A Comparison of Oxygen Transfer into Hemoglobin Solutions and Whole Blood Flowing in Rectangular Channels

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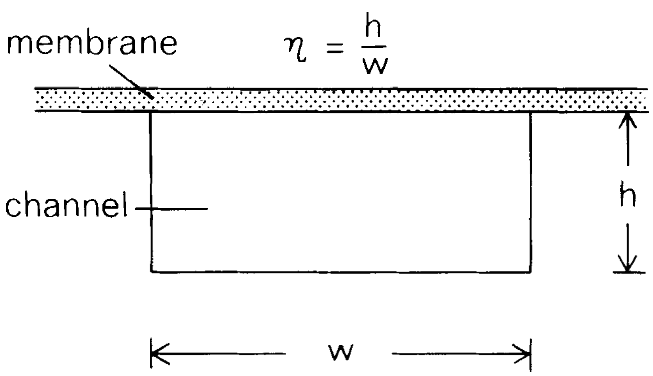

Fig. 1. Cross section of rectangular channel: *h* is the depth of the channel, w is the width, and η the aspect ratio.

In recent reviews on oxygen transport into blood flowing in artificial oxygenation devices, Colton (1976) and Dorson and Voorhees (1976) have concluded that the theory of oxygen transport into fluids flowing in laminar flow is well understood. Considerable experimental data are available to compare with theoretical predictions by either advancing front theory or numerical methods for blood flowing in devices with different configurations. The agreement between experimental data and theory for various well-defined flow geometries is generally satisfactory. According to Dorson and Voorhees (1976), there is only one report of an apparent discrepancy. Weissman (1973) found that oxygen transfer into blood flowing in rectangular channels greatly exceeds numerical predictions, despite the fact that such predictions are accurate when used with other geometries. A cross section of the rectangular channel is shown in Figure 1. Weissman reported that experimental oxygen uptake exceeded theoretical prediction when the aspect ratio η of the dimensions of the rectangular channel cross section was between 0.5 and 1. For aspect ratios considerably higher or lower than this range, the oxygen uptake approached that predicted by theory. The anomalously high oxygen uptake was not observed in water, and Weissman hypothesized that no obvious reasons, other than the possibility of secondary flows induced by non-Newtonian behavior, present themselves as explanation for the enhancement in gas transfer.

We have investigated the oxygen transfer to hemoglobin solutions and blood flowing in rectangular channels, with either an aspect ratio of 0.5 or 1, in order to test more closely the hypothesis of Weissman. The aim of this work is twofold: first, to reinvestigate the oxygen uptake anomaly of blood, and, second, to compare such results with the oxygen uptake of hemoglobin solutions of the same total hemoglobin content. Hemoglobin solutions are homogeneous, and their behavior in laminar flow is Newtonian (Schmid-Schönbein and Wells, 1971) so that they should conform to the theoretical predictions of Weissman.

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EXPERIMENTAL

Fresh bovine blood was obtained from a local slaughterhouse and heparinized. Hematocrits were determined with a microcentrifuge. Packed red blood cells, obtained from the same blood, were added if necessary to bring the hematocrit in the range of 39 to 43. The conditions used by Weissman were duplicated as closely as possible.

Hemoglobin solutions were prepared by repeated centrifugation and washing of the red blood cells with isotonic saline. A mixture of washed packed red blood cells and buffered saline ($pH = 7.4$) was then lysed by freeze thawing. Red blood cell membrane fragments were separated by centrifuging in tubes at 22 000 g for 20 min. The membranes and part of the solution in the bottom of the tubes were discarded. All preparations were performed at 4°C. To prevent bacterial growth 0.1 mg/ml streptomycin sulfate (Calbiochem, San Diego, Calif.) was added to the solutions (Richterich, 1969). Hemoglobin saturation was determined using the Lex-O_2-CON (Lexington Instruments Co., Waltham, Mass.).

The blood or hemoglobin solution was tonometered in a disk oxygenator with a gas mixture containing 5% carbon dioxide, nitrogen, and sufficient oxygen to bring the initial saturation of hemoglobin to 70%; this saturation was used in the experiments and maintained to within $\pm$ 1%. All experiments were conducted at room temperature (24° $\pm$ 1°C).

