrt{a/\nu_{P\infty}}\ y$ and $F(\eta)$ is the stream function. For convenience we also define a dimensionless protein concentration

$$C = C_P/C_{PW}$$

where C_{PW} is taken to be the known concentration in the problem. Our model for the system then takes the form

$$\mu F''' = \gamma \qquad (10)$$

$$-N_{Sc,\infty} FC' = D'C' + DC'' \qquad (11)$$

subject to the boundary conditions at $\eta = 0$:

$$F = F(0) \qquad (12a)$$

$$F' = 0 \qquad (12b)$$

$$F'' = \gamma(1 - \beta) \qquad (12c)$$

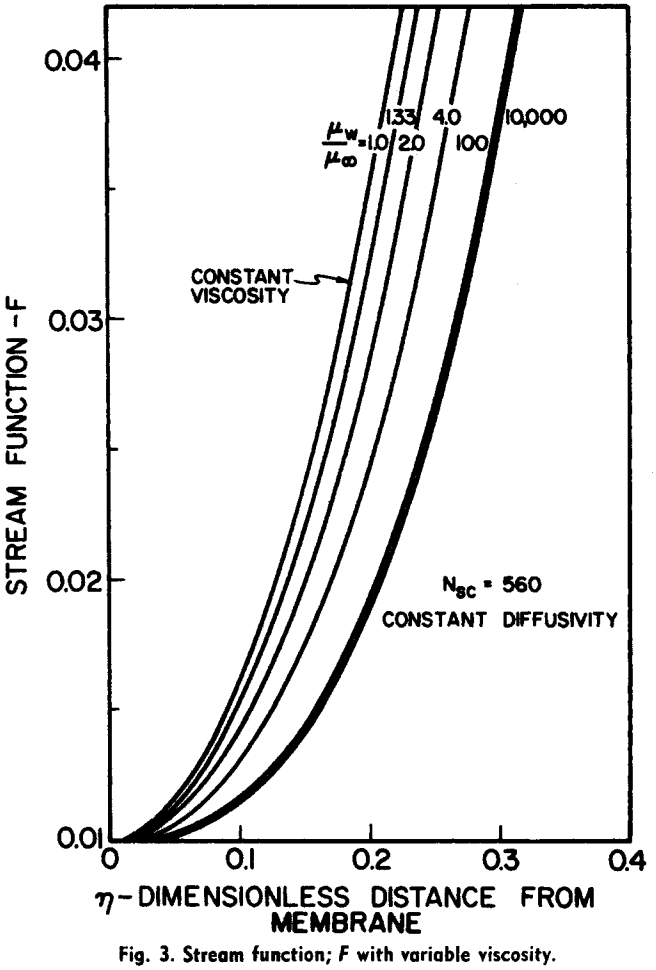

Fig. 3. Stream function; F with variable viscosity.

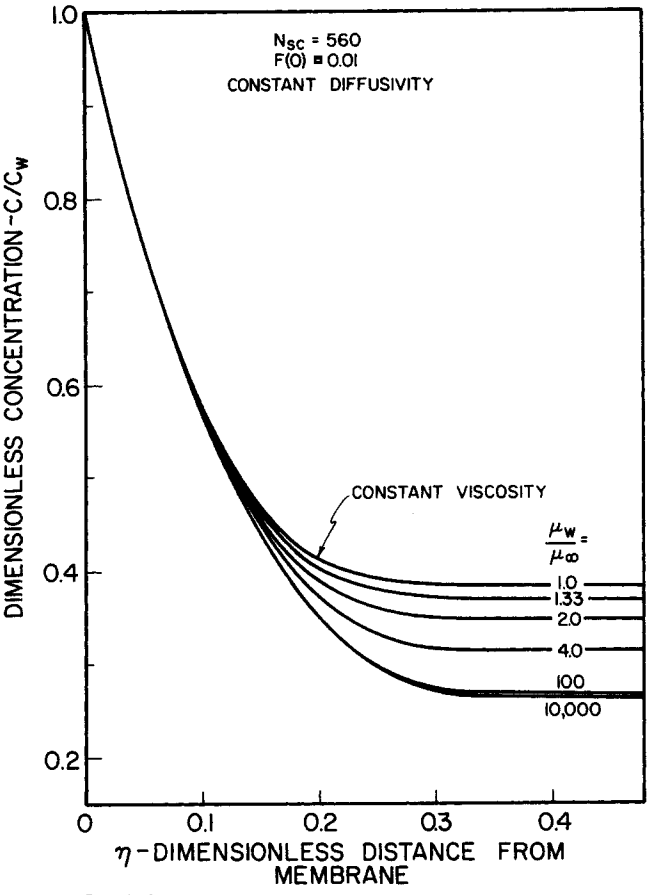

Fig. 4. Concentration profiles with variable viscosity.

