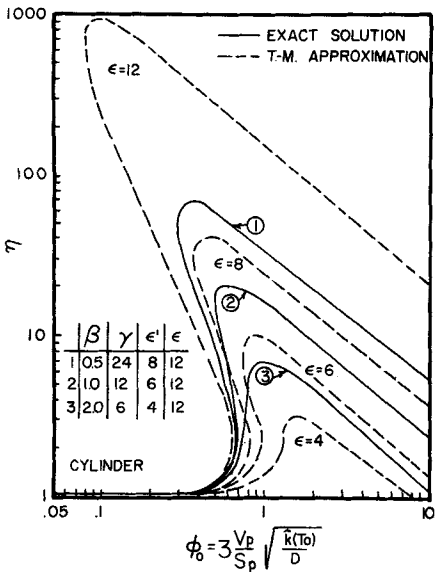

Fig. 6. Bounds on the effectiveness factor for cylinder.

the exact E.F. curve is bounded by the curves for ϵ and ϵ', it can be concluded that the Tinkler-Metzner method yields a good approximation in the range in which the curve for $\epsilon = \beta\gamma$ and $\epsilon' = \beta\gamma/(1+\beta)$ are close together.

Thus, the approximation is good for low values of $\epsilon(\epsilon < 4)$. Figures 1 and 2 indicate that for any value of ϵ the approximation is better for smaller values of β.

It is seen from Figure 5 that the asymptotic E.F. is better described by the ϵ' curve than by the ϵ curve. The reason being that for large values of ϕ_0 most of the reaction is completed in a narrow zone near the interface and the dimensionless temperature throughout most of the volume is much closer to $1+\beta$ than to one. Analytical methods to estimate the asymptotic E.F. by use of the T.-M. approximation are discussed (*4, 5*).

It should be noted that the theorem is proved here only for slab. It was shown by Aris (*1*) and Petersen (5) that all catalyst particles of arbitrary shape have the same asymptotic value of the E.F. if the characteristic length is V_p/S_p. Thus, it is clear that the bounds on the asymptotic E.F. obtained for a slab can be used also for other configurations.

Surprisingly, it was found that the theorem is valid also for cylinders (Figure 6) and spheres [Figure 2 in (2)] for all values of the Thiele modulus. However, no proof of this fact was found.

CONCLUSIONS

1. It is shown that for large values of $\epsilon = \gamma\beta$ the Tinkler-Metzner approximation yields large errors in the computed values of the effectiveness factors.

2. A simple method is developed by which the Tinkler-Metzner approximation can be used to obtain upper and lower bounds on the exact value of the effectiveness factor for an exothermic catalytic reaction.

3. It is shown that the asymptotic effectiveness factor curve computed by the T. M. method for $\epsilon' = \gamma\beta/(1+\beta)$ yields a better estimate than does the curve for $\epsilon = \gamma\beta$.

ACKNOWLEDGMENT

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NOTATION

c_o = concentration of reactant
D = effective diffusivity
E = activation energy
$f(y)$ = kinetic expression
ΔH = heat of reaction
k = reaction rate constant
r = radial position
R = radius, or half thickness of slab
S_p = surface area of particle
T = temperature
V_p = volume of particle
y = T/T_o
w = dy/dr
z = $(y-1)/\beta$

Greek Letters

β = $(-\Delta H)Dc_o/\lambda T_o$
γ = E/RT_o
ϵ = $\beta\gamma$
ϵ' = $\beta\gamma/(1+\beta)$
η = effectiveness factor
λ = thermal conductivity
ϕ_0 = $3V_p/S_p\sqrt{k(T_o)/D}$
ψ_0 = $R\sqrt{k(T_o)/D}$

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Diffusion Coefficients for Oxygen Transport in Whole Blood

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The rate of oxygen uptake by blood has been the object of much study. Early researchers hypothesized that the oxygen molecules, after traversing a multistage diffusion path in the lungs, would then combine with the hemo-