The rectangular channels employed had identical dimensions as those used by Weissman. The active test section was 152.5 cm long, the channel depth 0.165 cm, and the width 0.165 and 0.328 cm, giving aspect ratios of 1 and 0.5, respectively. The machining tolerance was such that cross-sectional dimensions were held constant with a maximum variance of $\pm$ 0.003 cm along the entire length of the channel, which included an inactive, membraneless inlet length which preceded the active test section to insure fully developed flow. The membrane material used was 127 μm thick silicone membrane obtained from Edward Laboratories (Santa Anna, Calif.). The membrane was stretched tightly over the channel.

The experimental apparatus is shown in Figure 2. The fluid of interest was pumped through the channel with an adjustable constant speed syringe pump (Braun, Melsungen, West Germany). A gas consisting of 95% oxygen and 5% carbon dioxide contacted the membrane at the gas side. After flowing through the channel, the fluid was collected with a second syringe which could be connected or disconnected to the same driving screw of the syringe pump. The collecting syringe was chosen to have a cross-sectional area about 2 to 3% smaller than the infusion

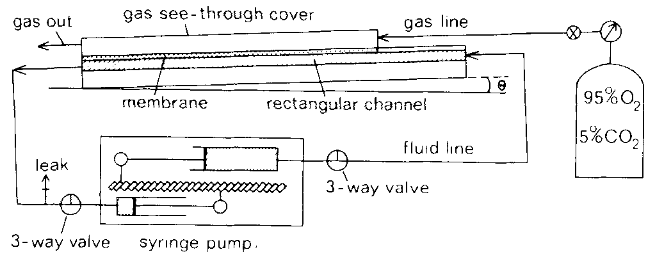

Fig. 2. Schematic diagram of the experimental apparatus.

syringe. A needle was utilized as a leak downstream of the channel through which the small stream of excess fluid was continually discarded during flow. This setup allowed for precise control of fluid flow. Further, by appropriately adjusting the height of the opening of the needle relative to the exit of the channel, and slightly tipping the channel a small degree θ (0 to 7 deg., depending on the flow rate), the membrane did not need to be supported and was completely flat along the entire length of the active test section of the channel. In this condition the membrane in contact with the fluid was nearly floating on the surface, and fluid disturbances could be visualized.

The experimental procedure was to adjust the setup so that the membrane was flat along the entire channel for the chosen flow rate and then to collect a sample after the channel was flushed out several times. Hemoglobin saturations were measured for both incoming and outcoming fluids. Since the Lex-O_2-CON has an accuracy of $\pm$ 1 saturation percent, the accuracy of the saturation difference ΔS is $\pm$ 2 saturation %.

RESULTS AND DISCUSSION

Ten different experimental runs were made, five each for blood and hemoglobin solutions. The average hematocrit for the blood was 42 and the total hemoglobin 14.7 g/100 ml (range 13.8 to 15.5 g/100 ml). The average hemoglobin concentration for the hemoglobin solutions was 14.5 g/100 ml which is the same as that of blood (range 13.6 to 15.0 g/100 ml). No systematic difference in the oxygen transfer was observed in these concentration ranges. Figures 3 and 4 show the experimental results of this study. The results of the oxygen uptake for blood and hemoglobin solutions are nearly identical. The blood results agree reasonably with the theoretical prediction by Weissman within experimental accuracy. The hemoglobin experiments also agree fairly well with Weissman's theory except that there is a definite deviation at the lowest flow rates investigated. The data measured by Weissman are seen to be considerably higher. We can only speculate about the higher data obtained by Weissman, but they may be due to the flow system he utilized. Weissman employed a roller pump downstream of the channel. When we utilized a roller pump (with ten individual rollers), we noticed that at the higher flow rates (~10 ml/min) the membrane would oscillate up and down. The pump was a Minipuls II (Gilson, Villiers-Le-Bel, France) with a roller housing diameter of 5 cm and roller diameter of 1.5 cm. If a small gas bubble was injected into the blood line, the flow of this bubble in the channel was not smooth but progressed in discrete movements, even at the lowest flow rates (~0.5 ml/min). Any of these events could disturb the boundary layer and lead to higher uptakes. None of the above phenomena occurred with the syringe pump; the flow was smooth. Another possibility in the Weissman system is that the membrane may have buckled inwards. This would have been difficult to observe, except in extreme cases, since the membrane was supported by porous metal foam. The oxygen transfer experiments into water were in agreement with Weissman's theory.

