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Micro-scale Modeling of Flow and Oxygen Transfer in Hollow Fiber Membrane Bundle

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Abstract

The aim of this work was to develop a modeling approach to solve the flow and oxygen transfer when the blood passes through the hollow-fiber membrane bundle. For this purpose, a “two-region” modeling approach was developed regarding the hollow fiber and blood regions. The oxygen transfer in these regions was defined with separate diffusion processes. Two dimensional single and multi-fiber geometries were created and flow solutions were obtained for a non-Newtonian fluid. The convection-diffusion-reaction equation was solved to produce the oxygen partial pressure distributions. As a benefit of coupling the interstitial flow field into the oxygen transfer through the hollow-fiber membrane bundle, the membrane resistance was taken into consideration. Thus, varying oxygen partial pressures were observed on the outer fiber surface, which is contrary to the common simplifying assumptions of negligible membrane resistance and uniform oxygen content on the fiber surface (Traditional approach). It was illustrated that, the current approach can be utilized to predict the mass transfer efficiencies without overestimating as compared to the predictions obtained with the traditional approach. Utilization of the current approach was found to be beneficial for the geometries with lower packing density which allows significant P_{O_2} variations on the fiber surfaces. For the geometries with dense packings, the above simplifying assumptions could be applicable. The model predictions were validated with the experimental measurements taken from a benchmark device.

Keywords

Artificial Lung; Oxygenator; Hollow-Fiber Membrane; Crossflow; Micro-scale Modeling

1. Introduction

Blood oxygenators are commonly used in cardiopulmonary bypass for open heart surgery and for extracorporeal membrane oxygenation for cardiac/cardiopulmonary support. Artificial lungs are actively developed as a bridge to lung transplantation [1]. Blood oxygenation in artificial lungs or blood oxygenator devices is achieved with oxygen diffusion, through hollow fiber membranes into blood. Blood flows around the outside of thousands of hollow fiber tubes, and oxygen flows inside the fiber lumen. During the blood passage around the tubes, the oxygen diffuses into blood through gas permeable fiber membranes from the oxygen rich inner wall (oxygen gas side) to the oxygen poor outer wall

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(blood side). Then the oxygen moves with the blood away from the membrane wall through diffusion and convection in the interstitial space between the membrane walls. Meanwhile, the carbon dioxide moves in the opposite direction. Reliable modeling of this physical phenomenon is essential to predict the gas transfer performance for development of efficient artificial lung devices and blood oxygenators.

The currently used approaches to model the blood flow and gas transfer in the hollow fiber membrane bundles can be classified as pseudo-homogeneous and heterogeneous models. In the pseudo-homogeneous models, the whole device (membrane bundle) is considered to be occupied by a porous medium material and modeled as porous media without considering localized processes involved with individual fiber membranes. In the heterogeneous models, the blood flow and oxygen transfer in the interstitial space between membrane walls is considered. These models are also known as micro-scale models or single fiber models.

In the pseudo-homogeneous model, the heterogeneous multi-phasic nature of the fiber bundles is approximated, and the presence of the individual fibers and corresponding local processes are accounted for with the lumped parameters. The superficial velocity or interstitial velocity of the fluid are estimated based on the flow rate, cross-sectional area and porosity of the medium. Several equations (Blake-Kozeny equation, Burke-Plummer equation, Ergun equation, Darcy's law) have been developed in the literature to relate the flow through a porous medium to the pressure drop in different flow regimes [2]. The gas transfer from the fiber membranes to the blood is estimated using the most common form of the dimensionless semi-empirical mass transfer correlation [3] which is obtained through an analogy from the heat transfer [4], and relates the Sherwood (Sh) number to the Reynolds (Re) and Schmidt (Sc) numbers:

$$Sh = a Re^{\alpha} Sc^{\beta} \quad (1)$$

The dimensionless numbers are obtained by a dimensional analysis of the governing equations of the mass transfer. The Sherwood number represents the ratio of convective to diffusive mass transport, the Reynolds number represents the ratio of inertial to viscous forces, and the Schmidt number represents the ratio of momentum to diffusive transport. The factor a and the exponents α and β in Equation (1) are empirically determined from experiments through multivariable regression. This approach has been used to evaluate the oxygen transfer to blood flowing in round tubes [5], and to characterize the various oxygenator designs and to develop several new oxygenator designs [6–8].