globin in the erythrocytes (red cells) of the blood in a chemical reaction to form oxyhemoglobin. Spaeth and Friedlander (*24*) have speculated on a theory of facilitated oxygen transport where the diffusion coefficient is a function of the local oxygen partial pressure. Weissman and Mockros (*27*) considered the red cells as oxygen sinks and assumed that the reaction between oxygen and hemoglobin in the red cell to be diffusion controlled. However, the nature of the oxygenation transport process is not well understood. Some investigators, such as Ostwald (*21*) and Bayliss (*1*) proposed that what actually occurred might be an adsorption phenomena rather than a chemical reaction. Blood oxygenation has also drawn much attention from persons interested in the design of extracorporeal blood oxygenation devices. In such devices thin films of blood are exposed to an oxygen atmosphere. Diffusion of oxygen into these films is in three steps (*7*): (a) diffusion through the plasma surrounding the red cell; (b) diffusion across the red cell membrane; and (c) diffusion within the red cell and chemical combination with hemoglobin. The roles of each of these steps in the total oxygen transport process have been individually investigated. Gertz and Loeschcke (*8*) have reported that in defibrinated plasma, where the diffusion of oxygen obeys Fick's law, they found a diffusion coefficient of 1.98×10^{-5} sq.cm./sec. at 25°C. From the results obtained in their photometric studies of oxygen diffusion in whole blood, Thews and Niesel (*26*) determined a diffusion coefficient for oxygen in plasma of 1.60×10^{-5} at 20°C.

The nature of the red cell membrane as a diffusion barrier has not yet been definitely established. Forester, et al. (*6*), and Hartridge and Roughton (*9*) have reported that they observed the rate of oxygen consumption to be up to ten times greater in hemolyzed blood than in unhemolyzed blood. But more recently, Thews (*24*), and Kreuzer and Yahr (*17*) have expressed the view that the red cell membrane does not represent a significant diffusion resistance.

Finally, within the red cell itself, the diffusion of oxygen and its chemical combination with hemoglobin have been studied both theoretically and experimentally. Mochizuki and Fukuoka (*20*) have stated that in the red cell, the diffusion rate of oxygen could be given as

$$\frac{d\bar{C}}{dt} = F\,(P_a - \bar{P}) \tag{1}$$

Also, Thews and Niesel (*25*) have reported that they experimentally determined a diffusion coefficient of 0.8×10^{-5} sq.cm./sec. for oxygen in the red cells. This they determined from the results they obtained in their photometric observations of the diffusion of oxygen into layers of whole blood. Several investigators have developed mathematical theories to describe the transport of oxygen through hemoglobin solutions. Fatt and Laforce (*5*) obtained a general mathematical relationship for the process by combining the equations describing diffusion, gas solubility, and mass conservation. Also, Collins (*3*) developed a mathematical theory to explain the apparently enhanced oxygen transport observed at low oxygen partial pressures by Scholander (*23*), and Hemmingsen and Scholander (*11*). Their oxygen transport studies were conducted on a hemoglobin solution held in a millipore membrane which separated two gas chambers. Keller and Friedlander (*14*) have also studied steady state oxygen transport through hemoglobin solutions, but by employing a diffusion cell and a Clark polarographic electrode. For oxyhemoglobin solutions, they observed a decrease in the value of the diffusion coefficient of oxygen from 2.1×10^{-5} sq.cm./sec. at zero oxyhemoglobin concentration, to 0.8×10^{-5} sq.cm./sec. at an oxyhemoglobin concentration of 35 g./100 ml. of solution. Pircher (*22*) observed an effect of the same magnitude in his diffusion studies with methemoglobin solutions.

Hershey, et al. (*12*), and Miller (*19*) studied the diffusion of oxygen into falling films of whole blood in a wetted-wall column and obtained a value of 2.1×10^{-5} sq.cm./sec. at 30°C. Marx (*18*), who studied diffusion into thin, stationary, blood films, obtained a value of 1.3×10^{-5} sq.cm./sec. at 27°C. by using a moving front diffusion model. In our extension of past diffusion studies, we have determined values for a coefficient for oxygen in whole blood (without chemical reaction) and observed the effect that intact red cells concentration (hematocrit) has upon that coefficient. This was accomplished, using a diffusion cell and a Beckman oxygen macroelectrode, by conducting the diffusion studies at oxygen partial pressures higher than that corresponding to complete saturation of the red cell hemoglobin with oxygen. The experiments were designed to follow the unsteady state diffusion of oxygen into a layer of whole blood (unhemolyzed). By using the appropriate boundary conditions to the diffusion equation, a solution was obtained which could be used with experimental data to obtain diffusion coefficients.

