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A DESIGN CALCULATION METHOD
FOR CAPILLARY-TUBE OXYGENATORS

by
Fernando Villarroel
Clifford E. Lanham

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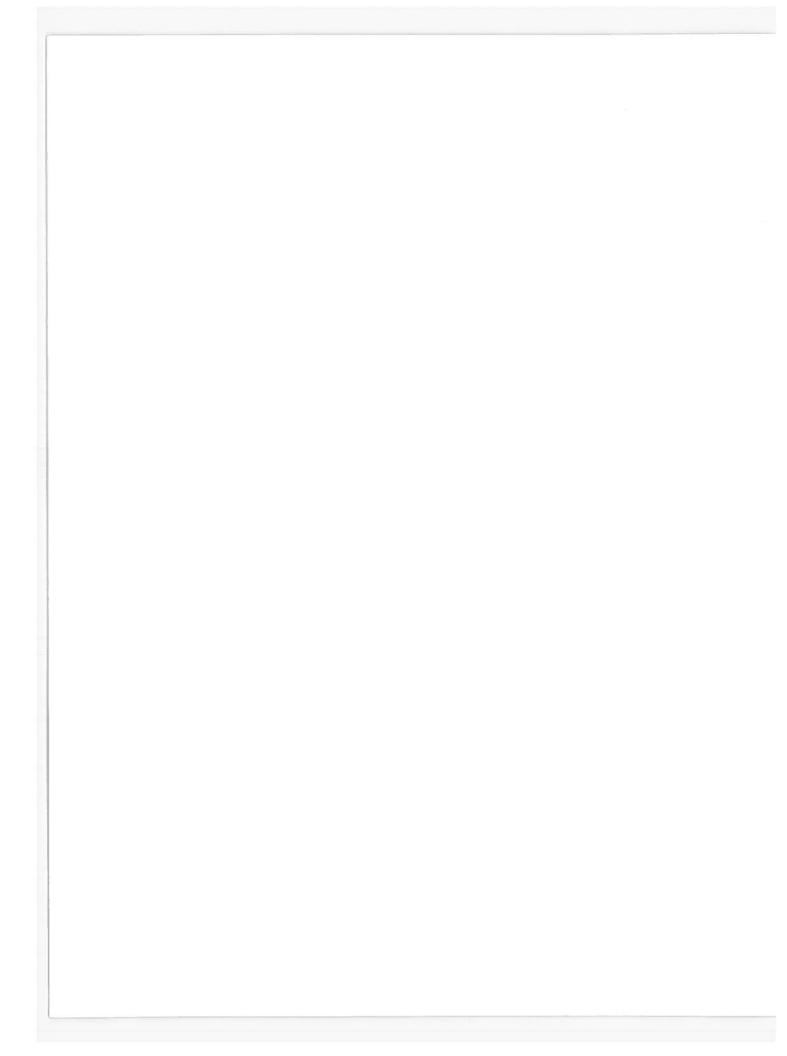
A DESIGN CALCULATION METHOD FOR CAPILLARY-TUBE OXYGENATORS

by
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Clifford E. Lanham

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ABSTRACT

A semi-empirical graphic method to predict the performance of capillary-tube artificial lungs has been developed from a mathematical model and an extensive amount of in vitro data obtained under precisely controlled conditions. This graphical technique predicts the performance of a given oxygenator for exchange of both oxygen and carbon dioxide for a wide range of blood flows and input blood conditions and greatly simplifies the analysis of data taken in evaluation procedures where precise control of test conditions is not achieved. Performance predictions for capillary-tube oxygenators obtained by this method are supported by preliminary in vivo data as well as by extensive in vitro data. The calculation further provides a simple means of designing or selecting a capillary oxygenator for application under known operating conditions. This method has indicated that, for the same blood flow rate, oxygenators staged in series are significantly more effective than when connected in parallel. This prediction has also been verified in the laboratory.

FOREWORD

This report summarizes work performed for the Surgical Directorate of the U.S. Army Medical Research and Development Command.

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1. INTRODUCTION

Heretofore, the design of blood oxygenators has been largely a trial-and-error procedure based on the intuition of the experienced investigator; a rigorous design method was not available. A comprehensive theoretical model of the gas exchange process in capillary blood oxygenators has been previously presented as has an accurate means of obtaining in vitro experimental data. Adjustment of the effective diffusivity has brought the theoretically predicted values into close agreement with those found in a series of precise in vitro experiments. This adjusted theoretical model allows for accurate graphical corrections to be made for all of the important parameters affecting gas transport. This has resulted in a simple and accurate method to predict the performance of capillary-tube oxygenators for both oxygenation and carbon dioxide removal over a wide range of conditions. Further, this calculation method provides an accurate means of designing oxygenators to meet any anticipated operating conditions.

2. THEORETICAL MODEL

2.1 Mathematical Analysis

The mathematical model used to describe and correlate the various phenomena occurring during the operation of capillary-tube oxygenators is based on the following equations:

$$\frac{1}{r} \frac{\partial}{\partial r} \left[r \frac{\partial C_1}{\partial r} \right] = (1 - r^2) \left[1 + \left(\frac{\partial S_1}{\partial C_1} \right)_{DH} \right] \frac{\partial C_1}{\partial \xi} + \left(\frac{\partial S_1}{\partial PH} \right)_{C_1} \frac{\partial PH}{\partial \xi}$$
 (1)

$$\frac{1}{r} \frac{\partial}{\partial r} \left[r \frac{\partial C_2}{\partial r} \right] = (1 - r^2) \left[1 + \left(\frac{\partial S_2}{\partial C_2} \right)_{pH} \right] \frac{\partial C_2}{\partial \xi} + \left(\frac{\partial S_2}{\partial S_1} \right)_{C_2} \frac{\partial S_1}{\partial \xi}$$
 (2)