$$C = 1 \qquad (12d)$$

$$N_{Sc,\infty} CF + DC' = 0 \qquad (12e)$$

The value of γ is obtained by trial and error matching with the constant-property solution outside the concentration boundary layer. The viscosity expression has been changed to concentration units by replacing $2.5\ \alpha\phi$ by βC. This requires only the assumption of a constant partial molal volume of the protein, which for most proteins should be a good approximation. Any deviations would not be significant at the level of approximation of this study. The value of β was chosen to give a condition of sludging at the wall which was defined as $\mu \to \infty$ at $C = 1$.

This set of equations was solved numerically by a standard fourth-order Runge-Kutta method.

RESULTS

The results of our analysis are shown in Figures 2 through 7 and summarized in Equations (13) through (15). The velocity profiles of Figures 2 and 3 show a displacement of the velocity boundary layers away from the wall as the wall viscosity is increased. There is only a small change in the shape of the profiles near the wall. The sample profiles shown are for the relatively low Schmidt number of 560 (typical of salt solutions), because at the higher Schmidt numbers of protein solutions (ca. 10^5) the region of concentration changes is compressed. This in turn compresses the changes in velocity profiles making those for different viscosity ratios indistinguishable. At all Schmidt numbers the velocity profiles become essentially concentration independent for dimensionless wall viscosity, $\mu > 100$. This was also found for

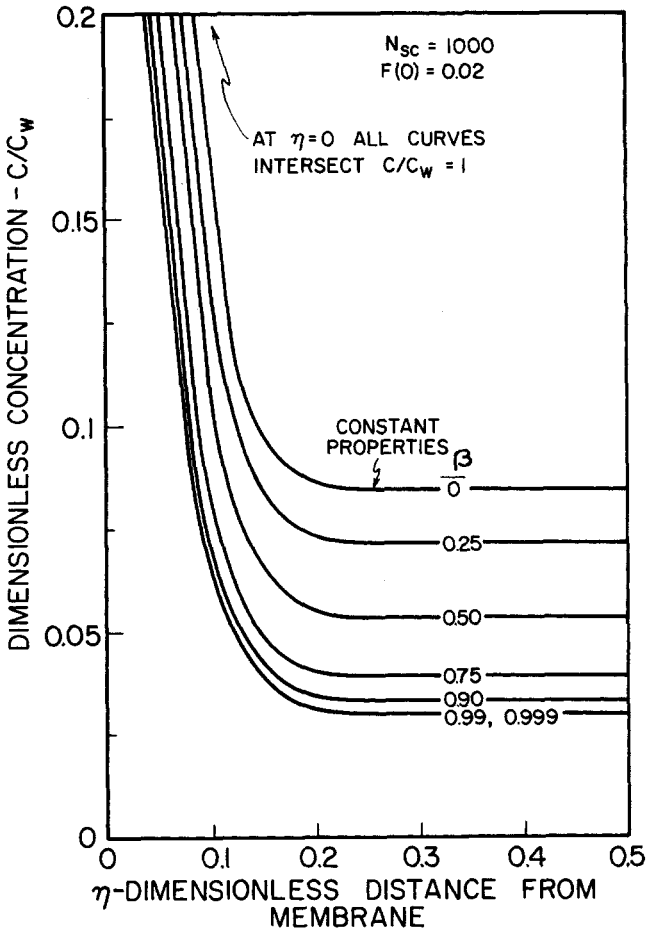

Fig. 5. Concentration profiles with variable viscosity and diffusivity.

dimensionless wall diffusivity, $D < 0.01$, but the profiles were compressed even more. However, it should also be noted that the slope of the velocity profile at the wall approaches zero as μ_W approaches infinity (sludge formation). The sludge layer once formed becomes effectively part of the wall and can continue to thicken without limit for the conditions of our model. In actual practice the hydraulic permeability of the sludge is very low, and the pressure drop required to maintain the design permeation rate becomes prohibitive. In addition, a high osmotic pressure develops which further increases the required pressure drop. Finally it must be realized that Equations (6) and (8) cannot reasonably be expected to apply to the protein gel, and also that irreversible denaturation reactions may be encountered here.

The calculated concentration profiles of Figures 4 and 5 indicate that the concentration boundary layer is indeed much thinner than the velocity boundary layer, even at the low Schmidt number of 560 of Figure 4. It can also be seen that the shape of the concentration profile and the degree of polarization become independent of μ_{PW} and $\mathcal{D}_{PW}$ for $\beta > 0.99$ at this Schmidt number. For the higher Schmidt numbers of protein solutions the effect of β on the shape of the concentration profile is even less.

