The experiments completed on the total liquid holdup and the step response of a column under periodic control have not been reported previously in the literature. The analysis of these experiments in terms of the (2S) model has provided the basic liquid transfer mechanism in the column.

ACKNOWLEDGMENT

A part of this research project was supported by the Australian Atomic Energy Commission.

NOTATION

a = parameter in the 1S model
A = matrix with elements composed of a and b
b = parameter in the 1S model
e = entrainment rate, kg s^{-1}
E = dimensionless entrainment
f = discrete residence time distribution
F = step response of the system
h = liquid holdup on a plate, kg
H = dimensionless holdup
$\bar{m}$ = mean cycle number
m = cycle number
M = mass of liquid admitted to the column per cycle
n = number of perfectly mixed tanks; or plate number
N = number of plates in the column
P = objective function
t = time
T = dimensionless time
w = weeping rate, kg s^{-1}
X = output response

Greek Symbols

η = fraction of liquid dropped from a plate in the 1S model
θ = dimensionless cycle number
σ_n = variance for n tanks
σ_m = variance about $\bar{m}$
σ = variance about $\bar{\theta}$

Subscripts

d = drain period
v = vapor period

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An Analysis of Carrier Facilitated Transport in Heterogeneous Media

A theoretical model is developed for steady state diffusion in reactive heterogeneous media in which simultaneous reversible chemical reactions occur between diffusible carrier species and the transported species. The heterogeneous systems analyzed are those for which one phase is dispersed as uniform spheres in a second continuous phase, and either or both phases may be reactive. The results have a simple physical interpretation in terms of additivity of resistances. The theory is applied to oxygen diffusion in blood.

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SCOPE

Transport processes in heterogeneous media pose an important problem in science and engineering. This paper is concerned with the problem of diffusion with reversible chemical reaction in such systems. Previous work has dealt separately with diffusion in nonreactive heterogeneous media and with diffusion and chemical reaction in homogeneous media, but the combined problem has not been studied in depth. The theoretical framework presented here provides a model for heterogeneous reactive systems and serves as a cohesive link between the two subjects. The heterogeneous media considered are those for which one phase is dispersed as uniform spheres

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in a second continuous phase. The spheres are required to be much smaller than any characteristic dimension of the overall system. Theoretical results are obtained for the specific case in which a second-order reaction $A + B \rightleftarrows AB$ between a permeating species A and a carrier species B occurs in both the dispersed and the continuous phase. *It is assumed that the interface* may present a significant resistance to the transport of the permeating species and that it is impermeable to the carrier species. The theory presented here is applicable to diffusion with reversible chemical reaction in dispersions and, in particular, the transport of oxygen, nutrients, and metabolites in blood.

CONCLUSIONS AND SIGNIFICANCE

Analytical results are obtained for the concentration field around a single sphere by using the technique of single-point linearization and for the effective permeability of the entire system by using the technique employed by Maxwell. The relationships take into account deviations from chemical equilibrium and their effect on transport facilitation in each phase. The effective permeability is a function of the overall permeabilities of A in the continuous phase and in the dispersed phase and is a maximum when the reactions in the two phases are at equilibrium. The total resistance to transport which is associated with the presence of the sphere in the continuous medium corresponds to serial addition of the resistances of the interface, the sphere interior, and an additional resistance due to deviations from chemical equilibrium in the continuous phase. The problem is so posed that departures from equilibrium in the continuous phase are induced solely by the presence of the sphere.

The theory is illustrated by application to the diffusion of oxygen in whole blood. The oxygen-hemoglobin reaction is modeled here as a one-step reaction scheme; more complex schemes may also be used (Stroeve, 1973). Physicochemical parameters are taken from the literature. Predictions are presented for the characteristic reaction-diffusion length and facilitation factor in the red cell and for the average effective oxygen permeability of blood as a function of red blood cell volume fraction, assumed red blood cell radius, and oxygen partial pressure driving force conditions. The results suggest that the oxygen-hemoglobin reaction in the red cell is near but not at equilibrium at 25°C. Small amounts of hemolysis of red blood cells are predicted to significantly increase the oxygen transport rate because the continuous phase (plasma) is now reactive and the released hemoglobin has a much larger diffusivity in the plasma than in the red blood cell. This prediction has important implications for experimental studies.

In a companion paper (Stroeve et al., 1976), experimental measurements of steady state oxygen permeation through red blood cell and model suspensions are compared with the theoretical model developed in this paper. The satisfactory agreement between data and prediction provides support for the assumptions made in the analysis.

Heterogeneous media such as emulsions, slurries, suspensions, and foams are frequently encountered as process streams. Biological systems are invariably heterogeneous because of their cellular nature. Mass transport in such systems is a complex phenomenon. For example, solute molecules in blood must diffuse around plasma proteins and around or through red blood cells. The equilibrium distribution of solute between plasma and red blood cells may be unequal. The solute may undergo reversible chemical combination with any of the many species present in the plasma or the red blood cell, and deviations from chemical equilibrium of the reactions between the solute and these species may be important. Further, the red blood cell membrane may offer a significant resistance to mass transfer. Diffusion with reversible chemical reaction in heterogeneous media is not limited to transport in blood; such phenomena may take place in the transport of nutrients, metabolites, and drugs to tissues or any ensemble of cells.

Numerous theoretical solutions have been given for mass transport without chemical reaction in heterogeneous media. For example, Maxwell (1881) obtained an effective permeability for the case of uniform spherical particles dispersed in a continuum. A relationship for a suspension of randomly oriented spheroids in a continuum was obtained by Fricke (1924). Relationships for two-phase media have been reviewed by Meredith and Tobias (1962) and more recently by Batchelor (1974). Diffusion and reversible chemical reaction in homogeneous media has also been extensively treated, and published experimental and theoretical studies on carrier facilitated transport have been reviewed (Schultz et al., 1974; Goddard et al., 1974). Except for the specific case of oxygen diffusion through blood with the oxyhemoglobin reaction assumed to be at equilibrium (La Force and Fatt, 1962; Fatt and La Force, 1963; Spaeth and Friedlander, 1967), integration of the work on such simpler systems toward the more complex heterogeneous situation has not been examined.