where C_1 = concentration of oxygen in plasma

C2 = concentration of carbon dioxide in plasma

 $S_1 = S_1(C_1, pH) = total concentration of oxygen in whole blood$

 $S_2 = S_2(C_2, S_1) = total$ concentration of carbon dioxide in whole blood

r = r'/R = dimensionless radial parameter

r' = radial distance from the center of the tube

R = inside radius of the tube

 ξ = DZ/2Q = dimensionless axial parameter

D = diffusivity of the gas in whole blood

Z = axial distance from the entrance of the tube

Q = blood flow rate per tube

Villarroel, F., Lanham, C.E., Bischoff, K.B., Regan, T.M., and Calkins, J.M., "A Mathematical Model for the Prediction of Oxygen, Carbon Dioxide, and pH with Augmented Diffusion in Capillary Blood Oxygenators," <u>Blood Oxygenation</u>, D. Hershey (ed.), Plenum Press, New York, 1970.

Lanham, C.E., Grose, R.M., and Villarroel, F., "The Precise Control of Blood-Gas Concentrations and Blood Flowrate as a Key to Oxygenator Evaluation," Proc. Symp. on Flow (in press), Pittsburgh, Pennsylvania, May 1971.

The initial and boundary conditions are as follows: (1) the concentration of gases is uniform and constant at the entrance of each tube, (2) the radial gas flux at the center of each tube is zero, and (3) the gas flux in the membrane is equal to that in the blood at the blood-membrane interface.

In establishing the theoretical model, the following assumptions have been made: (1) the axial diffusion in both the blood and the membrane is negligible, (2) the system is isothermal, (3) the gas reactivity in blood is homogeneous and is given by the standard gas dissociation curves, (4) the velocity profile is parabolic, (5) the gas concentration outside of the tubes is constant, and (6) the gas transport process is diffusion-limited.

The differential equations, although functions of the dimensionless parameter r, show no explicit dependence on the parameter r' which varies between 0 and R. It follows that the radially averaged values of the concentrations C_1 and C_2 should be independent of the radius of the tube when the initial and boundary conditions are maintained constant, and if the basic assumptions are valid. In particular, the tubes must be sufficiently large to permit the assumption that the gas reactivity with blood is homogeneous in order for the solution to be valid. The radially averaged concentration of either gas is then only a function of the venous concentration of both gases, the partial pressures of both gases outside of each tube, the dimensionless axial parameter, and the wall characteristic G defined as

$$G = \frac{Ds}{\psi} \ln \frac{OD}{ID}$$
 (3)

where ψ = membrane permeability

s = gas solubility in plasma

OD = outside diameter of the tube

ID = inside diameter of the tube.

The wall characteristic is a measure of the effective resistance that the membrane offers to the gas transport. If the wall permeability is expressed in ml(STP)-cm/sec-cm-mmHg, the value of the diffusivity D should be expressed in cm²/sec, and the solubility, in ml(STP)/ml(blood) mmHg. The numerical value of the oxygen solubility in these units is 3.1×10^{-5} , and that for carbon dioxide is 6.2×10^{-4} .

To facilitate utilization of the calculation method, the normalized flow, Q^* , is defined by

$$Q^* = \frac{Q_B}{NZ} \frac{D_0}{D} \tag{4}$$

where Q_B = total blood flow rate through the oxygenator

N = number of tubes

 D_0 = diffusivity of the gas in whole blood when the hematocrit is 42.

This new variable may be used to replace the abstract dimensionless parameter $\boldsymbol{\xi}$ by using the relationship

$$Q^* = \frac{\pi D_0}{2\xi} \tag{5}$$

A computer program for the numerical solution of the model was run for a variety of conditions assuming a value for the diffusivity D_0 . Correction factors intended to normalize experimental data to selected standard conditions were calculated from the computer results for the assumed value of the diffusivity. The computer-predicted curve for standard conditions was compared with a large amount of normalized data. This process was repeated changing the values of D_0 , until the standard curve predicted by the computer agreed with the normalized data for oxygen and carbon dioxide. The standard conditions selected for this study are:

Hematocrit = 42

Hemoglobin concentration = 15 g-percent (grams/100 ml blood)

Venous saturation = 60 percent

Venous carbon dioxide partial pressure = 45 mmHg

G = 0.0675 for oxygen

G = 0.0259 for carbon dioxide.

The above values of the wall characteristic G correspond to those of medical grade silicone rubber tubing (Silastic, Dow Corning) with OD/ID = 2.08 and with an oxygen permeability of 6.74×10^{-9} ml(STP)-cm/sec-cm-mmHg and a carbon dioxide permeability of 3.52×10^{-8} ml(STP)-cm/sec-cm-mmHg.

2.2 <u>Normalizing Procedure</u>

Several normalizing factors were determined for oxygen and carbon dioxide transport. The final factors were obtained from the computer results for the optimal gas diffusivities found in this study. These corrections are practically independent of each other and not a strong function of the diffusivity.

The normalizing factors relate the values of ΔPS and ΔPCO_2 measured at any conditions to $\Delta PS*$ and ΔPCO_2* . (The asterisk denotes the values that would be measured at standard conditions including standard wall characteristics.) The normalizing factors are defined as

$$\alpha_{x} = \frac{\Delta PS^{\circ}}{\Delta PS} \tag{6}$$

$$\beta_{\rm Y} = \frac{\Delta \rm PCO_2^{\circ}}{\Delta \rm PCO_2} \tag{7}$$

where

 α_x = oxygen normalizing factors (fig. 1 and 2)

 $\beta_{\rm V}$ = carbon dioxide normalizing factors (fig. 3 and 4)

x,y = subscripts indicate type of normalizing factor

 $(PS)_n$ = arterial blood oxygen percent saturation

 $(PS)_{V}$ = venous blood oxygen percent saturation

 $\Delta PS = (PS)_A - (PS)_V = \text{change in percent saturation of oxygen}$

Galletti, P.M., Snider, M.T., and Silbert-Aiden, D., "Gas Permeability of Plastic Membranes for Artificial Lungs," Med. Res. Eng., 5, 2, pp. 20-23, 1966.