The use of computational methods in the simulation of fluid flows in porous media has been recently introduced [9]. 2-D and 3-D computational fluid dynamic (CFD) models [10–16] have been utilized to calculate velocity fields and gas–blood transport with a porous media model. Although the overall hollow fiber membrane (HFM) regions were effectively simulated, the usefulness and accuracy for localized performance prediction of a new oxygenator design with unknown fiber configuration is limited.

Micro-scale or heterogeneous models, which are the interest of the present work, includes the presence of the walls of individual fibers. The fluid flow in the interstitial space between fibers is considered. Most of the available micro-scale models are implemented for single fiber or repeats of single fiber. Gas-liquid mass transfer has been studied theoretically in a microporous HFM module operated under partially wetted conditions in the laminar flow regime by Malek et al. [17]. A numerical approach to the determination of oxygen transfer to water through partially wetted microporous membranes was developed by Evren [18]. The finite difference technique was used for the numerical solution and the oxygen concentration profile along the single fiber was calculated. Direct CFD simulation of the

fluid flow and mass transport past a single circular cylinder was performed by Zierenberg et al. [19,20]. The mass transport of the free-stream flow past the single cylinder was considered as a building block for an artificial lung device. The pulsatile flow was simulated. The effect of the Newtonian and Non-Newtonian property of the fluid on the flow behavior, local oxygen partial pressure and concentration were investigated. The presence of more cylinders was also studied for pulsatile flow conditions for square arrays [21,22], and for steady flow conditions for square, triangle and staggered square geometries [23] in terms of concentration and streamline fields. Although the gas transfer was not studied, the reference [24] is an example of modeling 3300 fibers in a 2D model of an oxygenator.

All the above mentioned micro-scale modeling of the fluid flow in the interstitial space between the membranes assumed a constant surface oxygen partial pressure on the wall of the membrane and a negligible gas transfer resistance through the fiber membrane wall from the inner lumen to the outer wall. It was mentioned that, the over predictions observed on the Sherwood numbers could be due to these assumptions [22]. Eash et al. [25] recently demonstrated that the gas transfer resistance through a membrane wall existed and there were significant differences in the gas permeation (oxygen and carbon dioxide) for different types of fiber membranes. Thus the non-uniform blood flow profile around the fiber cylinder would cause the non-uniform surface gas partial pressure.

The aim of the present study was to develop a realistic micro-scale modeling approach for simulating the blood flow and oxygen transfer in a cylindrical hollow fiber array as a building block for artificial lung devices and blood oxygenators. The modeling approach developed incorporated the following important features: the oxygen diffusion resistance across the membrane wall was considered; the surface oxygen partial pressure was obtained during the calculations rather than being set as a boundary condition; and the oxygen content in the whole blood, including that dissolved in plasma and bound to hemoglobin, was incorporated in the model.

The capabilities of the approach developed were evaluated with a parametric analysis for fiber arrangements with different fiber dimensions, and different void fractions. Furthermore, the CFD simulation results for a mini-oxygenator using the newly developed modeling method were compared with the experimentally measured oxygen distributions.

2. Materials and Methods

The oxygen concentration profiles in the hollow fiber oxygenator were evaluated by solving the coupled mass transfer equations in two regions: the wall of the porous hollow fiber membrane and the blood flowing in the interstitial space between fibers. The blood flow in the interstitial space is governed by the momentum conservation and continuity equations. The oxygen transfer in the blood region is governed by a convection-diffusion-reaction equation. The oxygen diffusion across the membrane wall is governed by the Knudsen diffusion equation. These equations are coupled and solved numerically.

