Mathematical model and experimental setup of extracorporeal blood oxygenators

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Abstract
To study the oxygen mass transfer in extracorporeal membrane oxygenators, experiments were performed in a mini-oxygenator. Secondly, a mathematical model to simulate this system was developed. The mini-oxygenator used in this experimental setup is composed of a rectangular channel and an oxygen chamber, slit. The liquid flows in the rectangular chamber with dimension of $2B \times 2X \times Z$, with $2B \ll 2X, Z$. At the interface between these two compartments, there is a biocompatible membrane. For the experimental procedures, the slit was in a closed loop with a peristaltic pump upstream, and a reservoir downstream, where the oxygen concentration was measured by an oxygen sensor. Through a series of experiments, various charts were plotted with oxygen concentration over time. With these experimental results, the overall mass transfer coefficients were calculated on the slit system. A mathematical model to simulate the slit was developed and solved using the finite differences method. The effects of the oxygen pressure, height of rectangular channel, water flow, mass transfer coefficient and membrane dimensions were investigated on the oxygen concentration over time via the developed mathematical model. The model results are in line with the experimental results for: mass transfer coefficient, membrane dimension, oxygen pressure and channel height. However, for the velocity, the results are dissociated, which evidences the need for improvements on the model.

Keywords: mass transfer in gas/liquid; extracorporeal blood oxygenator; hemocompatible membranes; finite differences

1. Introduction
The function of the blood circulation is to deliver nutrients and oxygen to all cells in the body. Circulation is divided into systemic circulation and pulmonary circulation. Systemic circulation carries oxygenated blood away from the heart to the body, and returns deoxygenated blood back to the heart. Pulmonary circulation transports oxygen-poor blood from the right ventricle to the lungs where carbon dioxide diffuses out of the blood cell into the alveoli and oxygen diffuses into the blood. The oxygenated blood leaves the lungs and re-enters into the heart at the left atrium. This blood is then distributed to the body through the systemic circulation before returning to the pulmonary circulation [1].

Machines designed to provide extracorporeal membrane oxygenation (ECMO) have been in use since the early 1970s. The ECMO machine is similar to the heart-lung by-pass machine used in open-heart surgery. It pumps and oxygenates a patient's blood outside the body, allowing the heart and lungs to rest. When patients are connected to an ECMO, blood flows through
tubing to an artificial lung in the machine that adds oxygen and takes out carbon dioxide; then the blood is warmed to body temperature and pumped back into the body. There are two types of ECMO. The VA ECMO is connected to both a vein and an artery and is used when there are problems with both the heart and lungs. The VV ECMO is connected to one or more veins, usually near the heart, and is used when the problem is only in the lungs [2].

One key component of ECMO is the transport of oxygen into blood across a semi-permeable membrane. The concept of cardiopulmonary bypass was developed in the early 1950's. Devices used at that time were bubble or disk oxygenators with a direct oxygen-blood interface. Haemolysis occurred after a few hours of bypass. This precluded its use for long-term support. The development of the first membrane oxygenator, by Clowes in 1956, enabled prolonged cardiopulmonary bypass to become feasible [3].

The development of membrane oxygenators in the 1960s permitted longer extracorporeal life support in heart surgery. From 1972 onwards numerous clinical applications of extracorporeal membrane oxygenation in ECMO were investigated for respiratory failure. The membrane blood oxygenators (MBO) either used in cardiopulmonary bypass are a central part of the ECMO systems, and their clinical use is still nowadays associated to the systemic administration of heparin. This minimizes the damage of the blood like clot formation during its contact with the components of the ECMO systems [4].

In the future, cardiac surgery will be performed on older and less healthy patients (Voorhees & Brian, 1996). Further, the number of patients undergoing more than one operation will increase. This changing patient population as well as clinical and economic factors will demand improved BO designs. Designing improved BOs will be complex given the interdependence of the important design variables as described below [5]:

- Maximizing the gas transfer per unit priming volume of the device is essential;
- Minimizing the membrane surface area of the device has clinical and economic benefits;
- The blood flow path must be carefully designed.