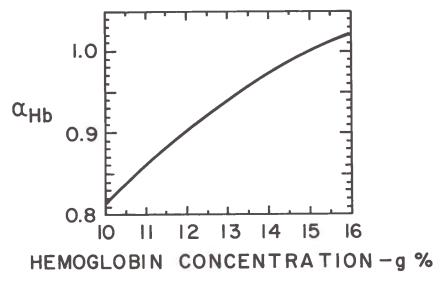


Figure I. Hemoglobin normalizing factor for oxygen transport.

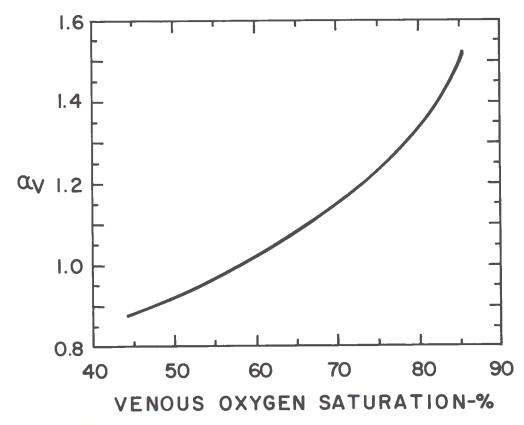


Figure 2. Venous saturation normalizing factor for oxygen transport.

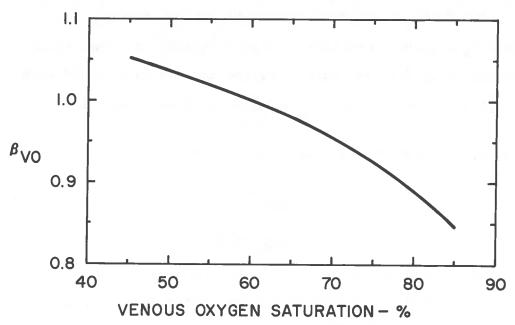


Figure 3. Venous saturation normalizing factor for carbon dioxide transport.

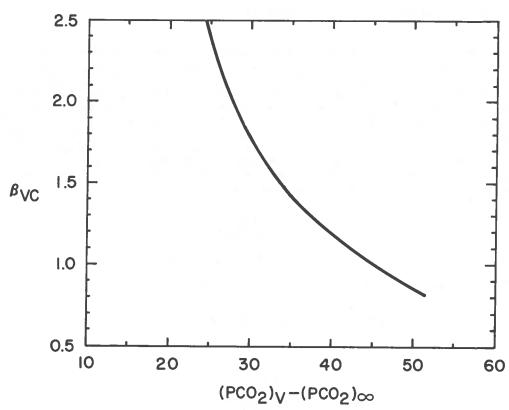


Figure 4. Venous carbon dioxide partial pressure normalizing factor for carbon dioxide transport.

 $\Delta PS^{\circ} = \Delta PS$ at standard conditions for any given G

(PCO₂)_v = partial pressure of carbon dioxide in venous blood

(PCO₂)_A = partial pressure of carbon dioxide in arterial blood.

 $\Delta PCO_2 = (PCO_2)_V - (PCO_2)_A = change in partial pressure of carbon dioxide$

 $\Delta PCO_2^{\circ} = \Delta PCO_2$ at standard conditions for any given G

and

$$\alpha_{G} = \frac{\Delta PS^* + A}{\Delta PS^\circ + A} \tag{8}$$

$$\beta_{G} = \frac{\Delta PCO_{2} * + B}{\Delta PCO_{2} ° + B}$$
 (9)

where

 $\alpha_{\rm G}$ = wall correction factor for oxygen (fig. 5)

 β_c = wall correction factor for carbon dioxide (fig. 6)

 $\Delta PS* = \Delta PS$ at standard conditions for G = 0.0675

 $\Delta PCO_2^* = \Delta PCO_2$ at standard conditions for G = 0.0259

A,B = constants (fig. 5 and 6).

The effects of parameters influencing blood oxygenation, other than those for which correction factors have been generated, were studied using the mathematical model. It was found that the removal of carbon dioxide has an insignificant effect on the oxygen transport. It was also found that when the oxygen dissociation curve is displaced between a P50 (oxygen partial pressure at 50 percent saturation) of 21 and 33 mmHg, no significant effect is observed in the arterial oxygen saturation for a given set of other initial conditions. Insight into the reason for this result may be obtained by manipulation of equation (1) as was suggested by M.H. Weissman of Carnegie-Mellon University. Rearranging this equation for constant pH gives

$$\left(\frac{\partial C_1}{\partial \xi}\right)_{\text{pH}} = \frac{\frac{1}{r} \frac{\partial}{\partial r} \left[r \left(\frac{\partial C_1}{\partial r}\right)_{\text{pH}}\right]}{(1 - r^2) \left[1 + \left(\frac{\partial S_1}{\partial C_1}\right)_{\text{pH}}\right]} \tag{10}$$

but $C_1 = C_1(S_1, pH)$, and at constant pH, we have

$$\left(\frac{\partial C_1}{\partial \xi}\right)_{\text{DH}} = \left(\frac{\partial C_1}{\partial S_1}\right)_{\text{DH}} \left(\frac{\partial S_1}{\partial \xi}\right)_{\text{DH}}$$
(11)

or

$$\left(\frac{\partial C_1}{\partial \xi}\right)_{\text{pH}} = \frac{\left(\frac{\partial S_1}{\partial \xi}\right)_{\text{pH}}}{\left(\frac{\partial S_1}{\partial C_1}\right)_{\text{pH}}} \tag{12}$$