Because of the asymptotic convergence of both velocity and concentration profiles at high polarization one can define the onset of sludging rather arbitrarily for characterization of these profiles. Here for convenience we define sludging as the attainment of $\beta = 0.999$, $\mu_{PW}/\mu_{P\infty} = 1{,}000$, and $\mathcal{D}_{PW}/\mathcal{D}_{P\infty} = 0.001$. This is a mathematical convenience corresponding to the arbitrary definition of boundary-layer thicknesses in constant-property analyses. It is legitimate for our present purposes but may prove inadequate in practice if more complex physical behavior is encountered than that we have modeled. Our definition of sludging must then be considered tentative pending a critical examination of reliable experimental data. As we shall see shortly, however, it appears useful on the basis of the data currently available to us.

Calculated relations between the concentration ratio C_x/C_W at the onset of sludge formation ($\beta = 0.999$) and wall permeation rate $F(0)$ are shown in Figure 6 at three Schmidt numbers for two different assumed situations: (1) D constant and μ variable as described by Equation (6). (2) D and μ both variable as described by Equations (8) and (6).

The constant-property calculations are also shown for comparison and indicate the minimum amount of polarization possible at a particular Schmidt number and permea-

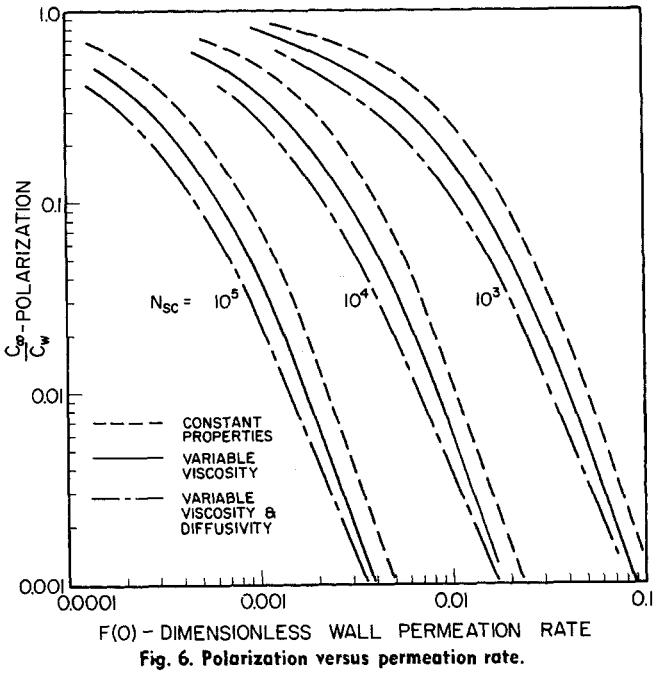

Fig. 6. Polarization versus permeation rate.

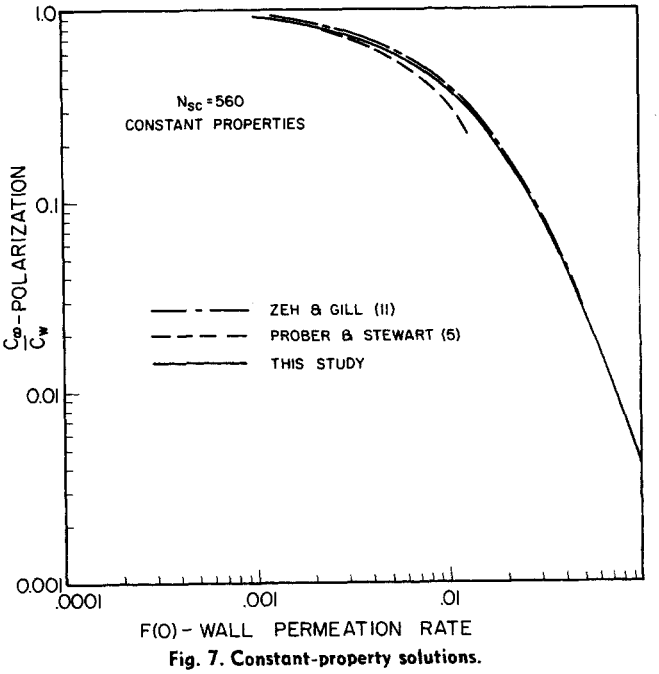

Fig. 7. Constant-property solutions.

tion rate. The constant-property calculation in addition permits a check of our numerical procedure with the constant-property calculations of previous investigators.