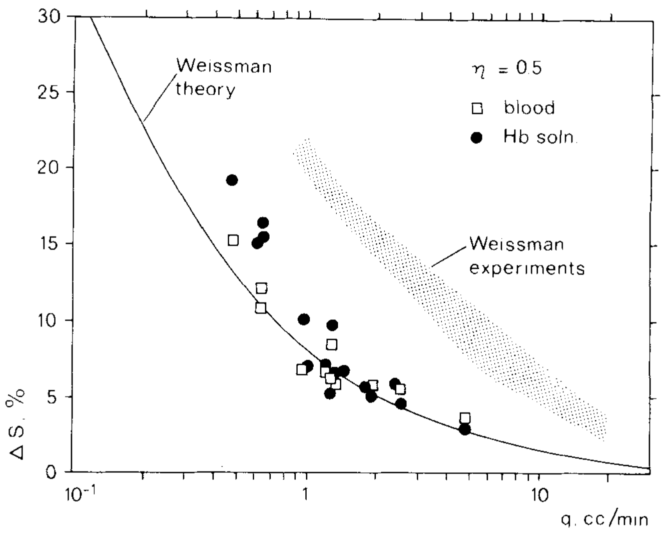

Fig. 3. Saturation increase ΔS vs. flow rate q in a rectangular channel with $\eta = 0.5$. The initial hemoglobin saturation is 70%. Oxygen transfer experiments into whole blood and hemoglobin solutions are compared with the experimental results and the theoretical predictions of Weissman.

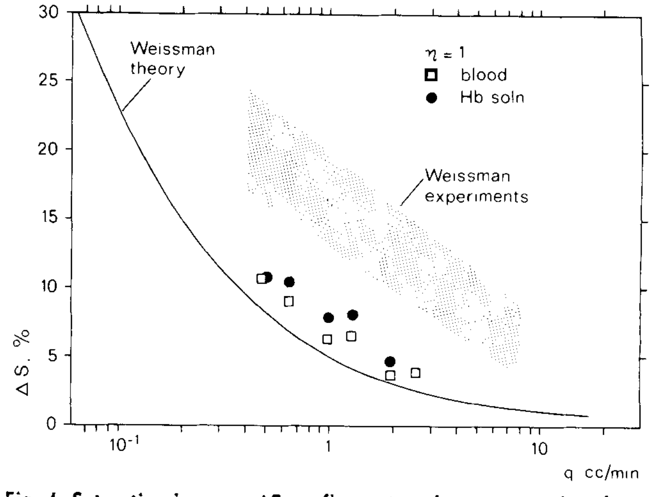

Fig. 4. Saturation increase ΔS vs. flow rate q in a rectangular channel with $\eta = 1$. The initial hemoglobin saturation is 70%. Oxygen transfer experiments into whole blood and hemoglobin solutions are compared with the experimental results and the theoretical predictions of Weissman.

The different results for blood and water, as obtained by Weissman, suggest either that the membrane did not buckle with the less viscous water, or that the flow disturbances significantly increase the oxygen transfer rate into reactive and heterogeneous fluids, but not into inert and homogeneous fluids.

The similar results obtained for both hemoglobin solutions and blood are internally consistent. The results on hemoglobin solutions should be in agreement with the theory of Weissman, since the solution is both homogeneous and Newtonian, in agreement with the assumptions made in the theory. The higher uptake by hemoglobin solutions vs. blood and theory at the lower flow rates in Figure 3 is caused by the higher oxygen diffusivity in the hemoglobin solutions. Although both systems have the same hemoglobin content, blood in addition contains plasma proteins which decrease the oxygen diffusivity (Stroeve, 1975). From previous available data (Goldstick and Fatt, 1970) we estimate the average oxygen diffusivity in the hemoglobin solutions as 1.37×10^{-5} cm^2/s at 24°C using a temperature correction of 2.5%/°C.