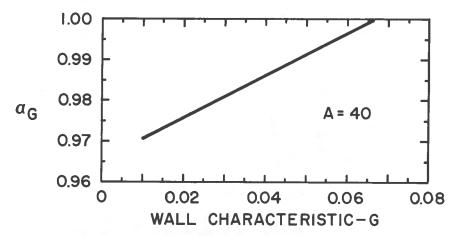


Figure 5. Membrane normalizing factor for oxygen transport.

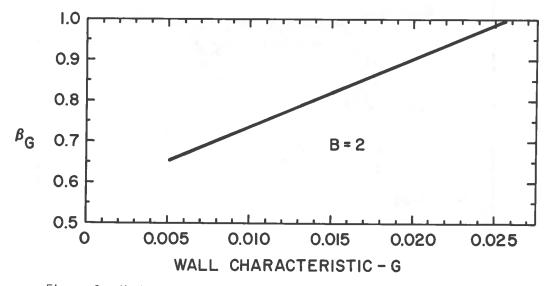
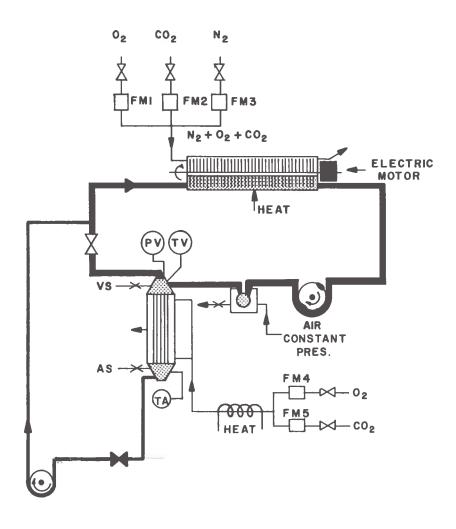


Figure 6. Membrane normalizing factor for carbon dioxide transport.

Substituting equation (12) into equation (10) and rearranging yields:

$$\left(\frac{\partial S_{1}}{\partial \xi}\right)_{pH} = \frac{\frac{1}{r} \frac{\partial}{\partial r} \left[r \left(\frac{\partial C_{1}}{\partial r}\right)_{pH}\right]}{(1 - r^{2})} \frac{\left(\frac{\partial S_{1}}{\partial C_{1}}\right)_{pH}}{1 + \left(\frac{\partial S_{1}}{\partial C_{1}}\right)_{pH}}$$
(13)

Over most of the range of the oxygen dissociation function, the value of its slope, $\partial S_1/\partial C_1$, is large, and the second term on the right of equation (13) is approximately one. In this way, the nonlinear effect of the oxygen dissociation curve is practically eliminated from the differential equation over a wide range of oxygen saturation.



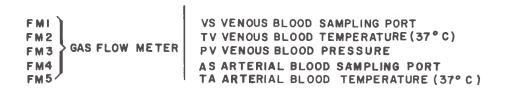


Figure 7. Experimental setup.

3. EXPERIMENTAL METHODS AND RESULTS

3.1 In Vitro Experimental Methodology

The *in vitro* experimental methodology² is based on the precise control of the initial conditions and flow rate of the blood. The blood flow through the oxygenator (fig. 7) is produced and measured using a calibrated, low-flow roller pump. The venous blood is continuously recirculated through a rotating-disk gas exchanger in which the gas partial pressures are controlled to any desired level within the range of interest to an accuracy of ±1 mmHg. The temperature throughout the system is maintained at 37°C.

The methodology uses stored human blood (American Red Cross) that is not more than five days old. This blood is mixed with an isotonic solution of glucose, phosphate, inosine, and sodium bicarbonate and equilibrated for one hour in the venous blood circuit of the test apparatus. After a final adjustment of the pH to 7.40, the blood has a P50 (oxygen partial pressure at 50 percent saturation) of 21.7 \pm 2.3 mmHg, and the oxygen dissociation curve does not shift significantly during the remainder of the experiment (approximately three hours).

Experimental data includes measurements of pH and the partial pressures of oxygen and carbon dioxide (Model 16 Gas Analyzer, Corning Scientific Instruments), and precise spectrophotometric measurements (IL-182 CO-Oxymeter) of total hemoglobin, carboxyhemoglobin, and percent oxygen saturation. Extreme care must be taken in measuring partial pressures of carbon dioxide to obtain meaningful results. Enough time must be allowed for each reading of $\rm CO_2$ to permit real equilibrium with the sample. Further, the instrument must be calibrated after each point to insure accurate readings.

The experimental oxygenators used for these tests were made in our laboratories from medical grade silicone rubber tubing. The tubes are arranged in two straight parallel rows separated by about 0.2 in. Gas distribution manifolds, located at each end of the rows of tubes, inject pure oxygen through a series of nozzles into the center area between the rows. The results of early tests with oxygenators in which no space was left between tubes of the same row showed very poor and erratic carbon dioxide transport but no significant effect on the transport of oxygen. Tests conducted with oxygenators in which the tubes were separated by at least one tube diameter showed consistent carbon dioxide data. This tube separation allows adequate circulation of the gas around the tubes and eliminates carbon dioxide accumulation, which considerably reduces the carbon dioxide transport driving force.