EQUATIONS DESCRIBING THE DIFFUSION PROCESS

The unsteady state diffusion of oxygen into a stationary layer of whole blood can be represented (assuming homogeneous chemical reaction) in differential equation form as

$$\frac{\partial C}{\partial t} = -D\,\nabla^2 C + R \tag{2}$$

However, if the hemoglobin in the intact red cells is completely in the form of oxyhemoglobin so that no chemical reaction occurs, the equation reduces to

$$\frac{\partial C}{\partial t} = -D\nabla^2 C \tag{3}$$

By making the assumption of unidimensional diffusion and by fixing the other system variables, Equation (3) can be reduced to the partial differential form

$$\frac{\partial C}{\partial t} = -D\,\frac{\partial^2 C}{\partial x^2} \tag{4}$$

The initial and boundary conditions, imposed by the experimental conditions, for the solution of this equation are

$$\begin{array}{lll} t = 0, & x > 0 & C = C_0 \\ t > 0, & x = 0 & C = C_1 \\ t > 0, & x > 0 & C = f(t) \end{array} \tag{5}$$

If the diffusion chamber is considered to be a semi-infinite medium (in the x direction), Equation (4) can be solved (*4*) to obtain the solution

$$\frac{C - C_1}{C_0 - C_1} = \operatorname{erf}\frac{x}{2\sqrt{Dt}} \tag{6}$$

Though the experiments were finite in the x-direction, Equations (4) to (6) are applicable, as indicated by our excellent results with the known water-oxygen system. Thus, Equation (6) and experimental data were used to calculate diffusion coefficients for oxygen in whole blood at various values of hematocrit. Details are given elsewhere (*13*).

EXPERIMENTAL EQUIPMENT

A Beckman oxygen macroelectrode was the basic unit of the experimental apparatus. This is a Clark-type polarographic

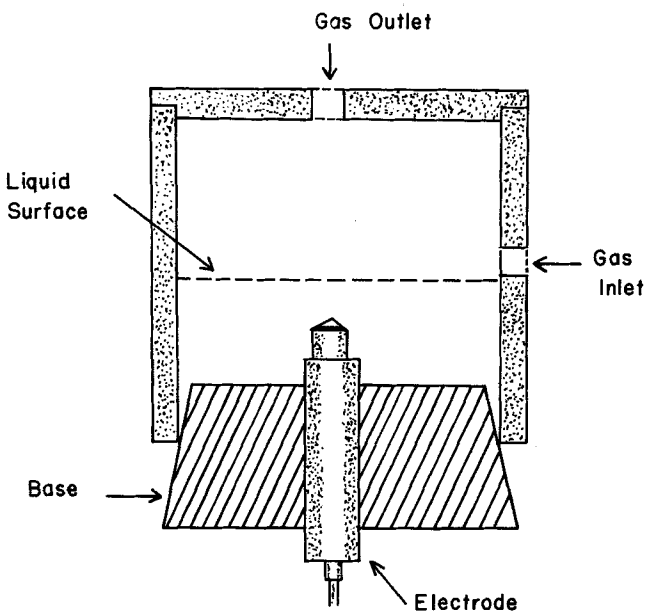

Fig. 1. Diffusion cell.

cell (7) with a silver-silver chloride anode and a platinum cathode.

The Instrumentation Laboratories model 125B portable gas analyzer was used in conjunction with the oxygen electrode in order to obtain continuous readings. The precision with which oxygen partial pressure measurements could be made was 0.1 mm. Hg. on the scale covering the range of partial pressures from zero to 160 mm. Hg., and 1.0 mm. Hg. on the scale covering the range of partial pressures from zero to 800 mm. Hg.

A cathetometer was used to determine the length of the diffusion path (that is the distance from the top of the liquid film to the tip of the electrode). The scale could be read to the nearest 0.005 cm. A built-in leveling device on the instrument eliminated line-of-sight viewing errors. Figure 1 is a sketch of the diffusion cell and Figure 2 shows the overall experimental setup.

Gas mixtures used in this experimentation were air and pure oxygen with less than 10 ppm. nitrogen. They were chosen because of the large difference in their oxygen partial pressures and because the hemoglobin in the red cells will be entirely in the form of oxyhemoglobin if the blood is equilibrated with either one. The diffusion cell used was made of transparent acrylic plastic and the base of the cell (a rubber stopper) contained a hole into which the oxygen electrode fit snugly.