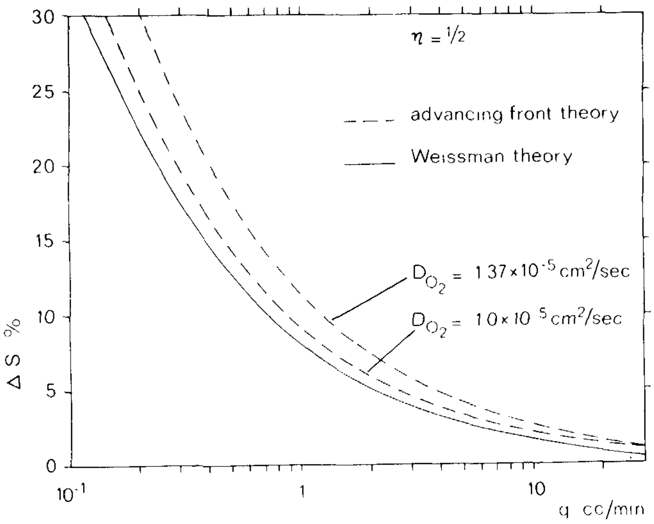

Fig. 5. Saturation increase ΔS vs. flow rate q in a rectangular channel with $\eta = 0.5$ as predicted by advancing front theory: Oomens and Spaan (1976) for oxygen diffusivities of 1.0×10^{-5} and 1.37×10^{-5} cm²/s and the theory of Weissman ($D_{O_2} = 1.0 \times 10^{-5}$ cm²/s.) Parameters used in the advancing front theory are those given in the text.

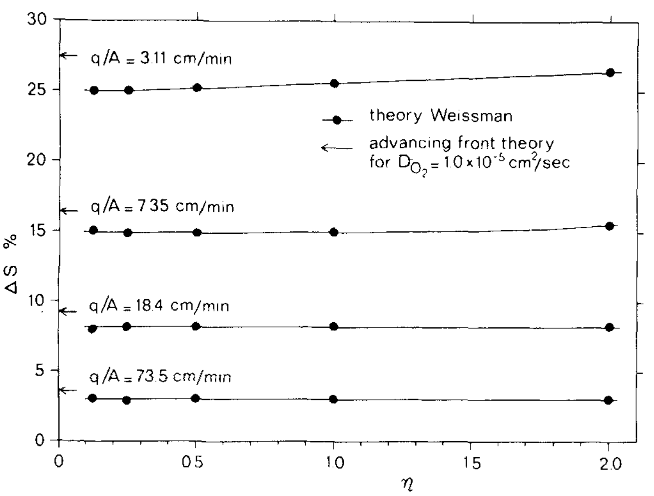

Fig. 6. Effect of aspect ratio on the saturation increase for various average flow velocities in the channels. The depth for all channels is 0.165 cm.

Weissman used an average diffusivity of 1.0×10^{-5} cm²/s to arrive at his theoretical lines. [For the blood in our experiments, we estimate that the average oxygen diffusivity is 1.19×10^{-5} cm²/s at 24°C, using heterogeneous diffusion theory (Stroeve et al., 1976a, 1976b).] Figure 5 shows a comparison of advancing front theory (Oomens and Spaan, 1976) with the theoretical results of Weissman for both a diffusivity of 1.0×10^{-5} and 1.37×10^{-5} cm²/s. If we accept Weissman's theory as correct, the advancing front theory gives a reasonable agreement at a diffusivity of 1.0×10^{-5} cm²/s. A diffusivity of 1.37×10^{-5} cm²/s for the hemoglobin solution gives a significant deviation only at the lower flow rates, in agreement with the experimental results (within experimental accuracy). The correction to Weissman's theoretical curve for an oxygen diffusivity of 1.37×10^{-5} cm²/s should be of the same order as the correction found for the advancing front theory. Similar curves can be constructed for $\eta = 1$.

The curves calculated from advancing front theory have been constructed using the following parameters: length of channel 152.5 cm, depth of channel 0.165 cm, hemoglobin concentration 2.1 mmole/l, initial hemoglobin saturation 70%, initial oxygen partial pressure in fluid 36 mm Hg, oxygen solubility in fluid 1.35×10^{-6} moles/l/mm Hg, gas phase oxygen partial pressure 722 mm Hg, membrane thickness 127 μm, and membrane permeability 2.91×10^{-14} gmole/s/cm/mm Hg. Inclusion of membrane resistance has no effect on the prediction of saturation increase for this channel depth. The influence of the saturation curve is also negligible for this oxygen gas pressure.

The advancing front theory used here is that derived for oxygen transport into blood flowing between infinite parallel plates, where one plate is permeable to gas. An objection can be raised with respect to comparing advancing front theory with a numerical solution for rectangular channels, where apparently three-dimensional laminar flow was used. However, Weissman calculated theoretical results numerically for a number of rectangular channels, all with the same depth. Figure 6 compares the saturation increase with aspect ratio for four different average velocities. The theoretical results appear to be virtually insensitive to the aspect ratio except at ΔS values greater than 15%. The insensitivity is interesting if we consider that the aspect ratio changes from 0.125 to 2.0, a factor of 16. The predictions of advancing front theory are shown for $\eta = 0$, for the same channel depth. If the numerical results of Weissman are realistic, the advancing front theory can be utilized to estimate oxygen transfer into blood or hemoglobin solutions flowing in rectangular channels for aspect ratios up to 1 (for the conditions of these experiments).