In the work described here, gas transfer studies were conducted using water as a substitute for blood. Results for the oxygenation and deoxygenation of water were obtained using pure oxygen or nitrogen as the gas phase. Based on these results, a mathematical model of the oxygenator has been developed.

The transfer of oxygen to the liquid stream may be described by the following equation [6]:

\[ N = K \Delta C \]  

(1)

where \( N \) is the total molar flux, \( \Delta C \) is the overall concentration difference and \( K \) is the overall mass transfer coefficient. The overall mass transfer coefficient may be determined experimentally using the equation [6]:

\[ K = \frac{Q}{A \ln \left( \frac{C_0 - C_{O_2}^*}{C - C_{O_2}^*} \right)} \]  

(2)

2. Experimental

The mini-oxygenator is a laboratory model of a flat-sheet blood oxygenator composed by a slit and an oxygen chamber. The slit with dimensions \( 2X \times 2B \times Z \) is the compartment where the liquid surrogate of blood circulates. The bottom wall of this slit is constituted by a biocompatible membrane that separates the oxygen chamber from the liquid compartment. During the experimental procedures, the mini-oxygenator was connected to a water reservoir where the oxygen concentration in water was monitored on line by a fibre optic oxygen sensor (figure 1). The curves concentration \( O_2 \) (mol/cm\(^3\)) in function of time (min) was obtained from the oxygen sensor response, connected to the computer [7].

The commercial biocompatible silicone reinforced membrane from the ECMO 1500, from Medtronic, was tested at a temperature of
25°C, and oxygen at a pressure \( p_{O_2} = 1.2 \pm 0.1 \text{ bar} \). The height of the water compartment and the water flow rate were varied to assess the influence of the flow conditions in slits of different heights on the oxygen mass transfer across the ensemble oxygen/membrane/liquid flowing in the slit. The overall mass transfer of oxygen through the membrane to the liquid phase was determined experimentally.

3. Mathematical Model

The compartment where the liquid circulates, slit, is characterized by the Y-dimension being very small compared to the other two dimensions, \( 2B \ll 2X,Z \). This geometry assures a fully developed uni-dimensional flow situation, \( v_Z = v_Z(y) \) (figure 2 and 3). A global mass transfer coefficient, \( K_{O_2} \), for the transfer of oxygen from the gas chamber into the liquid phase, is, in steady state, defined by \[8\] \[9\]:

\[
J_{O_2} = K_{O_2}(C_{O_2}^* - C_{O_2b}(z)) \quad (3)
\]

where \( C_{O_2b}(z) \) is the average bulk concentration in the liquid stream at a distance \( z \) of the entrance in the slit and \( C_{O_2}^* \) is the concentration of oxygen in the liquid phase that would be in equilibrium with \( p_{O_2} \) at a gas/liquid interface:

\[
p_{O_2} = HC_{O_2}^* \quad (4)
\]

where \( H \) is Henry's constant \[8\] \[9\].

The liquid stream oxygenated through the passage in the slit chamber enters a reservoir with a well-mixed liquid volume, \( V \). A time
differential mass balance to the oxygen in this volume yields:

\[
V \frac{dC_{O_2}}{dt} = J_{O_2} A_{perm}
\]

where \(J_{O_2}\) is the oxygen flux permeating through the surface area of the membrane, \(A_{perm}\) and \(V\) is the constant volume of the liquid inside the reservoir where the oxygen sensor is inserted.

Introducing in equation (5) the flux given by equation (3), for an initial period of liquid oxygenation, when the average bulk concentration is very small compared to the oxygen concentration next to the membrane/liquid interface, \(C_{O_2b}(z)\) can then be neglected with respect to \(C_{O_2}\) and then:

\[
K_{O_2} = \frac{dC_{O_2}}{dt} \times \frac{V}{A_{perm} C_{O_2}}
\]

In steady state, applying a differential mass balance to \(O_2\) in the liquid stream, dividing it by \(4XY. \Delta z < v_z >\) and taking the limits when \(\Delta z \to 0\) yields [8][9]:

\[
\frac{dC_{O_2b}}{dz} = \frac{J_{O_2}}{2Y < v_z >}
\]

Finite differences methods were applied to develop a numerical model to the slit system. The domain was discretised into a uni-dimensional grid with \(n+1\) points, as per Figure 5.