Initially, the electrode was placed in the empty diffusion cell at a height corresponding to a zero point on the cathetometer. After calibrating the electrode with pure oxygen and air, blood was poured into the cell, covering the electrode tip. The same volume of blood was added for each experiment giving an average blood film of 0.199 cm. This blood was previously equilibrated by bubbling water-saturated air through it for about 1 hr. in a 25°C. constant temperature bath. Room temperature was also maintained at 25°C. Water saturated air was then blown over the blood in the cell until the start of each experiment. After the height of the blood film above the electrode had been measured with a cathetometer, the experiment would be started by switching a three-way valve to allow water saturated oxygen to flow past the blood film. The unsteady state diffusion process was then followed by observing the changes in oxygen concentration at the electrode. At the end of the experiment, the electrode would be advanced to the surface of the liquid layer. After allowing stable hydrodynamic conditions to be attained the concentration was measured at the surface. Calibration of this type of electrode in a gas gives a reading different by about 5% from that given by the calibration in a liquid at the same oxygen partial pressure. Since the concentration (electrode) data was obtained from differences in final and initial electrode readings, the calibration error in oxygen concentration is probably negligible.

Experiments with all blood samples were made 10 min. in length because of the necessity of minimizing the red cell sedimentation effects in the experiments. Wintrobe (28) has stated that sedimentation of the red cells is insignificant until about 20 min. after the sample is allowed to become stationary in a vertical position. The plasma was examined after each run and found to have maintained its original color with minimal lysis. The red cells were microscopically examined and appeared to be in good condition. Each blood sample was used only once.

Whole sheep's blood with intact red cells was used in these experiments. Blood samples having hematocrits of less than 30 were obtained by diluting the defibrinated blood with defibrinated plasma. Plasma was obtained by centrifugation of blood at 1,500 g. for 30 min., decantation, and recentrifugation. Since the blood was defibrinated, the results obtained should be considered applicable for blood in this condition.

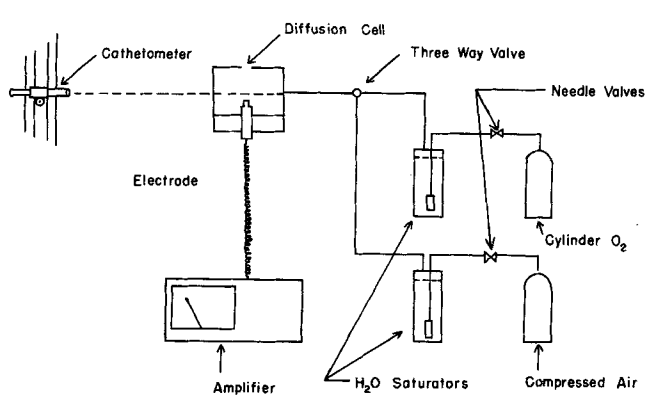

Fig. 2. Diffusion experiment equipment setup.

EXPERIMENTAL RESULTS

In this study, experiments were conducted on whole blood samples having hematocrits ranging from zero (plasma) to about 45% (normal human hematocrit). Two experiments were also done using water, as a check of the experimental equipment and procedure.

Figure 3 shows the changes in concentration with time for a typical run. The calculated diffusion coefficients are plotted in Figure 4 for various hematocrits. It was found that even the slightest liquid surface perturbations caused by the gas flow over the film would seriously affect experimental results. In order to eliminate the possibility of surface disturbances caused by the oxygen flow, the inlet gas flow rate had to be reduced to approximately 10 cc./sec. This was the approximate flow rate used in all subsequent experiments and corresponds to about 10 vol. changes/min. in the gas chamber of the diffusion cell. This flow rate was still high enough to assure that the oxygen displacement through the diffusion cell was several orders of

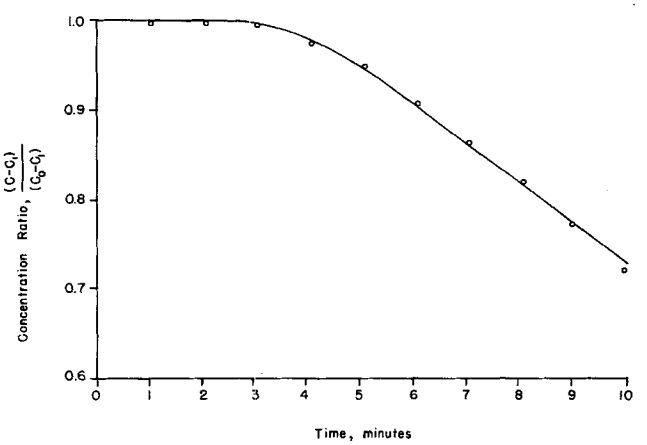

Fig. 3. Unsteady state oxygen diffusion in water.