ANALYSIS

Problem Statement

A conceptual diagram of the problem is shown in Figure 1. Species A diffuses through a layer of medium composed of uniform spherical particles dispersed in a continuous phase. Solubilities and diffusivities of A in the two phases are different. A carrier species present in each phase can reversibly combine with the diffusing species. The problem is to predict the steady state mass transport of A through the layer. Because of our interest in gas transport, the final result is given in terms of the effective permeability which relates the average flux to the partial pressure difference across the layer. With a small change in nomenclature, the results apply equally to nongaseous solutes. The diameter of each particle is assumed small compared to the layer thickness so that an effective permeability can be derived for the heterogeneous system. More complex kinetics, or a sequence of reactions, can be treated in a similar fashion.

The analysis is divided in two distinct problems. The first is to solve for the concentration field both inside and outside a single sphere isolated in a continuum. The effective permeability of an assemblage of spheres is then obtained using the technique developed by Maxwell.

Concentration Field

Consider a single sphere of radius a and permeability $P_A{}^d$, immersed in an infinite medium of permeability $P_A{}^c$. At large distances from the sphere, the flux of the diffusing species A is everywhere uniform. A single step reversible reaction occurs in each phase.

$$A^j + B^j \underset{k_{-1}{}^j}{\overset{k_1{}^j}{\rightleftarrows}} AB^j$$

where $j = c, d$. This reaction is chosen to be illustrative and is assumed to follow the kinetics suggested by the stoichiometry. The reaction-diffusion equations are thus

$$D_i{}^j\left[\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C_i{}^j}{\partial r}\right)+\frac{1}{r^2\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial C_i{}^j}{\partial\theta}\right)\right] = \delta[k_1{}^jC_A{}^jC_B{}^j - k_{-1}{}^jC_{AB}{}^j] \quad (1)$$

where

$$\delta = +1 \quad \text{if} \quad i = A, B$$

$$\delta = -1 \quad \text{if} \quad i = AB$$

It will also be assumed that $D_B{}^j = D_{AB}{}^j$, from which it is easily shown that the total carrier concentration is independent of position; that is

$$C_B{}^j + C_{AB}{}^j = C_T{}^j \quad (2)$$

In most physical situations, this idealization is approached rather closely. With it, the reaction-diffusion equations may be reduced to

$$P_A{}^j\left[\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial p_A{}^j}{\partial r}\right)+\frac{1}{r^2\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial p_A{}^j}{\partial\theta}\right)\right] = k_1{}^j\alpha_A{}^jp_A{}^jC_B{}^j - k_{-1}C_T{}^j + k_{-1}{}^jC_B{}^j \quad (3)$$

and

$$\frac{\partial}{\partial r}\left[r^2\frac{\partial}{\partial r}(D_B{}^jC_B{}^j - P_A{}^jp_A{}^j)\right] + \frac{1}{\sin\theta}\frac{\partial}{\partial\theta}\left[\sin\theta\frac{\partial}{\partial\theta}(D_B{}^jC_B{}^j - P_A{}^jp_A{}^j)\right] = 0 \quad (4)$$

where the substitutions $C_A{}^j = \alpha_A{}^jp_A{}^j$ and $P_A{}^j = \alpha_A{}^jD_A{}^j$ have been made in anticipation of the desirability of relating the flux of A to the external partial pressure difference.

Solutions are sought of the form

$$p_A{}^c = p_A{}^* - \frac{N_{A,\infty}}{P_A{}^c(1+F_{\text{eq}}{}^c)}[r - af(r)]\cos\theta \quad (5)$$

$$C_B{}^c = (C_B{}^c)^* + \frac{N_{A,\infty}F_{\text{eq}}{}^c}{D_B{}^c(1+F_{\text{eq}}{}^c)}[r + ag(r)]\cos\theta \quad (6)$$

$$p_A{}^d = p_A{}^* + H(r)\cos\theta \quad (7)$$

$$D_B{}^d[C_B{}^d - (C_B{}^d)^*] - P_A{}^d(p_A{}^d - p_A{}^*) = G(r)\cos\theta \quad (8)$$

where the asterisk indicates the value at $r = 0$, and $F_{\text{eq}}{}^c$ is the equilibrium facilitation factor in the continuous phase [see Equation (16)]. The form of Equations (5) and (6) is selected on the assumption that the reaction in the continuous phase attains equilibrium (f, $g \to 0$) within such a short distance from the sphere that the equilibrium solution may be taken to be linear in r.

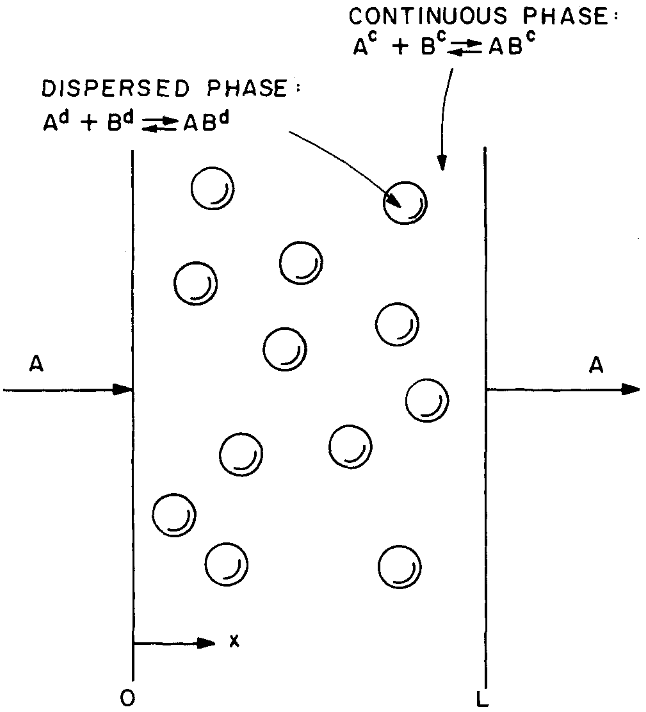

Fig. 1. Diffusion of species A in a reactive heterogeneous slab. Superscript c denotes continuous phase; superscript d denotes dispersed phase.