The blood is approximated as a non-Newtonian fluid in which the shear rate dependency of the fluid viscosity is expressed with a modified Casson model [26]:

$$\mu = \left(\left(\frac{\tau_0}{\phi + 1} \right)^{1/2} + \mu_c^{1/2} \right)^2 \quad (2)$$

where τ_0 is the yield stress taken to be 0.005 Pa, ϕ is the magnitude of the shear rate and μ_C is the Casson viscosity, taken to be the high shear limit, 3.5 cP. The density of the blood was taken as 1056 kg/m³ in the calculations.

From rheological point of view, blood is considered as a shear thinning non-Newtonian fluid that shows both viscous and elastic properties. In this regard, consideration of viscoelastic characteristics of the blood, especially in the microchannel flows as in this case, may become critical [27,28]. There are numerous viscoelastic constitutive equations available in the literature. Among them the one proposed by Oldroyd [29], which considers the normal stresses acting on the blood particles with a four constant model, was additionally utilized in this work to evaluate if the modified Casson model is appropriate for the present study. The maximum difference in the calculated local oxygen partial pressures on the fiber surfaces is about 10% when these two non-Newtonian fluid models were utilized. This resulted in a 2% difference in the oxygen concentrations. Therefore, under the studied operating conditions and the system geometries of this work, we continued with modified Casson model given in Equation (2).

The modeling approach was developed in three stages: the single fiber model; the simple multi-fiber model and the mini-oxygenator model. The single fiber model was used as an initial implementation of the modeling approach, and to compare the results with those obtained by assuming uniform fiber surface oxygen concentration. The latter approach, referred as traditional approach in here, does not use the hollow structure of the fibers (i.e. no wall thickness), and has been commonly used in the literature. The simple multi-fiber model was used to determine the effects of the presence of multiple fibers in the domain, and to compare the overall gas transfer performances with different fiber arrangements. The mini-oxygenator model was an extension of the simple multi-fiber model and was used to perform detailed investigations on local and overall gas transfer performances, and to compare the predicted oxygen transfer with the experimentally measured results.

2.1 Single-fiber model

The schematic presentation of the 2-D single-fiber model and corresponding mesh structure are shown in Figure 1a. A 300 μ m diameter (D) fiber positioned at the center of the computational domain, and the boundary walls were placed far enough from the fiber (20D $\times$ 20D) so as the boundary conditions do not influence the solutions. Uniform velocity inlet and outflow outlet conditions were selected to define the fluid advection. The outflow boundary condition was selected as the velocity and pressure conditions were not known a priori [30]. The top and bottom walls were set as symmetry walls. The flow domain was meshed into 11,000 quadrilateral elements. Finer mesh elements were utilized closer to the hollow-fiber wall. One hundred computational nodes were created on the fiber surface. The fiber membrane wall was meshed into 10 radial grid layers. The steady flow past the single fiber was simulated.

2.2 Multi-fiber models

The simple multi-fiber model was built on the above mentioned single fiber model. It consisted of a staggered array of fibers with the same fiber dimensions as utilized in the single-fiber model. A schematic drawing of this multi-fiber model is illustrated in Figure 1b as well as the magnified section of the fiber region which represents the particularly interesting front, central and rear fibers. The axial spacing between the hollow fiber tubes was arranged to create fiber regions with two different void fractions. One arrangement was configured with an axial spacing of 5/6 fold of the outer diameter (D) based on the typical dimension of the sheet of the hollow fibers (50 fibers/inch, fiber OD=300 μ m, wall thickness =30 μ m (Celgard Inc., Charlotte, NC). The spacing between the fiber sheets was determined

according to the desired void fraction ($\epsilon=0.53$) of the fiber bundle in typical oxygenators and in our benchmark device. In the other arrangement, the axial spacing shortened to $2/3D$, while keeping the other dimensions unchanged to create the overall void fraction of $\epsilon=0.40$. The former arrangement consisted of 46 fibers, whereas the latter one composed of 53 fibers. Since the individual fiber (D) and the fiber region ($6D \times 14D$) dimensions were the same for both arrangements, the membrane surface area of the lower void fraction arrangement was 15% more than that of the higher one.