3.2 In Vitro Experimental Results

Table I summarizes the range of oxygenation test conditions for which data were obtained. Normalized oxygen data for hematocrits between 40 and 42 are plotted in figure 8. Figure 8 also shows the theoretical prediction for a diffusivity of oxygen in whole blood of 2 \times 10 $^{-5}$ cm $^2/\mathrm{sec}$. Although the theoretical curve is in close agree-

Lanham, C.E., Grose, R.M., and Villarroel, F., "The Precise Control of Blood-Gas Concentrations and Blood Flowrate as a Key to Oxygenator Evaluation," Proc. Symp. on Flow (in press), Pittsburgh, Pennsylvania, May 1971.

Table I. Summary of Oxygenator Test Conditions

 $(PCO_2)_V = 45 \pm 5 \text{ mmHg}$ T = 37°C

 $P50 = 21.7 \pm 2.3 \text{ mmHg}$

		TU	BING [†]		В	LOOD	
Symbol (fig. 8 and 9)	N	L	ID	OD	PS _V	Hct	Active Hb
		(in.)	(in.)	(in.)	(%sat)	(%)	(g%)
\bigcirc	60	5.0	0.037	0.020	73	40	12.8
	100	11.4	0.025	0.012	67-72	40	13.3
+	62	9.8	0.037	0.020	65-71	42	13.7
	100	9.8	0.025	0.012	71-74	41	12.8
∇	100	10.0	0.025	0.012	50-58	42	13.8
×	99	9.8	0.025	0.012	56-60	41	13.4
*	62	10.0	0.037	0.020	52-60	42	12.7
*	62	10.0	0.037	0.020	76	41	12.8
⊛	62	9.8	0.037	0.020	52-62	41	12.8
Δ	31	74.5	0.037	0.020	79-83	37	12.2
0	60	5.0	0.037	0.020	66-70	33	11.7
	100	10.0	0.025	0.012	75	35	12.1
	100	9.8	0.025	0.012	89-91	35	12.1
Δ	62	10.0	0.037	0.020	52-54	34	10.7
$\otimes_{\mathbb{R}^n}$	62	10.0	0.037	0.020	81	32	10.3
Θ	62	9.8	0.037	0.020	54	32	10.3

⁺ Silicone rubber (medical grade), Silastic, Dow Corning, Michigan

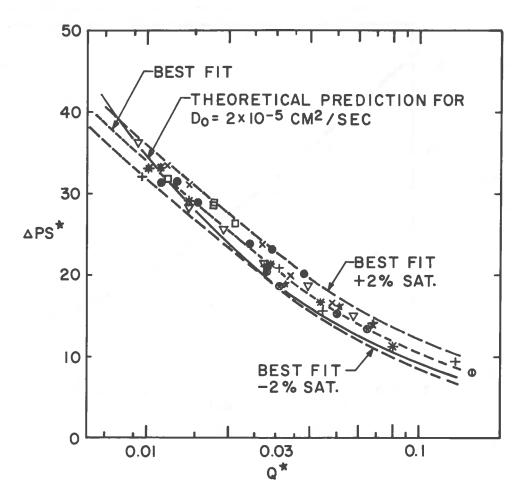


Figure 8. Oxygen data for hematocrits from 40 to 42.

ment with the experimental values, the best-fit curve was used for the calculation method. All the data shown in figure 8 are less than two percent saturation from the adjusted theoretical curve.

The diffusivity calculated with this procedure is surprisingly high and is close to that reported for pure plasma. This result suggests that the diffusivity, or at least the effective diffusivity, is not a strong function of the hematocrit. To prove this point, several groups of data were obtained at low hematocrit, normalized, and plotted in figure 9 assuming that the ratio D_0/D in equation (4) remains constant and equal to one at any hematocrit. The agreement between the data and the adjusted theoretical curve suggests that this assumption is valid.

Normalizing data for carbon dioxide, obtained in experiments made after fixing the distribution of the tubes, are shown in figure 10. Most of the points fall close to the curve for a carbon dioxide diffusivity in whole blood of $1.60 \times 10^{-5}~{\rm cm}^2/{\rm sec}$.

Hershey, D. and Karnant, T., "Diffusion Coefficients for Oxygen Transport in Whole Blood," AIChE J., 14, 6, p. 969, 1968.

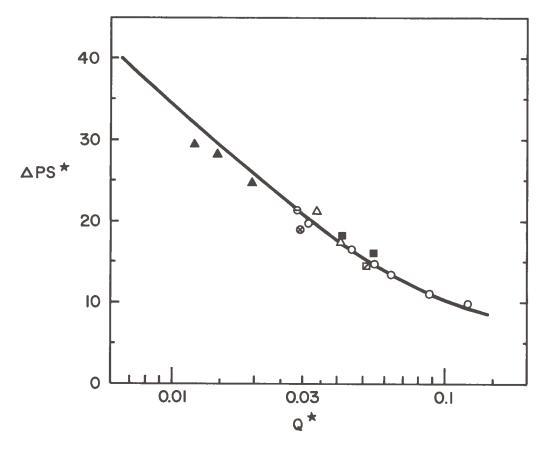


Figure 9. Oxygen data for low hematocrits.

3.3 Preliminary In Vivo Results

A small oxygenator model (62 tubes, 10 in. long, 0.037 in. OD, and 0.020 in. ID) was brought to the Animal Test Facility of Brown University to be tested in vivo by Dr. P.M. Galletti's group. 5 test was conducted using a live sheep, and the HDL oxygenator model was connected in parallel with a larger oxygenator unit that processed most of the blood. Their carbon dioxide measuring system could not be used because the construction of our device did not permit the collection of all the gas from the oxygenator model and because the gas flow to the oxygenator was high to provide the necessary ventilation (very low output concentration of carbon dioxide). On the other hand, their carbon dioxide partial pressure measurements (which they do not use for transport calculations) are not accurate because the instrument is not recalibrated after each point. However, the $in\ vivo$ data on oxygen transport showed good agreement with in vitro data previously obtained in our laboratory using the same oxygenator. The normalized data together with the standard curve (adjusted curve for $D = 2 \times 10^{-5}$ cm²/sec) is shown in figure 11.