It is further required that perturbations from the values at $r = 0$ be small so as to permit linearization of the kinetics in the manner of Friedlander and Keller (1965). In this event

$$(C_B{}^j)^* = \frac{k_{-1}{}^jC_T{}^j}{k_1{}^j\alpha_A{}^jp_A{}^* + k_{-1}{}^j} \quad (9)$$

Furthermore, the boundary conditions for $r \to \infty$ and $r = 0$ require

$$f, g \to 0 \quad \text{as} \quad r \to \infty \quad (10)$$

and

$$H(0) = G(0) = 0 \quad (11)$$

The solutions are

$$f(r) = -\frac{a^2K_1}{1+F_{\text{eq}}{}^c}\left(\frac{1}{r^2}\right) + K_2\left(\frac{a}{r}\right)^{1/2}\left(\frac{\lambda^c}{r}\right)^{1/2}\left(1+\frac{\lambda^c}{r}\right)\left[\cosh\frac{r}{\lambda^c} - \sinh\frac{r}{\lambda^c}\right] \quad (12)$$

$$g(r) = \frac{1}{F_{\text{eq}}{}^c}\left[f(r) + K_1\frac{a^2}{r^2}\right] \quad (13)$$

$$H(r) = -K_3\frac{N_{A,\infty}}{P_A{}^d(1+F_{\text{eq}}{}^d)}r + \frac{N_{A,\infty}a}{P_A{}^d}K_4\left(\frac{a}{r}\right)^{1/2}\left(\frac{\lambda^d}{r}\right)^{1/2}\left[\cosh\frac{r}{\lambda^d} - \frac{\sinh r/\lambda_d}{r/\lambda^d}\right] \quad (14)$$

$$G(r) = K_3N_{A,\infty}r \quad (15)$$

where

$$F_{eq}{}^j = \frac{D_B{}^j\alpha_A{}^jk_1{}^jk_{-1}{}^jC_T{}^j}{P_A{}^j(k_1{}^j\alpha_A{}^jp_A{}^* + k_{-1}{}^j)^2} \quad (16)$$

$$\lambda^j = \left[\frac{k_1{}^j\alpha_A{}^jp_A{}^* + k_{-1}{}^j}{D_B{}^j} + \frac{\alpha_A{}^jk_1{}^jk_{-1}{}^jC_T{}^j}{P_A{}^j(k_1{}^j\alpha_A{}^jp_A{}^* + k_{-1}{}^j)}\right]^{-1/2} \quad (17)$$

F_{eq} and λ are obviously identical to those used by Friedlander and Keller in their analysis of facilitated transport in a single phase of planar geometry.

The four constants are determined from the boundary conditions at $r = a$. If the continuous and dispersed phases are separated by an infinitely thin shell of resistance $R_A{}^m$, then continuity of flux across the surface requires that

$$P_A{}^c \frac{\partial p_A{}^c}{\partial r} = P_A{}^d \frac{\partial p_A{}^d}{\partial r} = \frac{p_A{}^c - p_A{}^d}{R_A{}^m}; \quad r = a, \quad \text{all } \theta \tag{18}$$

Furthermore, if the carriers (which may be chemically distinct if present in both phases) cannot transit from one phase to the other, then

$$D_B{}^c \frac{\partial C_B{}^c}{\partial r} = D_B{}^d \frac{\partial C_B{}^d}{\partial r} = 0; \quad r = a, \quad \text{all } \theta \tag{19}$$

The solutions for the constants are

$$\frac{K_1}{1 + F_{eq}{}^c} = \frac{P_A{}^c(1 + F_{eq}{}^c) - P_A{}^d(1 + F^d)\left\{(1 - W^c F_{eq}{}^c) - \dfrac{P_A{}^c R_A{}^m}{a}(1 + F_{eq}{}^c)\right\}}{2P_A{}^c(1 + F_{eq}{}^c) + P_A{}^d(1 + F^d)\left\{(1 + 2W^c F_{eq}{}^c) + \dfrac{2P_A{}^c R_A{}^m}{a}(1 + F_{eq}{}^c)\right\}} \tag{20}$$

$$K_2 = \frac{F_{eq}{}^c\left(1 - \dfrac{2K_1}{1 + F_{eq}{}^c}\right)}{\left(\dfrac{\lambda^c}{a}\right)^{1/2}\left[\left(2 + 2\dfrac{\lambda^c}{a} + \dfrac{a}{\lambda^c}\right)\left(\cosh\dfrac{a}{\lambda^c} - \sinh\dfrac{a}{\lambda^c}\right)\right]} \tag{21}$$

$$K_3 = 1 - \frac{2K_1}{1 + F_{eq}{}^c} \tag{22}$$

$$K_4 = \frac{\left(\dfrac{1}{1 + F_{eq}{}^c}\right)\left(\dfrac{F_{eq}{}^d}{1 + F_{eq}{}^d}\right)(1 + F_{eq}{}^c - 2K_1)}{\left(\dfrac{\lambda^d}{a}\right)^{1/2}\left[2\left(\dfrac{\lambda^d}{a}\sinh\dfrac{a}{\lambda^d} - \cosh\dfrac{a}{\lambda^d}\right) + \dfrac{a}{\lambda^d}\sinh\dfrac{a}{\lambda^d}\right]} \tag{23}$$