The inlet and outlet boundaries were placed $20D$ away from the fiber region and the free stream boundary conditions were set upstream and downstream of the fiber array. Symmetry boundary conditions were set on the top and bottom walls of the fiber array since the fiber array was considered to be a building block for artificial lung devices. The uniform velocity inlet and outflow outlet conditions were set. The same meshing scheme was applied in both the blood flow and the hollow fiber regions as in the single-fiber model. The computational domain was meshed into 80,000 hexahedral elements.

The second multi-fiber model was constructed from a mini-oxygenator placed in a parallel flow chamber as a benchmark device. The device is shown in Figure 2(a), and the schematic drawing of the device and the constructed 2-D segment of the upper half cross-section is presented in Figure 2(b–c). Two different fiber arrangements were utilized to create the same void fractions as in the first multi-fiber model. In the first arrangement, 2100 hollow tubes were placed in a staggered array. In this arrangement the fiber dimensions were the same as the above models, and the void fraction was kept at 0.53. In the second arrangement, fibers with larger outer diameter ($380\mu\text{m}$) were placed (wall thickness was not changed). To keep the total mass transfer area constant, 1660 of the higher outer diameter tubes were utilized. The overall void fraction of the fiber region was maintained at 0.40. Note that, the arrangement with a void fraction of 0.53 was created to model the mini-oxygenator device that we used in the experiments. Whereas, the one with a void fraction of 0.40 was a theoretical arrangement, and used as a part of the parametric analysis. The representative fiber arrangements are shown with enlarged views in Figure 2c.

The models were meshed into 1.20 ($\epsilon=0.40$ model) to 1.74 ($\epsilon=0.53$ model) million hybrid (triangular/quadrilateral) elements. The quadrilateral cells were used to mesh the interstitial flow domain in the fiber bundle region and the fiber walls were meshed as the same as for the above multi fiber model. The rest of the flow domain was meshed with varying size triangular cells. A uniform velocity profile was set at the inlet. The solid wall boundary condition was set on the top of the computational domain. A symmetrical boundary condition was set on the bottom.

All of the models were developed and meshed with the commercial geometry and mesh development software Gambit v.2.4.6 (Ansys Fluent Inc., Lebanon, NH, USA).

2.3 The flow solution

The blood flow solution was obtained by solving the continuity and momentum equations with the laminar flow model. The momentum conservation is written as:

$$\rho \nabla \cdot (\vec{v} \vec{v}) = -\nabla P + \nabla \cdot \vec{\tau} \quad (3)$$

where $\vec{v}$ is the velocity vector, ρ is the density of the blood, $\vec{\tau}$ is the stress tensor, and p is the pressure.

2.4 The oxygen transfer-fiber side

As mentioned before, a “two-region” approach was implemented in this work. The lumen and wall of the fiber membrane compose the fiber side of this approach. The oxygen diffusion through the pores of the fiber wall was assumed as a Knudsen diffusion process. This is a typical choice when the gas molecules flow in the porous material, if the mean molecular path is large compared to the pore diameter so diffusion mainly occurs as a result of a frequent collision of the molecules with the pore walls, as opposed to the diffusion due to the inter-molecular collision [31]. In our case, the mean oxygen gaseous path length was estimated to be approximately two fold larger than the mean pore diameter (0.04 μm) which supports our selection. Knudsen law was also applied for the polyamide membranes for biogas purification applications [32] and hollow fiber membranes in oxygenators [33].

The diffusion coefficient was calculated based on the membrane permeation, effective pore length, tortuosity, and effective porosity as;

$$D_i = K_m \frac{\tau}{\varepsilon'} h \left(\frac{T}{T_0} \right) P_0 \quad (4)$$