Galletti, P.M., Richardson, P.D., and Snider, M.T., "Blood Oxygenator Testing and Evaluation," NIH Annual Report NIH-69-2047-1, 1971.

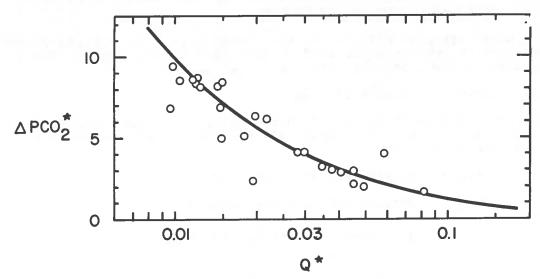


Figure IO. Carbon dioxide data.

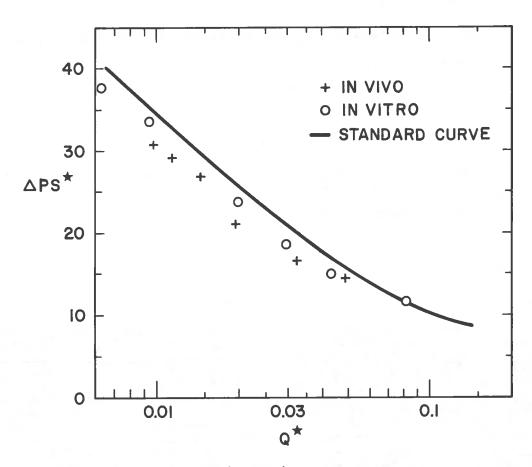


Figure II. In vivo and in vitro test results.

4. CALCULATION AND DESIGN METHOD

A simple graphic calculation and design method for capillary-tube oxygenators evolved from the studies described in this paper. The calculation method, step by step, is as follows:

Step 1: Compute
$$Q* = \frac{Q_B}{LN}$$

where the flow Q* is in ml/min/in./tube, the total blood flow $Q_{\rm B}$ is in ml/min, L is the length of the tubes in inches, and N is the number of tubes.

Step 2: Obtain APS* and APCO2* from figure 12.

Step 3: Compute the wall characteristic G.

$$G = \frac{6.2 \times 10^{-10}}{\psi_{Oo}} \ln \frac{OD}{ID} \text{ for oxygen}$$

$$G = \frac{9.9 \times 10^{-9}}{\psi_{\text{CO}_2}} \, \ln \frac{\text{OD}}{\text{ID}} \quad \text{for carbon dioxide}$$

where $\psi_{\mbox{\scriptsize O}_2}$ and $\psi_{\mbox{\scriptsize CO}_2}$ are in ml(STP)-cm/sec-cm-mmHg.

Step 4: Obtain $\alpha_{\mbox{\scriptsize G}}^{}$, $\beta_{\mbox{\scriptsize G}}^{}$, A, and B from figures 5 and 6.

Step 5: Compute ΔPS° and ΔPCO_{2}°

$$\Delta PS^{\circ} = \frac{\Delta PS^* + A}{\alpha_G} - A$$

$$\Delta PCO_2^{\circ} = \frac{\Delta PCO_2^{*} + B}{\beta_G} - B$$

Step 6: Obtain α_{Hb} and α_{V} from figures 1 and 2 and β_{VO} and β_{VO} from figures 3 and 4.

Step 7: Compute APS and APCO2

$$\Delta PS = \frac{\Delta PS^{\circ}}{\alpha_{Hb}\alpha_{V}}$$

$$\Delta PCO_2 = \frac{\Delta PCO_2^{\circ}}{\beta_{VO}^{\beta}_{VC}}$$

The design of capillary-tube oxygenators may also be accomplished for any chosen venous conditions, any desired ΔPS , ΔPCO_2 , and blood flow rate, and any chosen tube-wall properties by applying the above equations. The designer begins with ΔPS and uses the given blood conditions and wall properties to obtain Q*. With this value of Q*, one follows the above calculation method for carbon dioxide transport through the calculation of ΔPCO_2 °. Then, using the relation in step 7 with the desired ΔPCO_2 , one may obtain the necessary partial pressure of carbon dioxide outside the tubes $(PCO_2)_{\infty}$ by calculating the value of β_{VC} and using figure 4. From the value of Q* and the desired blood flow rate Q_B , one obtains the LN product from which the length and number of tubes may be chosen with due consideration of the relation of the length to pressure drop.

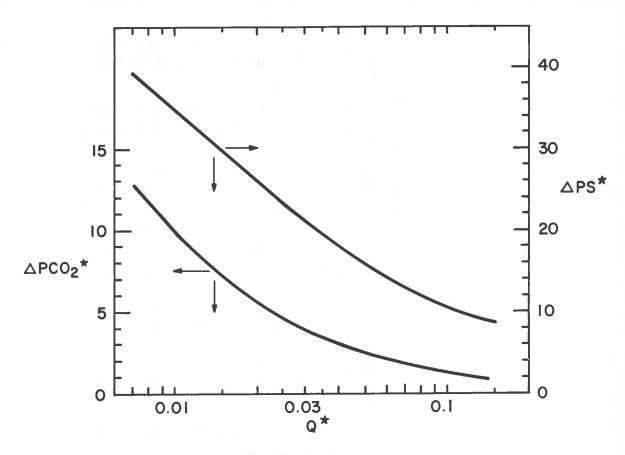


Figure 12. Standard curves.