where

$$W^c = \frac{1 + \lambda^c/a}{2 + 2\lambda^c/a + a/\lambda^c} \tag{24}$$

$$F^d = \frac{F_{eq}{}^d\left\{\dfrac{\left[3\left(\dfrac{\lambda^d}{a}\right)^2 + 1\right]\tanh\dfrac{a}{\lambda^d} - 3\dfrac{\lambda^d}{a}}{\left[2\left(\dfrac{\lambda^d}{a}\right)^2 + 1\right]\tanh\dfrac{a}{\lambda^d} - 2\dfrac{\lambda^d}{a}}\right\}}{1 + F_{eq}{}^d\left\{1 - \dfrac{\left[3\left(\dfrac{\lambda^d}{a}\right)^2 + 1\right]\tanh\dfrac{a}{\lambda^d} - 3\dfrac{\lambda^d}{a}}{\left[2\left(\dfrac{\lambda^d}{a}\right)^2 + 1\right]\tanh\dfrac{a}{\lambda^d} - 2\dfrac{\lambda^d}{a}}\right\}} \tag{25}$$

F^d is the facilitation factor for the dispersed phase, and $F^d \to F_{eq}{}^d$ as $\lambda^d/a \to 0$.

The solution for the case in which the shell is permeable to the carrier is given elsewhere (Stroeve, 1973).

Effective Permeability

At any point in the continuous phase, the total flux of A is given by

$$\mathbf{N}_A{}^c = -P_A{}^c \nabla\left[p_A{}^c + \frac{D_{AB}{}^c}{P_A{}^c} C_{AB}{}^c\right] \tag{26}$$

$$= N_{A,\infty}\nabla\left\{\left[r + \frac{a^3}{r^2}\frac{K_1}{1 + F_{eq}{}^c}\right]\cos\theta\right\}$$

For a spherical cluster of reactive spheres, such that the cluster has a radius R as shown in Figure 2

$$\mathbf{N}_A{}^c = N_{A,\infty}\nabla\left\{\left[r + \sum_n \frac{a^3}{r_n{}^2}\frac{K_1}{1 + F_{eq}{}^c}\right]\cos\theta\right\} \tag{27}$$

$$\cong N_{A,\infty}\nabla\left\{\left[r + n\frac{a^3}{r^2}\frac{K_1}{1 + F_{eq}{}^c}\right]\cos\theta\right\}$$

where it has been assumed that the point of observation is so distant from the cluster that $r_n \cong r$ and that the individual spheres are sufficiently distant from each other that their interactions are negligible. Alternatively, the entire cluser may be viewed as a single sphere with an effective permeability P_{eff}. In this case

$$N_A{}^c = N_{A,\infty}\nabla\left\{\left[r + \frac{R^3}{r^2}\frac{K'_1}{1 + F_{eq}{}^c}\right]\cos\theta\right\} \tag{28}$$

and

$$\frac{K'_1}{1 + F_{eq}{}^c} = \frac{P_A{}^c(1 + F_{eq}{}^c) - P_{eff}}{2P_A{}^c(1 + F_{eq}{}^c) + P_{eff}} \tag{29}$$

Equivalence of the two formulations requires

$$K'_1 = n\left(\frac{a}{R}\right)^3 K_1 = \Phi K_1 \tag{30}$$

or

$$\frac{P_{eff}}{P_A{}^c(1 + F_{eq}{}^c)} = \frac{1 - 2\Phi\dfrac{K_1}{1 + F_{eq}{}^c}}{1 + \Phi\dfrac{K_1}{1 + F_{eq}{}^c}} \tag{31}$$

In all important respects, this derivation is equivalent to that employed by Maxwell for the case of nonreactive media.

Lastly, it should be noted that P_{eff} is defined only for a single value of p_A, that is, $p_A{}^*$. If, in a given experiment, the range of p_A is significant, then P_{eff} may also

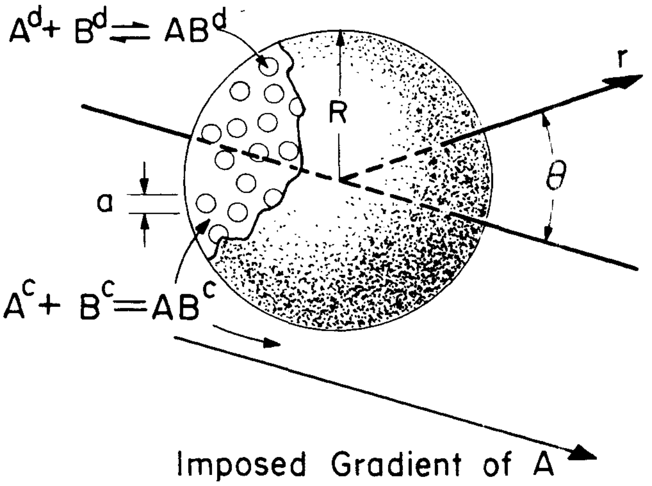

Fig. 2. Spherical cluster of reactive spheres in a reactive continuum.

vary significantly. In such a case, the appropriate average value of P_{eff} is given by

$$\overline{P}_{\text{eff}} = \frac{1}{p_A{}^o - p_A{}^L}\int_{p_A{}^L}^{p_A{}^o} P_{\text{eff}}\,dp_A \qquad (32)$$

provided that the geometry corresponds to a simple slab, as sketched in Figure 1.