The membrane permeation, K_m , was adopted from the literature [25] for the Celgard membranes ($1.77 \times 10^{-2} \text{ cm}^3/(\text{s} \cdot \text{cm}^2 \cdot \text{cmHg})$). The Celgard fiber is a microporous hollow fiber that has increased “plasma resistance” with a reduced pore size. The pores of the microporous fibers, especially made from hydrophobic polypropylene material as in this case, remains as gas filled in an aqueous gas-liquid environment [34]. This minimizes the potential error of utilizing the above mentioned permeation value in our calculations. The tortuosity, τ , is estimated to be 4.0 [35]. The effective pore diameter, h , and effective porosity, ε' , were from the properties of the fiber material ($h = 0.03 \mu\text{m}$, $\varepsilon' = 0.40$). T is the temperature (assumed as 310 K). T_0 and P_0 are the standard temperature and pressure (298 K and 760 mmHg). The partial pressure on the fiber surface is an intermediate variable which was used in the oxygen transfer equation in the blood region. The Fick’s diffusion law governs the oxygen flux through the fiber wall as such;

$$J_i = -D_i \nabla C_{O_2} \quad (5)$$

where C_{O_2} is the oxygen concentration. The negative sign indicates the direction of the diffusion along the gradient of oxygen concentration.

2.5 The oxygen transfer-blood side

The steady convection-diffusion equation for the oxygen transfer is as follows;

$$v \cdot \nabla(C_{O_2}) = D \cdot \nabla^2(C_{O_2}) \quad (6)$$

where D the diffusion coefficient. The left side of the equality represents the convective process, while the right side presents the diffusive process. Equation (6) can be rewritten as a function of the oxygen partial pressure (P_{O_2}) as follows:

$$v \cdot \nabla(P_{O_2}) = D_{eff} \cdot \nabla^2(P_{O_2}) \quad (7)$$

In this equation, the diffusion term of oxygen in the blood was represented with a variable effective parameter (D_{eff}), considering the unique hemoglobin-oxygen binding characteristics of the blood:

$$D_{eff} = D_b / (1 + [Hb] S'_{O_2} / \alpha) \quad (8)$$

where D_b is the free oxygen diffusion coefficient ($1.9 \times 10^{-5} \text{ cm}^2/\text{s}$), $[Hb]$ is the oxygen binding capacity per volume of blood in terms of STP (standard temperature and pressure) volumes of oxygen. The nominal value is 0.167 ml Hb/ml. α is the oxygen solubility in plasma ($3.0 \times 10^{-5} \text{ ml O}_2/\text{ml plasma/mmHg}$), and S'_{O_2} is the first derivative of oxygen saturation (dS_{O_2}/dP_{O_2}). The saturation, S_{O_2} , is obtained by the Hill equation;

$$S_{O_2} = (P_{O_2} / P_{50})^n / (1 + (P_{O_2} / P_{50})^n) \quad (9)$$

where P_{50} , the oxygen partial pressure at the half saturation level, and the exponent n is taken from literature [35]. Based on a piecewise-defined curve fitting of the experimentally measured data for ovine blood, the following P_{50} values obtained;

$$n = 2.6, \begin{cases} P_{50} = 43, P < 68 \\ P_{50} = 29, P \geq 68 \end{cases} \quad (10)$$

The mass transfer rates, $\dot{m}_{O_2}$, were calculated according to Equation (11) with the averaged P_{O_2} and S_{O_2} values at the inlet and the outlet of the models.

$$\dot{m}_{O_2} = \{13.4 \cdot Hb(S_{O_{2,out}} - S_{O_{2,in}}) + \alpha \cdot 10^3(P_{O_{2,out}} - P_{O_{2,in}})\} Q_b \quad (11)$$

In the equation, the volumetric blood flow rate, Q_b , is in L/min, the total hemoglobin, Hb , is in g/dl, α is in ml/(ml.mmHg), S_{O_2} values are fractions, and P_{O_2} values are in mmHg.

2.6 Solution procedure

As a first step, the flow solutions were obtained for different Reynolds number conditions. Re is defined based on fiber outer diameter and free stream velocity. Once the residuals and pressure predictions were stabilized and the mass balance between the inlet and outlet is established within an error of less than 10^{-6} kg/s , the scalar transport equation was solved in the entire computational domain. The scalar transport solutions were iterated until the residuals were reduced below 10^{-6} and the scalar value at the outlet of the models was stabilized. The oxygen partial pressure in the inner fiber wall (scalar value) was set as 760 mmHg (pure oxygen). The oxygen partial pressure of the blood at the inlet was set as 56 mmHg which is the typical oxygen partial pressure level of the venous blood.