NOTATION

A = cross-sectional area of channel
D_{O_2} = oxygen diffusivity in blood
h = height of channel
q = blood flow rate
S = saturation: percentage of total hemoglobin in oxyhemoglobin form
w = width of channel
ΔS = change in saturation S
η = aspect ratio
θ = angle

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Direct Solution of the Isothermal Gibbs-Duhem Equation by an Iterative Method for Binary Systems

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The direct technique for numerically integrating the isothermal Gibbs-Duhem equation as demonstrated by Ljunglin (1962) is advantageous because it provides a single differential equation directly relating the experimental vapor pressure data to the vapor compositions to be calculated. For a binary system with vapor and liquid phases in equilibrium at low pressure, this equation is:

$$\frac{dy}{dx} = \frac{y(1-y)}{(y-x)} \frac{d \ln P}{dx} \tag{1}$$

As discussed by White and Lawson (1970) and Van Ness (1970), the stepwise integration of Equation (1) must always proceed in the direction of increasing pressure, or numerical instabilities occur. This presents only minor problems for binary systems; however, possibly for this reason, the technique has never been developed for multicomponent systems.

Mixon (1965) used a numerical relaxation technique to indirectly (through the excess Gibbs free energy) solve the isothermal Gibbs-Duhem equation and successfully applied the method to a ternary system. In this note, we have applied Mixon's numerical relaxation technique to a rigorous form of Equation (1). This new direct method of solution can, in theory, be extended to multicomponent systems. The validity of the basic equations and the viability of the numerical method are demonstrated by application of the method to four systems with highly nonideal vapor pressure curves.

Using the standard thermodynamic relationships developed in texts on phase equilibrium, we can show that the rigorous counterpart to Equation (1) is

$$[1 + (\alpha - 1)x]\Delta Z d \ln P/dx = (\alpha - 1) + x(1-x)$$
$$(\alpha - 1)\ [d \ln(\phi_1/\phi_2)/dx + d \ln \alpha/dx] \tag{2}$$

where

$$\alpha \equiv y(1-x)/x(1-y) \tag{3}$$

is the relative volatility

$$\Delta Z \equiv Z^V - Z^L \tag{4}$$

is the difference between the compressibility factors for the vapor and liquid phases, and

$$\phi_i = f_i/y_i P \tag{5}$$

is the vapor phase fugacity coefficient for component i.

In Equation (2), the relative volatility (α) has been chosen to describe the vapor phase composition because it is closely related to the cost of an appropriately designed distillation column for the separation of the components and because, unlike Equation (1), Equation (2) is well defined at the points $x = 0$, $x = 1$, and $\alpha = 1$. In particular

$$\text{at} \quad x = 0, \quad \alpha = 1 + \Delta Z\, d \ln P/dx \tag{6}$$

$$\text{at} \quad x = 1, \quad \alpha = 1/(1 - \Delta Z\, d \ln P/dx) \tag{7}$$

and

$$\text{at} \quad \alpha = 1, \quad \Delta Z\, d \ln P/dx = 0 \tag{8}$$

The term $d \ln(\phi_1/\phi_2)dx$ in Equation (2) is related to a vapor phase equation of state through

$$d \ln(\phi_1/\phi_2)/dx = [\partial \ln(\phi_1/\phi_2)/\partial y]_P\, dy/dx$$
$$+ [\partial \ln(\phi_1/\phi_2)/\partial \ln P]_y\, d \ln P/dx \tag{9}$$

in which dy/dx can be expressed in terms of α by

$$dy/dx = \frac{\alpha[x(1-x)d \ln \alpha/dx + 1]}{[1 + (\alpha - 1)x]^2} \tag{10}$$

An additional constraint on the $P - x$ curve at an azeotrope ($\alpha = 1$) can be developed by rearranging Equation (2) and applying l'Hospital's rule to give

$$1 - x\{\Delta Z d \ln P/dx - (1-x)$$
$$[d \ln \alpha/dx + d \ln(\phi_1/\phi_2)/dx]\}$$
$$= \frac{\Delta Z\, d \ln P/dx}{\alpha - 1} = \frac{\Delta Z\, d^2 \ln P/dx^2}{d \ln \alpha/dx} \tag{11}$$

Equation (11) is quadratic in $d \ln \alpha/dx$, and by requiring the discriminant in the quadratic formula to be positive,

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