DISCUSSION OF RESULTS

General

The physical situation becomes much clearer if one sets

$$\frac{K_1}{1 + F_{\text{eq}}{}^c} = \frac{P_A{}^c(1 + F_{\text{eq}}{}^c) - \mathcal{P}^d}{2P_A{}^c(1 + F_{\text{eq}}{}^c) + \mathcal{P}^d} \qquad (33)$$

so that $\mathcal{P}^d$ is the equivalent permeability of a sphere immersed in a continuum of permeability $P_A{}^c(1 + F_{\text{eq}}{}^c)$. Comparison with Equation (20) then gives

$$\frac{a}{\mathcal{P}^d} = R_A{}^m + \frac{a}{P_A{}^d(1 + F^d)} + \frac{a}{P_A{}^c(1 + F_{\text{eq}}{}^c)}\,W^cF_{\text{eq}}{}^c \qquad (34)$$

The left-hand side is simply the total resistance to transport which is associated with the presence of the sphere. The first two terms on the right correspond to serial addition of the resistances of the shell and of the sphere interior. Furthermore, it is again evident that F^d does represent the transport facilitation within the sphere. The last term represents an additional resistance in the continuous phase which is associated with deviations from chemical equilibrium in that phase. These departures from equilibrium are induced solely by the presence of the sphere. Clearly, there is no induced resistance if $F_{\text{eq}}{}^c = 0$ or if $W^c = 0$, where the latter would correspond to very fast external kinetics ($\lambda^c/a \to 0$).

As derived here, F^d has the form

$$F^d = \frac{\gamma(\lambda^d/a)F_{\text{eq}}{}^d}{1 + [1 - \gamma(\lambda^d/a)]F_{\text{eq}}{}^d} \qquad (35)$$

as does the relation obtained by Friedlander and Keller (1965) for the case of a slab. A comparison of the values of γ appropriate to the two geometries is shown in Figure 3. A qualitative correspondence was to be expected, but the quantitative similarities are surprising. In fact, the two curves approach unity in exactly the same manner.

The possibility of reaction in the continuous phase also raises a question as to the range of volume fraction for which the analysis is valid. For inert media, it is known experimentally (Meredith and Tobias, 1962) that Maxwell's treatment is surprisingly good for all volume fractions, provided that the particles are not highly anisotropic and that P^d/P^c is not extremely large relative to unity. The same conclusion, with the latter constraint generalized to $\mathcal{P}^d/P^c(1 + F_{\text{eq}}{}^c)$, presumably applies to the present analysis, except for the complications associated with the deviations from chemical equilibrium which are induced in the continuous phase by the presence of the sphere. Conservative criteria for validity when reaction occurs in the continuous phase would be to require both that the nonequilibrium reactive volume in the continuous phase be a modest fraction of that phase

$$\left[\left(1 + \frac{\lambda^c}{a}\right)^3 - 1\right]\frac{\Phi}{1 - \Phi} \le \epsilon_1 \qquad (36)$$

and that the induced resistance be a small fraction of the continuous phase resistance

$$W^cF_{\text{eq}}{}^c \le \epsilon_2 \qquad (37)$$

This should also ensure that the simplifications inherent in Equations (5) and (6) be valid.

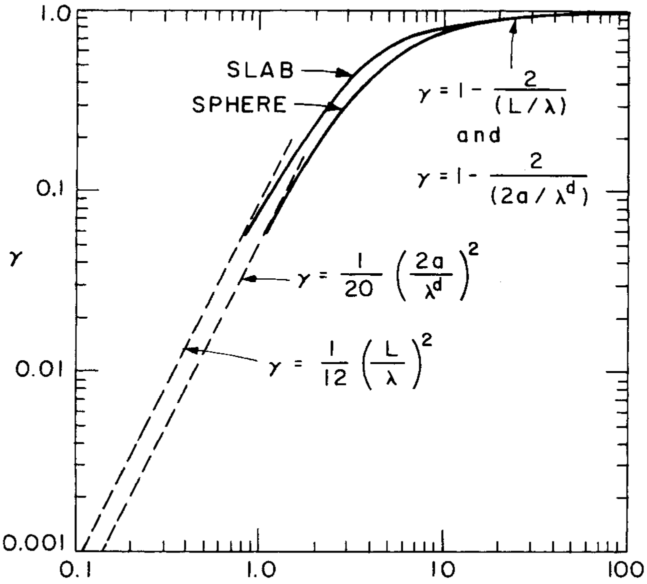

Fig. 3. Comparison of the facilitation factor for a slab with that for a sphere.

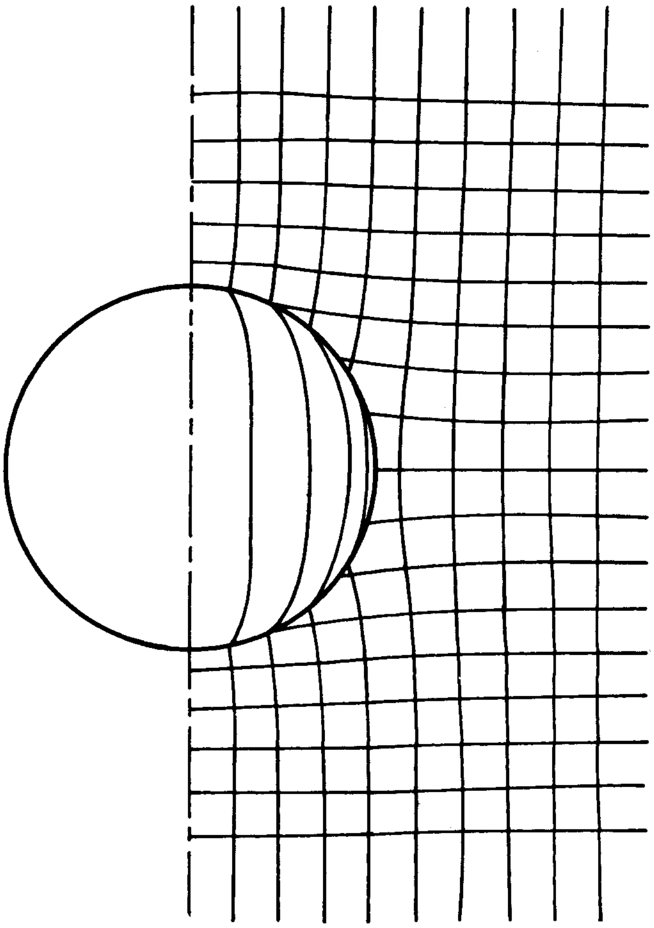

Fig. 4. Flux and potential plots for a single reactive sphere in a nonreactive continuum with $F^d = 4$, $P^d/P^c = 1/9$, and $a/\lambda^d = 14$.