Commercial CFD software (Fluent v.6.3.26) was used to obtain the flow and scalar solutions. The computations were carried out on a PC workstation with two Intel Xeon quad-core 2.66GHz CPUs and 16.0 GB RAM with Windows XP 64 bit operating system. The Semi Implicit Method for Pressure-Linked Equations (SIMPLE) pressure-velocity coupling algorithm was utilized to obtain the blood flow field. All of the simulations were performed with the second order accuracy. The user-defined functions were utilized to calculate the saturation in the blood as a post-processing procedure.

2.7 Blood oxygenation experiments

The blood oxygenation experiments were performed on a benchmark device. The mini HFM bundle was fabricated by folding the Celgard® X30-240 microporous HFM sheet into a rectangular block: 2 inch (length) by 1.8 inch (width) by 0.5 inch (thickness). Both ends of the bundle were potted using a lab-made potting centrifuge and the potted ends were cut to expose fiber lumina after potting. The bundle was placed in a long rectangular flow chamber for testing. The photo of this flow chamber together with the bundle is shown in Figure 2a. Since the flow direction is perpendicular to the fibers, the superficial flow path length is equal to the bundle length. There are totally 13 sampling ports on the whole benchmark test device, and the location of the sampling ports is shown in the same figure (in inches).

To characterize the performance of the mini bundle, a mock flow loop was constructed as shown schematically in Figure 3. Static pressures were measured at these ports and blood gas data can be obtained by analyzing blood samples from these ports. Initially 1 ml blood was drawn from the ports and disregarded. Then, another 1 ml blood was drawn and measured immediately. For the hydrodynamic measurement, both saline (at room temperature) and ovine blood (at body temperature) were used as testing fluid. The pressure loss across the bundle was recorded at various flow rates up to 3 L/min. For the oxygen transfer measurement, only ovine blood with a hematocrit value of $36 \pm 1\%$ was used as the testing fluid and the experiments were performed under various blood flow rates up to 1.5 L/min.

Fresh ovine blood collected from slaughter house was anticoagulated with heparin (10,000 U/L) and filtered before each experiment. The hematocrit of the blood was measured by centrifugation with an Adams™ Micro-Hematocrit II centrifuge (Model No. 420556, BD, Franklin Lakes, NJ, USA) and the viscosity of the blood was measured by a calibrated Cannon-Manning Semi-Micro viscometer (9721-Y56, Cannon Instrument Company, State College, PA, USA).

Flow was generated by a centrifugal blood pump (BP-80 Biopump, Medtronic, Inc., Minneapolis, MN, USA). Blood temperature was maintained at 37°C using a heat exchanger (Model 1104, VWR International, West Chester, PA, USA) and monitored by a temperature probe located inside the reservoir. The flow rate was measured by a calibrated ultrasonic flow meter (T101, Transonic Systems, Inc., Ithaca, NY, USA) and probe (H9XL, Transonic Systems, Inc., Ithaca, NY, USA). Inlet and outlet pressures were monitored using physiological pressure transducers (Edwards Lifescience, Irvine, CA, USA) with a Spacelabs patient monitor (Model No. 90316, Spacelabs, Hillsboro, OR, USA). Oxygenation of the testing fluid was realized by flowing pure oxygen into the fiber lumina of the bundle. The oxygen flow rate was measured by a GR series gas flow meter (GR112-1-A-PV, Fathom Technologies, Round Rock, TX, USA). The ratio of oxygen flow rate versus fluid flow rate was kept at 1. Deoxygenation of the testing fluid was achieved by using a CardioVenton CORx Oxygenator (CardioVenton, Inc. Santa Clara, CA, USA) connected in series with the benchmark testing device. Instead of oxygen or air, a mixture of carbon dioxide (CO₂) and Nitrogen (N₂) was flowing through the oxygenator for the purpose of deoxygenation. The deoxygenation gas flow rate was measured by a TopTrak gas flow meter (822 Top-Trak, Sierra Instruments, Monterey, CA, USA). The oxygen partial pressures, oxygen saturation, and other values were assessed by analyzing the blood samples taken from each port using a Stat Profile Phox Plus L blood gas analyzer (Nova Biomedical, Waltham, MA, USA).