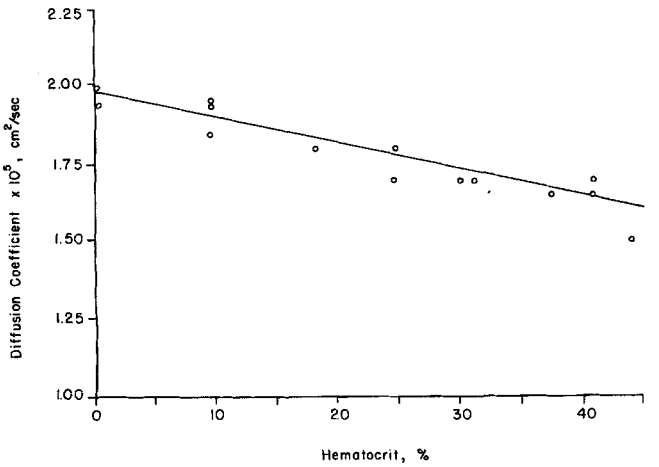

Fig. 4. Effect of hematocrit upon the diffusion coefficient at 25°C.

magnitude greater than the diffusion flux into the blood.

The results obtained from the experiments with water and plasma seemed to indicate that the technique was reasonably reliable. For the diffusion coefficient of oxygen in water, the literature (*15, 16, 22*) gives a value of 2.25 $\times$ 10^{-5} sq.cm./sec. The data obtained in the two experimental runs done with water gave values of 2.20 $\times$ 10^{-5} sq.cm./sec. and 2.30 $\times$ 10^{-5} sq.cm./sec. This was deemed acceptable since the error involved in measuring the film thickness is about 5%. Values for the diffusion coefficient of oxygen into plasma were 2.0 $\times$ 10^{-5} sq.cm./sec. and 1.95 $\times$ 10^{-5} sq.cm./sec. at 25°C. for two runs. This was also in quite good agreement with the previously reported value of 1.98 $\times$ 10^{-5} sq.cm./sec. obtained, at 25°C. by Gertz and Loeschcke (*8*). These results were, in addition, in qualitative agreement with the value of 1.60 $\times$ 10^{-5} sq.cm./sec. reportedly observed by Thews and Niesel (*26*) who reported their values at 20°C. rather than 25°C. Since the diffusion coefficient increases with increasing temperature this value seems to support our results.

The calculated values of the diffusion coefficient of oxygen, for the whole blood samples studied, tended to decrease with increasing hematocrit. The equation of the least squares line drawn through the data points of Figure 4 is

$$D = (1.98 - 0.0085\,H) \times 10^{-5}\ \text{sq.cm./sec.}$$

where D is the diffusion coefficient of oxygen in whole blood at 25°C. and H is the hematocrit. It seems reasonable to assume that this observed decrease in the value of the diffusion coefficient with increasing hematocrit was a result of the fact that, as the red cells become more concentrated, less of a path is open to direct oxygen diffusion in the plasma. The experiments were conducted over a hematocrit range of 0-45% and hence the results are considered applicable only in this range. Extrapolation into pathological ranges should be done cautiously.

The scatter observed in the experimentally determined diffusion coefficients reported here is probably due to the inability to more accurately determine the thickness of the liquid film. Also, possible sedimentation effects and error of the oxygen electrode readings could have contributed to the scatter.

The data obtained in this study should be an aid in the analysis of oxygen transport through whole blood and in the design of artificial oxygenators. Since the diffusion coefficients obtained in this study did not include the effects of simultaneous chemical reaction, it should now be possible to employ these diffusion coefficient values to determine the independent effect of simultaneous chemical reaction. By considering whole blood as a suspension of chemically reactive sinks and with the actual diffusion coefficients in whole blood determined, the equations of mass transport can be written and used in the analysis of experimental data to gain an increased understanding of the kinetics of this complex oxygen-blood system.

ACKNOWLEDGMENT

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NOTATION

c = concentration of dissolved oxygen in the plasma
$\bar{C}$ = average oxygen concentration within the red cell
C_0 = initial concentration of dissolved oxygen in the plasma
C_1 = equilibrium dissolved oxygen concentration in the plasma
D = diffusion coefficient
erf = error function
F = proportionality coefficient
P_a = average oxygen tension (partial pressure) in the plasma
$\bar{p}$ = average oxygen partial pressure in the red cell
R = chemical reaction rate expression
t = time
x = distance from the oxygen blood interface
∇^2 = del operator

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