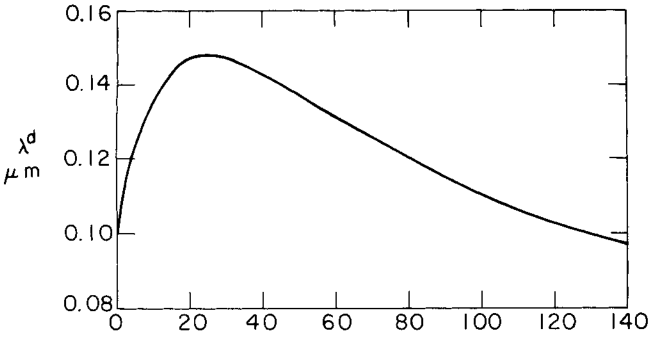

Fig. 5. Characteristic length λ^d for conditions inside the red blood cell.

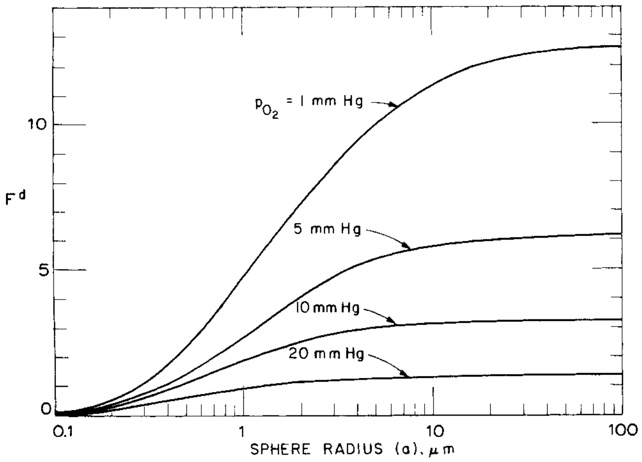

Fig. 6. The facilitation factor in the red cell as a function of oxygen partial pressure and equivalent sphere radius.

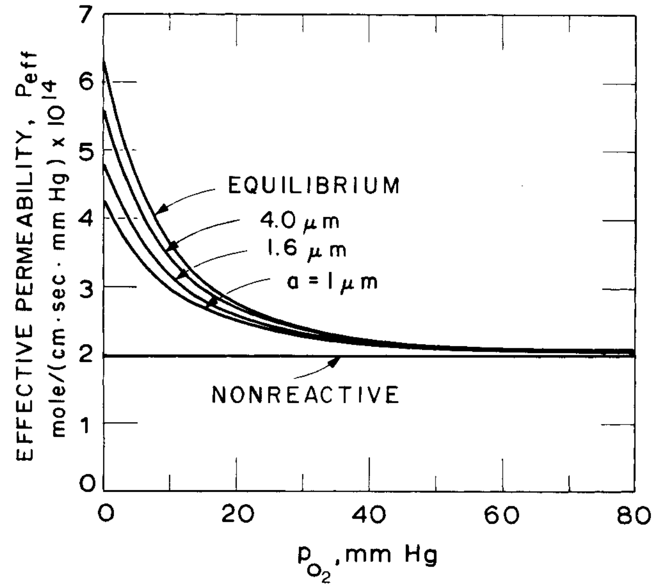

Fig. 7. Local effective permeability for whole blood at 25°C with $\Phi = 0.45$.

Finally, it should be noted that the reaction within the sphere may be shut off either by letting $F_{eq}{}^d \rightarrow 0$ or by letting $\lambda^d/a \rightarrow \infty$. The external reaction may be shut off only by letting $F_{eq}{}^c \rightarrow 0$, because the analysis initially assumed a single sphere in an infinite medium.

It is evident from Equations (4) and (26) that

$$\phi^j = p_A{}^j - \frac{D_B{}^j}{P^j} C_B{}^j + \text{const} \qquad (38)$$

TABLE 1. PHYSICOCHEMICAL PARAMETERS EMPLOYED FOR THE DIFFUSION OF OXYGEN IN WHOLE BLOOD AT 25°C

Parameter*	Value	Source
$k_1{}^d$	3.0×10^6 l mole^{-1} s^{-1}	Gibson (1959)
$k_{-1}{}^d$	42.8 s^{-1}	Gibson (1959)
$D_A{}^d$	0.65×10^{-5} cm^2 s^{-1}	Kreuzer (1970)
$\alpha_A{}^d$	1.75×10^{-6} mole l^{-1} (mm Hg)$^{-1}$	Altman and Dittmer (1971)
$D_B{}^d$	0.76×10^{-7} cm^2 s^{-1}	Kreuzer (1970)
$C_T{}^d$	0.020 mole heme l^{-1}	
$P_A{}^c = \alpha_A{}^c D_A{}^c$	2.80×10^{-14} mole s^{-1} cm^{-1} (mm Hg)$^{-1}$	Altman and Dittmer (1971), Hershey and Karhan (1968)

* $A = O_2$, B = hemoglobin.

describes a suitable potential function. That is, it satisfies Laplace's equation and its gradient is proportional to the total flux. Furthermore, a suitable conjugate (stream or flux) function is given by

$$\frac{\partial \psi^j}{\partial \theta} = r^2 \sin\theta \frac{\partial \phi^j}{\partial r} \qquad (39)$$

$$\frac{\partial \psi^j}{\partial r} = -\sin\theta \frac{\partial \phi^j}{\partial \theta} \qquad (40)$$

This representation is particularly useful in the continuous phase. In the dispersed phase, however, lines of constant ψ are simply parallel to $\theta = 0$, and lines of constant ϕ are parallel to $\theta = \pi/2$. Furthermore, the potential function is discontinuous across $r = a$. Figure 4 shows the flux and potential lines in the continuous phase and lines of constant p_A within the sphere. Since the sphere is less permeable than the continuous phase $[P^d(1 + F_{eq}{}^d) < P^c]$, the flux lines bend away from the sphere. Within the sphere, lines of constant p_A are concentrated near the surface $r = a$ as a result of the fact that the reaction is fast ($\lambda^d/a = 1/14$).