The partial derivatives [11]:

\[
u_x = \frac{\partial u}{\partial x} \quad \text{and} \quad v_{xx} = \frac{\partial^2 u}{\partial x^2}
\]

are always approximated by central difference quotients, i.e.

\[
u_x \approx \frac{u_{j+1} - u_{j-1}}{2\Delta x}
\]

\[
u_{xx} \approx \frac{u_{j+1} - 2u_j + u_{j-1}}{(\Delta x)^2}
\]

at a grid point \((j,n)\). Where \(u_j^n = (x_j, t_n)\).

With the use of the implicit scheme, \(u_t\) is approximated by a backward difference quotient:

\[
u_t \approx \frac{u_j^{n+1} - u_j^n}{\Delta t} \quad \text{with} \quad (j, n+1)
\]

Introducing equations (9) and (10) to equation (7) a mathematical equation for the development of the oxygen concentration in the slit is achieved in the form of:

\[
C_{O_2b}(i + 1) = \left(1 - \frac{K\Delta z}{2Y < v_z >}\right)C_{O_2b}(i) + \frac{K\Delta z}{2Y < v_z >} P_{O_2}
\]

with \(i = 1, ..., n + 1\) and \(\Delta z = \frac{L}{n+1}\), where \(L\) is the length of the slit.

Applying the following boundary limit to equation (11), \(C_{O_2b}(0) = 0\) (which represents that at \(i=0\), i.e. at the entrance of the slit, the oxygen concentration is zero) it becomes one equation with one unknown.

To compare the mathematical model results with

![Figure 5 – Discrete grid applied to slit](image-url)
the experimental ones, a time step delay is introduced in the model, since in the laboratorial system the oxygen concentration is only measured in the reservoir and not at the end of the slit.

For \( t_0 = 0 \), the time for a full cycle of the system of figure 1 is:

\[
t_{\text{cycle}} = t_0 + t_{\text{slit}} + t_{\text{tub1}} + t_{\text{res}} + t_{\text{tub2}}
\]  \hspace{1cm} (12)

Regarding figure 1, \( t_{\text{slit}} \), \( t_{\text{tub1}} \), \( t_{\text{res}} \) and \( t_{\text{tub2}} \) are the time that an element of volume takes in the slit, pipework A, reservoir and pipework B&C, respectively.

To introduce the closed system specificities presents in the experimental loop, the following formulation was implemented:

- For the first cycle, \( C_{O_2,b}(i + 1)|_1 \) is measured at \( t_1 = t_0 + t_{\text{slit}} + t_{\text{tub1}} \) with \( C_{O_2,b}(0)|_1 = 0 \);
- For any following cycle, \( C_{O_2,b}(i + 1)|_n \) is measured at \( t_n = t_{n-1} + t_{\text{ciclo}} \) with \( C_{O_2,b}(0)|_n = C_{O_2,b}(i + 1)|_{n-1} \)

4. Results and Discussion

For the experimental results the following parameters were assessed: height of liquid flow chamber (slit) and liquid flow rate. The evolution of the oxygen concentration as a function of time was plotted (figures 6 to 11) and the overall mass transfer coefficient and overall resistance for the mass transference were calculated (table 1).
By evaluating the figures 6 to 11 and table 1, it can be verified that for the same geometry of the slit, and same oxygen pressure in the gas chamber, higher volumetric flows positively influence the overall mass transfer coefficient. This behaviour was expected as higher flows imply higher velocity, which will lead to higher shear stress on the membrane surface. This increase in shear stress has the effect of reducing the boundary layer of oxygen in this region.

For the same flow, it is identified that an incensement on the slit height will decrease the overall mass transfer coefficient. This can be explained by a lower maximum velocity in the slit which will mean lower shear stress values at the membrane surface.