3. Results

3.1 Single fiber model

The effect of the Reynolds number on the oxygen partial pressure profile from the front to the back of the fiber cylinder is presented in Figure 4a. The Reynolds numbers covered the possible range of operating conditions in the artificial lung devices or oxygenators [21,36]. The P_{O_2} on the fiber inner wall is shown as a solid line, corresponding to the constant boundary condition. The $\theta=0^\circ$ and $\theta=180^\circ$ correspond to the forepart and the back part of the fiber surface respectively. A general trend of reduction in the partial pressure was noticed at the front of the fiber for all the flow conditions. The lowest oxygen partial pressure was located at $\theta=0^\circ$. The reduction increased with the increase of Reynolds number. The oxygen partial pressure decreased to 655 mmHg at $Re=20$ while it was 740 mmHg at $Re=0.5$. Although the profiles for all Reynolds numbers were qualitatively similar, there were some differences. The most noticeable difference was observed at high Reynolds numbers, i.e. $Re=20$. The oxygen partial pressure increased from the front to the back side until $\theta=135^\circ$. Then, the P_{O_2} began to decrease. This is related to the increased wake vortex at the region. Figure 4b illustrates the velocity vector fields and their effect on the P_{O_2} contours for $Re=5.0$ and 20.0 conditions. As the Reynolds number increased, vortex formation emerged in the wake region and became apparent at $Re=20$.

It was also observed in Figure 4a that, there was a slight change of the slope of the P_{O_2} profile between $50^\circ \leq \theta \leq 80^\circ$ at $Re=10$.

The dimensionless mass transfer correlation, as given in Equation (1), can be utilized to make comparative analysis in different fiber arrangements [23]. Therefore, in this work we have used the same idea to compare the predictions of our approach to those obtained using the assumptions of uniform surface oxygen partial pressure and a negligible gas transfer resistance through the fiber. For the uniform surface oxygen calculations, the oxygen partial pressure was set to a uniform value (760 mmHg) on the fiber surface. The local Sherwood numbers were calculated as the ratio of the concentration gradient on the cylinder surface to the concentration difference between the cylinder surface and the upstream fluid. The surface averaged Sherwood numbers were utilized in the Figure 5. A common form of the Sherwood and Schmidt number relation was utilized ($Sh \cdot Sc^{-1/3}$). An increasing trend was noticed for both approaches with an increase in Re , as was illustrated before [23]. For the low flow conditions ($Re \approx 1$) the predicted oxygen partial pressures with the two approaches were closer to each other. However, for the higher flow conditions, the predictions obtained with the traditional approach were almost doubled.

3.2 Multi-fiber models

3.2.1 The simple multi-fiber model—The local P_{O_2} distributions and velocity, P_{O_2} , and S_{O_2} contours were investigated for the arrangement of $\varepsilon=0.53$ at the flow condition of $Re=5.0$ as presented in Figure 6. The local P_{O_2} distributions on three neighboring fibers (Fig. 6a) were similar to each other. The lower values were seen on the front fiber, whereas the higher values were noticed on the rear fiber surface. The P_{O_2} profile on the middle fiber stayed in between those of the front and rear fibers. For all of three fibers, there was an increase of the partial pressure levels on the position of $\theta=90^\circ$. This position corresponds to the opening between the two neighboring fibers positioned on the top (or the bottom) of the central fiber. The lowest partial pressure levels were seen closer to the front end, and the highest values were observed at the rear end of the fiber surface. Figure 6b shows the velocity contour, and P_{O_2} and S_{O_2} distributions in the control region of this multi-fiber model. The highest velocity was observed in the regions where the fiber walls were closest to each other. The lower velocity regions were observed at the front stagnation region ($\theta=0^\circ$)

and the back of the fiber cylinder ($\theta=180^\circ$). The P_{O_2} distribution shows that the high oxygen level regions were located along the center lines of the fibers positioned after one another in the flow direction. This looked like a wired connection among front, central, and rear fibers on which the level of the oxygen partial pressures and saturations were gradually increased. At the rest of the fluid in the control region, the oxygen contents were closer to the inlet condition (56 mmHg P_{O_2} and 66 % S_{O_2}).