Application to Oxygen Diffusion in Blood

For oxygen diffusion, whole blood may be treated as a reactive suspension with no reaction in the continuous phase. Physicochemical parameters used in the calculations are listed in Table 1. The one-step reaction scheme employed above is a useful approximation to represent oxygen-hemoglobin kinetics (Hartridge and Roughton, 1923, 1925). Furthermore, the techniques developed here can be extended to more realistic kinetic schemes (Stroeve, 1973) such as that of Adair (1925).

The characteristic length λ^d for the oxygen-hemoglobin reaction inside the red blood cell at 25°C is shown in Figure 5 as a function of the oxygen partial pressure p_{O_2}. It varies from 0.1 to 0.15 μm over the p_{O_2} range plotted and reaches a maximum value at about 24 mm Hg. The facilitation factor F^d is plotted as a function of sphere radius and p_{O_2} in Figure 6. The upper and lower bounds for the equivalent spherical radius are taken to be the smallest (1 μm) and largest (4 μm) half thicknesses of the biconcave red blood cell. Within these bounds, F^d varies from 40 to 80% of its equilibrium value. $F_{eq}{}^d$ is approached asymptotically at large a. The curves depend markedly upon p_{O_2}, primarily because of its effect on the equilibrium facilitation factor $F_{eq}{}^d$ and only secondarily because of the dependence of λ^d on partial pressure. For a one-step reaction scheme and fixed radius, F^d attains a maximum value as the oxygen partial pressure approaches zero.

Values of P_{eff} consistent with these facilitation factors are shown in Figure 7 as a function of p_{O_2}. The local effective permeability is obtained from Equation (31) with $R_A{}^m$ equal to zero since the red blood cell membrane resistance to oxygen transport is negligible (Kreuzer and Yahr, 1960; Stein et al., 1971; Stroeve et al., 1976). The curves are plotted for the bounding estimates of equivalent sphere radius, for a sphere with equivalent red cell specific area (1.6 μm), and for the nonreactive and equilibrium limiting conditions. All curves approach the nonreactive case at high p_{O_2} as oxyhemoglobin becomes saturated and the effect of the chemical reaction becomes negligible.

Figure 8 shows the ratio of the average effective permeability of a layer of blood to that of plasma as a function of sphere radius and volume fraction red blood cells in plasma with $p_{O_2}{}^L = 0$ and $p_{O_2}{}^o = 40$ or 140 mm Hg. $\overline{P}_{\mathrm{eff}}/P^c$ was evaluated numerically from Equation (32), except for the equilibrium limit which may be obtained in closed form:

$$\frac{\overline{P}_{\mathrm{eff}}}{P^c} = \frac{s}{q} + \frac{t - \dfrac{us}{q}}{K_{\mathrm{eq}}{}^d \alpha_A{}^d \sqrt{qu}} \left\{ \frac{\tan^{-1}\left[(K_{\mathrm{eq}}{}^d \alpha_A{}^d p_A{}^o + 1)\left(\dfrac{q}{u}\right)^{1/2} \right] - \tan^{-1}\left[(K_{\mathrm{eq}}{}^d \alpha_A{}^d p_A{}^L + 1)\left(\dfrac{q}{u}\right)^{1/2} \right]}{p_A{}^o - p_A{}^L} \right\} \tag{41}$$

where

$$q = \frac{D_A{}^d}{D_B{}^d K_{\mathrm{eq}}{}^d C_T{}^d} \left[2 + \Phi + \frac{P^d}{P^c}(1 - \Phi) \right] \tag{42}$$

$$s = \frac{D_A{}^d}{D_B{}^d K_{\mathrm{eq}}{}^d C_T{}^d} \left[2 - 2\Phi + \frac{P^d}{P^c}(1 + 2\Phi) \right] \tag{43}$$

$$t = \frac{P^d}{P^c}(1 + 2\Phi) \tag{44}$$

$$u = \frac{P^d}{P^c}(1 - \Phi) \tag{45}$$

The intercept at $\Phi = 1$ for the nonreactive case is simply P^d/P^c. As anticipated from Figure 7, $\overline{P}_{\mathrm{eff}}$ is higher when p_{O_2} at both boundaries falls within the range where oxyhemoglobin is not completely saturated. Under such conditions, transport facilitation within red blood cells can actually increase the average effective permeability of blood above that of plasma.