Comparison of our constant-property results with the numerical analysis of Zeh and Gill (*12, 13*) and the perturbation solution of Stewart and Prober (*6*) indicates that our numerical procedure is sound. These various solutions are shown in Figure 7. The Stewart and Prober solution is a limiting analysis for small $F(0)$ and hence should not be expected to be valid for the larger $F(0)$ shown.

It may be noted that the curves of Figure 5 are of relatively simple shape for $(C_{P\infty}/C_{PW})$ less than about 0.1, which is the region of greatest current interest. In this region of high polarization one finds for each of the three cases that

$$F(0) \propto N_{Sc,\infty}{}^{-2/3} \tag{13}$$

for any $(C_{P\infty}/C_{PW})$. These results can also be put in the form

$$N_{Nu} = A\, N_{Re,\infty}{}^{1/2}\, N_{Sc,\infty}{}^{1/3} \tag{14}$$

Then from these asymptotic regions of Figure 5

$$A_1 = 1.0 \left(\frac{C_{P\infty}}{C_{PW}}\right)^{-0.355} \quad (\mu, D \text{ constant}) \tag{15a}$$

$$A_2 = 0.76 \left(\frac{C_{P\infty}}{C_{PW}}\right)^{-0.355} \quad (\mu \text{ variable } D \text{ constant}) \tag{15b}$$

$$A_3 = 1.0 \left(\frac{C_{P\infty}}{C_{PW}}\right)^{-0.41} \quad (\mu, D \text{ variable}) \tag{15c}$$

Equation (14) is the usual form of laminar boundary-layer mass transfer correlations for zero wall permeation rate. Furthermore the effect of property variations on the coefficients is surprisingly small and suggests that the forms of the $\mathcal{D}_P$ and μ_P relations are of secondary importance.

The unexpectedly simple form of Equations (15) is due to the combination of very high Schmidt numbers and very low permeation rates. The high Schmidt numbers result in a very thin concentration boundary layer as previously stated and provide a high degree of concentration polarization at such low permeation rates that distortion of the velocity profile is negligible. These results are applicable to any other uniformly accessible surface such as a rotating disc. It appears in retrospect that further simplifications should have been possible in our analysis, and we are currently reviewing this possibility. Mass transfer relations of the same simple form have been observed experimentally for protein solutions by Bixler et al. (*1*) and Nelson (*5*) for considerably more complex flow systems. This suggests that these flow systems, and perhaps also those found in the mammalian body, may also be susceptible to a relatively simple analysis.

CONCLUSION

Estimation of the effects of viscosity and diffusivity variation on the ultrafiltration of protein solutions is greatly simplified by the high Schmidt numbers and low permeation rates characteristic of these systems.

The agreement in Schmidt number dependence between our predictions of incipient sludging in stagnation flows and available data for more complex systems suggests the possibility of developing simple design criteria for configurations of practical interest. Further work along these lines is clearly indicated.

It also appears from this preliminary analysis that the specific concentration dependence of viscosity and diffusivity postulated are of only secondary importance. Caution is however always indicated in analyzing the behavior of protein molecules.

NOTATION

a = velocity coefficient of ideal fluid outside momentum boundary layer
A = coefficient as defined by Equation (14)
C = C_P/C_{PW} dimensionless concentration
D = $\mathcal{D}_P/\mathcal{D}_{P\infty}$ dimensionless diffusivity
$\mathcal{D}_P$ = effective binary diffusivity
F = stream function as defined by Equation (9)
$F(0)$ = dimensionless wall permeation rate
K_c = mass transfer coefficient, $F(0)\sqrt{av}$
N_{Nu} = Nusselt number, $K_c x/\mathcal{D}_P$
N_{Re} = Reynolds number, ax^2/ν_P
N_{Sc} = Schmidt number, $\nu_P/\mathcal{D}_P$
P = pressure
u = x component of velocity
v = y component of velocity
$\hat{v}_{sp}$ = specific volume of protein
x = distance from stagnation point parallel to wall
y = perpendicular distance from wall

Greek Letters

α = empirical correction to viscosity relation for protein type
β = $2.5\, \alpha \hat{v}_{sp}\, C_{PW}$
γ = dimensionless shear stress for matching boundary-layer solution, $\dfrac{\tau_\infty}{a\, \rho_P \sqrt{a\nu_\infty}}$
η = dimensionless coordinate, $\sqrt{a/\nu}\ y$
μ = dimensionless viscosity of solution
ν = kinematic viscosity of solution
ρ = density of solution
τ_∞ = shear stress in concentration boundary layer
ϕ = volume fraction of protein in solution

Subscripts

P = value in solution
W = value at wall
∞ = free stream value

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