5. STAGING OXYGENATORS IN SERIES

The shape of the curves shown in figure 12 suggests that the overall gas transport of an oxygenator system with two oxygenator units staged in series is more efficient than if the oxygenator units are connected in parallel. This may be demonstrated by the following example.

Consider venous blood at the standard conditions defined in this paper flowing at 5.5 liter/min through two oxygenator units made of 20,000 tubes, 10 in. long, with a standard oxygen wall characteristic of 0.0675. With $\Delta PS^*=22.0$ from figure 12, the differential saturation for the first unit is 22.0 percent. The arterial saturation for the first unit, which is 82 percent, is the sum of the standard venous saturation (60 percent) and the differential saturation (22.0 percent). This is the venous saturation for the second unit. From figure 2, α_{γ} for this venous saturation is 1.39. Then the differential saturation for the second unit becomes 15.8 (22.0/1.39), and the final arterial saturation is 97.8 percent.

In contrast, if the same two oxygenator units were connected in parallel, the flow through each one of these units would be only one half of the total flow, and Q* for each of them would be 0.0138. In this case, the differential saturation would be 30.4 percent, and the final output arterial saturation would be only 90.4 percent. To obtain

Table II. Data for Staged Oxygenators

7.35		(PCO ₂) _A	(mmHg)	44.6	44.0	43.3	42.4
Ig (@pH = 7.4) pH _V = 7.26 to 7.35	VALUES	PSA	(%sat)	75.8	75.3	76.7	76.6
mMHg (@ph	PREDICTED VALUES	ΔPC0 ₂	(mmHg)	6.1	2.5	3.7	4.1
Hct = 41 P50 = 20.5 mmHg (@pH = 7.4) T = 37° C pH $_{ m V}$ = 7.26 to		ΔPS	(%sat)	13.7	16.8	21.2	24.6
Hct P50 T =		∆PC0 ₂	(mmHg)	3.0	4.0	6.0	3.0
0.037 in. 0.020 in. 13 g-percent		∇PS	(%sat)	13.9	17.4	20.8	23.9
OD = 0.037 in. ID = 0.020 in. Hb = 13 g-perc	UES	Ò	(ml/min) (%sat) (mmHg)	41.75	30.60	20.30	17.56
0 1 4	EXPERIMENTAL VALUES	(PCO ₂) _A	(mmHg)	43.5	42.5	43.0	41.5
62 tubes 9.8 in. 10.0 in.	EXPERI	(PC0 ₂) _V	(mmHg)	46.5	46.5	47.0	46.5 41.5
Z		PSA	(%sat)	76.0	75.9	76.3 92.0	75.9 94.0
		PS_{V}	(%sat)	62.1 76.0	58.5 75.9	55.5 76.3	52.0 75.9
		Stage No.		1st 2nd	lst 2nd	1st 2nd	lst 2nd

the same final output arterial saturation as that given by the units in series, Q* for each unit in parallel should be 0.0078, and the total flow would be 3.12 liter/min. This result shows that the same oxygenation is obtained with an increase of 76 percent in the total flow through the units staged in series with respect to the flow through the units connected in parallel.

Some experimental data was taken to confirm the validity of the predictions for staged oxygenators. Table II shows good agreement between the experimental results and the predictions calculated using the graphic method.

6. INTERNAL PROFILES

Theoretical studies have suggested that the removal of carbon dioxide generates a radial pH gradient^{1,6} that in some cases may produce a high pH near the wall. Calkins' studies⁶ were made with pure plasma and water, while Villarroel et al.¹ computed the pH using a simplified form of the Henderson-Hasselback equation and ignored the last term in equations (1) and (2). Thus, in each case, the buffering effect of the hemoglobin contained in the erythrocytes was not considered.

The internal pH gradient obtained in this investigation for the standard initial conditions (sec 2.1) and with zero concentration of carbon dioxide outside of the capillary tubes is plotted in figure 13. The curves indicate that the pH at the wall is below 7.85 in spite of the low local partial pressure of carbon dioxide at the wall (fig. 14). It is interesting to note in figure 14 that the cup-mixed average partial pressure of carbon dioxide for $\xi=0.5$ is already below the normal physiological arterial condition. A similar family of curves in which the local oxygen partial pressure is plotted against the dimensionless radius is shown in figure 15.

7. CONCLUSIONS

A hybrid semi-empirical graphic method to predict the performance of capillary-tube artificial lungs has been developed from a mathematical model, and an extensive amount of in vitro data has been obtained under precisely controlled conditions. This method predicts the performance of a given oxygenator with a wide range of blood flows and input blood conditions and greatly simplifies the analysis of data obtained in evaluating procedures where precise control of of conditions is not achieved. The method also provides a simpler means of designing or selecting a capillary oxygenator for application under known operating conditions.

The effective oxygen diffusivity in whole blood was determined to be 2 \times 10⁻⁵ cm²/sec practically independent of hematocrit between 32 and 42. Also, the diffusivity of carbon dioxide is 1.6 \times 10⁻⁵ cm²/sec.

Villarroel, F., Lanham, C.E., Bischoff, K.B., Regan, T.M., and Calkins, J.M., "A Mathematical Model for the Prediction of Oxygen, Carbon Dioxide, and pH with Augmented Diffusion in Capillary Blood Oxygenators," <u>Blood Oxygenation</u>, D. Hershey (ed.), Plenum Press, New York, 1970.

⁶ Calkins, J.M., "Nonequilibrium CO₂ Transfer in Tubular Membrane Oxygenators," PhD Thesis, University of Maryland, 1971.