Figure 9 shows the average effective permeability divided by the normal plasma permeability as a function of the initial volume fraction for a case in which 5% of the original red cells have been hemolyzed. The driving force conditions are the same as in Figure 8*a*. Oxygen permeability and hemoglobin diffusivity in plasma were estimated as a function of the total protein concentration (plasma proteins and hemoglobin) from the correlation of Kreuzer (1970). It is obvious from Figure 9 that even small amounts of hemolysis can substantially increase the oxygen transport rate in red blood cell suspensions. This occurs because the hemoglobin released into the plasma renders the continuous phase reactive with respect to oxygen transport. It might be thought that the facilitation in the plasma would be minimal because the hemoglobin concentration in the plasma would ordinarily still be small, even if not zero. However, since the flux augmentation is proportional to $D_{\mathrm{Hb}}C_{\mathrm{Hb}}$ [see Equation (16)] and since D_{Hb} exhibits an inverse dependence on C_{Hb}, it follows that the product remains nearly constant over a wide range of C_{Hb}. For instance, a thirtyfold reduction in concentration level relative to that present in the red blood cell results in only a 2.5 fold reduction in $D_{\mathrm{Hb}}C_{\mathrm{Hb}}$. The effect of the oxygen-hemoglobin reaction in the continuous phase poses severe constraints on the extent of hemolysis allowable in experimental studies of oxygen transport in blood.

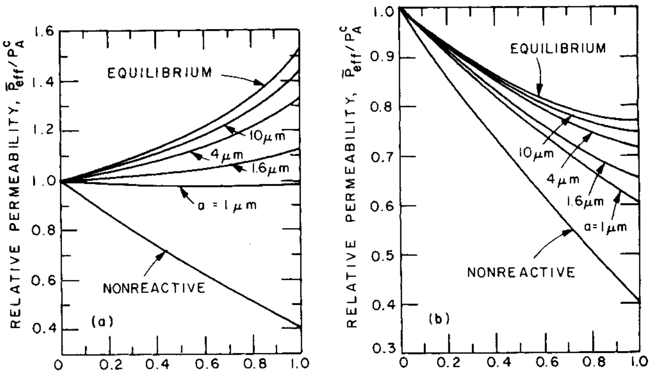

Fig. 8. Average effective permeability ratio for $p_{O_2}{}^L = 0$ and (a) $p_{O_2}{}^o = 40$ mm Hg; (b) $p_{O_2}{}^o = 140$ mm Hg.

It should be noted that the curves with and without hemolysis cross at high initial volume fractions. This behavior is physically unrealistic and reflects the fact that for hemolysis and high initial volume fractions, the criterion given by Equation (37) is not satisfied.

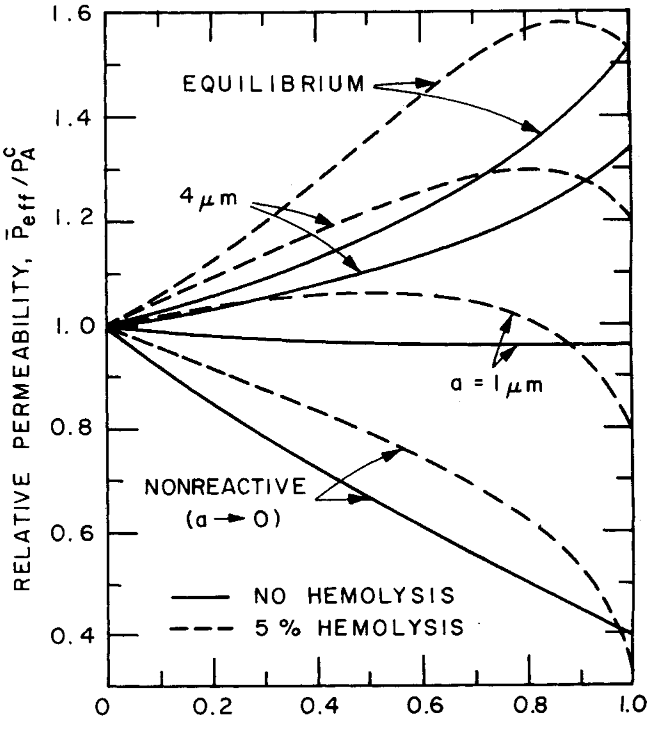

Fig. 9. Average effective permeability ratio in the presence and absence of hemolysis. $p_{O_2}{}^o = 40$ mm Hg and $p_{O_2}{}^L = 0$ mm Hg, 5% hemolysis.

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NOTATION

a = sphere radius
C = concentration
$C_T{}^j$ = $\int_v (C_B{}^j + C_{AB}{}^j)\,dv$, total carrier concentration (all forms) in phase j
D = diffusivity
f = function given by Equation (12)
F = facilitation factor
g = function given by Equation (13)
G = function given by Equation (15)
H = function given by Equation (14)
k_1 = forward rate constant
k_{-1} = backward rate constant
K_1, K_2, K_3, K_4 = constants defined by Equations (20) to (23)
K_{eq} = k_1/k_{-1}, equilibrium constant
L = slab thickness
n = number of spheres
N_A = flux of species A
p = partial pressure
P = $D\alpha$, permeability
P_{eff} = effective permeability of dispersion at single value of partial pressure
$\mathfrak{P}^d$ = equivalent permeability of a sphere in an infinite medium
$\overline{P}_{\text{eff}}$ = average effective permeability of dispersion
q = parameter defined by Equation (42)
r = radial coordinate
r_n = distance from sphere n to point of observation
R = radius of cluster of spheres
$R_A{}^m$ = interfacial mass transfer resistance for species A
s, t, u = parameters defined by Equations (43 to 45)
v = volume
W^c = parameter defined by Equation (24)
x = cartesian coordinate

Greek Letters

α = Bunsen solubility coefficient, $C = \alpha p$
γ = function defined by Equation (35)
δ = switching function, Equation (1)
ϵ = tolerance specification, Equations (36) and (37)
θ = cone angle in spherical coordinate system
λ = characteristic length, defined by Equation (17)
ϕ = potential function
Φ = volume fraction of dispersed phase
ψ = stream function

Subscripts

A, B, AB = species A, B, or AB
eq = equilibrium
i = species i
O_2 = oxygen
∞ = at large distances from a particle ($r \to \infty$)

Superscripts

c = continuous phase
d = dispersed phase
j = either phase, c or d
L = at $x = L$
o = at $x = 0$
$*$ = condition at $r = 0$

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