Table 1 – Overall mass transfer coefficients and overall global resistance of mass transfer from experimental data

<table>
<thead>
<tr>
<th>Volumetric Flow (L/min)</th>
<th>1.50</th>
<th>1.75</th>
<th>1.00</th>
<th>0.75</th>
<th>0.50</th>
<th>0.25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2L = 6.0 × 10^-3 cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( K_m ) (cm/min)</td>
<td>0.78</td>
<td>0.70</td>
<td>0.65</td>
<td>0.59</td>
<td>0.53</td>
<td>-</td>
</tr>
<tr>
<td>( 1/K_m ) (min/cm)</td>
<td>1.29</td>
<td>1.43</td>
<td>1.53</td>
<td>1.69</td>
<td>1.89</td>
<td>-</td>
</tr>
<tr>
<td>Case 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2L = 3.0 × 10^-3 cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( K_m ) (cm/min)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.81</td>
<td>0.78</td>
<td>0.69</td>
</tr>
<tr>
<td>( 1/K_m ) (min/cm)</td>
<td>-</td>
<td>-</td>
<td>1.24</td>
<td>1.29</td>
<td>1.46</td>
<td>-</td>
</tr>
<tr>
<td>Case 3</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2L = 1.0 × 10^-3 cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( K_m ) (cm/min)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.73</td>
</tr>
<tr>
<td>( 1/K_m ) (min/cm)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.36</td>
</tr>
</tbody>
</table>

The results acquired from the mathematical model (red) were plotted against their experimental match (black), figures 12 to 17. This evaluation was only performed for the first moments of the oxygenation, since an actual oxygenator will never attain the saturation due to blood being constantly recirculated.
The charts from figure 12 to figure 17 show that the results from the numerical model have the same tendency as the experimental ones. Nonetheless, all numerical results reveal an overshoot against the experimental ones. This was further investigated via an analysis parametric to the mathematical model.

A set of key parameters (height of slit channel, length of membrane, average velocity, oxygen pressure and global mass transfer coefficient) was tested, one at each time, to analyse the reactiveness of the model.

<table>
<thead>
<tr>
<th>Base case</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>2B (cm)</td>
<td>$6.00 \times 10^{-2}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Z (cm)</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V_{avg}$ (cm/min)</td>
<td>$4.17 \times 10^3$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$P_{O_2}$ (bar)</td>
<td>1.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K (cm/min)</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2 – Base case values for parametric analysis to mathematical model
The parametric analysis performed on the mathematical model gives the following results:

- The oxygen concentration increases with an increase of global mass transfer coefficient; this result is in line with the experimental ones;
o Increases of oxygen pressure will intensify the growth of the oxygen concentration; which is verified by equation (7);

o Larger membranes will lead to better oxygen transfer, since the bigger the permeable area is, the more particles will be available for mass transfer;

o Smaller slit height channel will increase the development of the oxygen concentration, which is also in line with the experimental results;

o Higher average velocities will decrease the rate of oxygen concentration evolution, this reaction of the system is unexpected, since the experimental results show the opposite. However, analysing the equation (11) it is identified the factor $<v_z>$ on the denominator side, and as it is, evolves inversely to the oxygen concentration. This reaction could be related to the residence time of fluid volume elements in the slit, which increases with the decrease in velocity, and would justify a greater absorption of oxygen the longer they are in the slit.

5. Conclusion and future work

Membrane blood oxygenators require design improvements including at the level of the mass transfer resistance of the fluid and membranes. This means that the governing mechanisms of oxygen mass transfer must be understood and quantified in an explicit way. For that, the primordial objective of this work consists in the attempt to develop a mathematical model that simulates the blood oxygenation in a slit.

From the analysis of the model results, in general, the governing parameters are confirmed suitable and fit, against the experiments data. Even though, the overshoot tendency of the model outputs and the effect of the average velocity parameter on the system, opposite to the experimental results, still needs further investigation. Improvements on the model could also be pursuit by including the effects of the shear stress on the membrane surface.

References