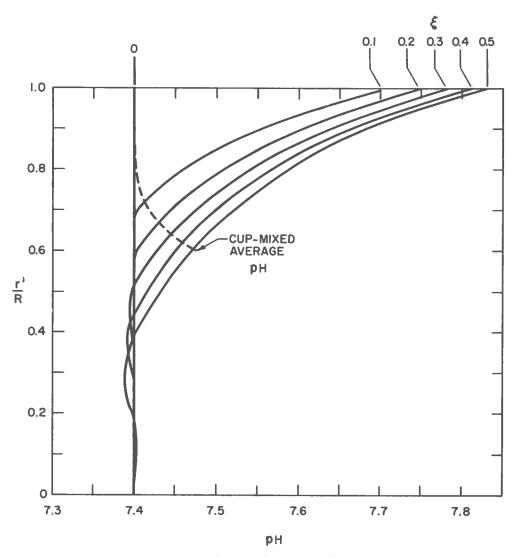


Figure 13. Internal pH profiles.

Preliminary $in\ vivo$ data showed a remarkable agreement with $in\ vitro$ data obtained with the same oxygenator unit. This agreement demonstrates the effectiveness of the $in\ vitro$ testing apparatus and of the data normalizing procedures.

8. LITERATURE CITED

- Villarroel, F., Lanham, C.E., Bischoff, K.B., Regan, T.M., and Calkins, J.M., "A Mathematical Model for the Prediction of Oxygen, Carbon Dioxide, and pH with Augmented Diffusion in Capillary Blood Oxygenators," <u>Blood Oxygenation</u>, D. Hershey (editor), Plenum Press, New York, 1970.
- Lanham, C.E., Grose, R.M., and Villarroel, F., "The Precise Control of Blood-Gas Concentrations and Blood Flowrate as a Key to Oxygenator Evaluation," Proc. Symp. on Flow, Pittsburgh, Pennsylvania, May 1971 (in press).

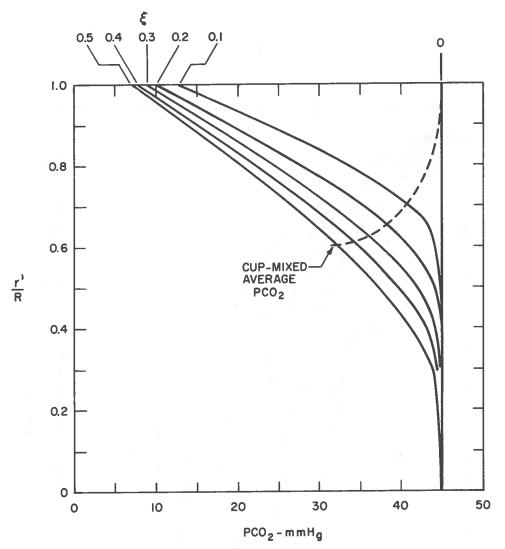


Figure 14. Internal PCO₂ profiles.

- 3. Galletti, P.M., Snider, M.T., and Silbert-Aiden, D., "Gas Permeability of Plastic Membranes for Artificial Lungs," Med. Res. Eng., 5, 2, pp. 20-23, 1966.
- Hershey, D. and Karnant, T., "Diffusion Coefficients for Oxygen Transport in Whole Blood," AIChE J., <u>14</u>, 6, p. 969, 1968.
- Galletti, P.M., Richardson, P.D., and Snider, M.T., "Blood Oxygenator Testing and Evaluation," NIH Annual Report NIH-69-2047-1, 1971.
- 6. Calkins, J.M., "Nonequilibrium CO₂ Transfer in Tubular Membrane Oxygenators," PhD Thesis, University of Maryland, 1971.

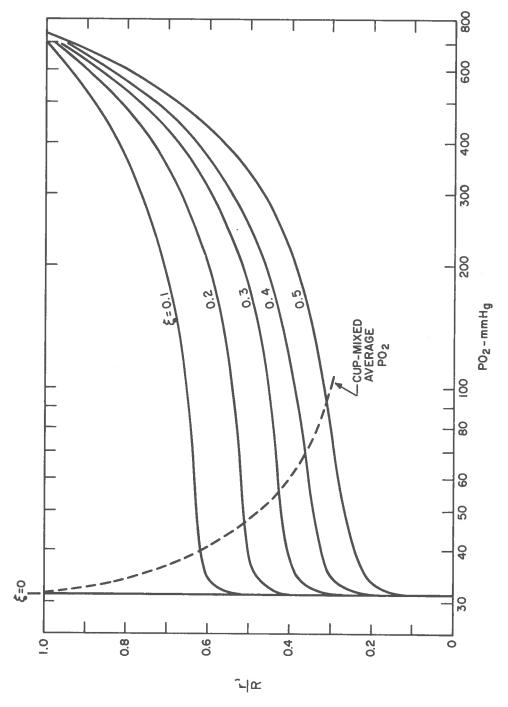


Figure 15. Internal PO_2 profiles.

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A semi-empirical graphic method to predict the performance of capillary-tube artificial lungs has been developed from a mathematical model and an extensive amount of in vitro data obtained under precisely controlled conditions. This graphical technique predicts the performance of a given oxygenator for exchange of both oxygen and carbon dioxide for a wide range of blood flows and input blood conditions and greatly simplifies the analysis of data taken in evaluation procedures where precise control of test conditions is not achieved. Performance predictions for capillary-tube oxygenators obtained by this method are supported by preliminary in vivo data as well as by extensive in vitro data. The calculation further provides a simple means of designing or selecting a capillary oxygenator for application under known operating conditions. This method has indicated that, for the same blood flow rate, oxygenators staged in series are significantly more effective than when connected in parallel. This prediction has also been verified in the laboratory.

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