To study the overall effect of the fiber arrangement on the oxygen transfer a second arrangement, with $\varepsilon=0.40$ was modeled. The relative comparison of the two arrangements was carried out with the mass transfer rate versus blood flow rate curves. Since the membrane surface areas (A) were different in the two arrangements considered here, the mass transfer rates were normalized in Figure 7 by the membrane surface area ($\dot{m}_{O_2}/A$). It was noticed that, the $\varepsilon=0.40$ arrangement results in larger mass transfer as compared to $\varepsilon=0.53$. The difference between the curves was increasing with the increase of flow rate, favoring the $\varepsilon=0.40$ arrangement more for higher flow rate conditions.

3.2.2. The mini-oxygenator model—The multi-fiber model was then applied to analyze the flow and oxygen transfer of a real mini-oxygenator ($\varepsilon=0.53$). Figure 8 illustrates the P_{O_2} and S_{O_2} contours taken from the sections of the mini-oxygenator located at dimensionless bundle length, $L=0.00$, $L=0.25$, and $L=0.50$ for $Re=2.0$ and $Re=5.0$. The fiber bundle length, L , is normalized based on the total length of the fiber bundle region (Fig. 2b). Figure 8 clearly shows the increases of the oxygen partial pressure and saturation from the inlet to the middle to the exit of the fiber region. When the blood began in contact with the fiber bundle ($L=0.00$), only a portion of the blood close to the front and back of the fibers became oxygenated. The bulk P_{O_2} value remained unchanged (56 mmHg). As the blood flow into the fiber region ($L=0.25$), the area with high P_{O_2} value increased close to the front and back of the fibers as axially connected to each other. The majority of the flow domain became oxygenated as indicated by the increased oxygen saturation. As the blood entered deep into the fiber bundle ($L=0.50$) the P_{O_2} levels in the entire fluid domain increased significantly, and blood became almost fully saturated mid-way in to the bundle. The effect of the inlet flow conditions can also be seen in the figure. For the higher Re condition ($Re=5.0$) relatively lower bulk P_{O_2} and S_{O_2} fields were noticed in all three sections.

The two fiber arrangements for the mini-oxygenator model were compared. The local values on the selected fibers were obtained. The fibers located at different axial positions but at the same transversal position were utilized. Note that, the fibers at $L=0.00$ were not exactly the first fibers that faced with the blood flow. We have selected the fiber at the third layer as $L=0.00$ to eliminate the entrance effects.

The local mass transfer capabilities can be analyzed with the mass transfer coefficients, K . Therefore, the variations of K on the fiber surfaces were calculated with Equation 12, and illustrated at Figure 9a for $Re=1.0$, as a representative example for the other conditions.

$$K=(-D_i \cdot \nabla C_{O_2})/(C_{O_{2,b}} - C_{O_{2,w}}) \quad (12)$$

In the above equation, D_i is mass diffusivity, ∇C_{O_2} is the concentration gradient normal to the fiber surface, $C_{O_{2,b}}$ is the bulk concentration, and $C_{O_{2,w}}$ is the fiber surface concentration. The largest variation in the mass transfer coefficient with circumferential position was seen on the fibers positioned at $L=0.00$. For $\varepsilon=0.53$ arrangement, the mass transfer coefficient increased at the rear side of the fibers. However, for $\varepsilon=0.40$ arrangement, the first half ($\theta \leq 90^\circ$) of the profiles were similar to the second half ($\theta \geq 90^\circ$) of them. The

local P_{O_2} variations were presented in Figure 9b for the selected fibers only. The lower P_{O_2} values were noticed for the arrangement with $\varepsilon=0.53$ than that with $\varepsilon=0.40$. It was also seen that, the shapes of the profiles were different. The flat profiles were observed between $0^\circ \leq \theta \leq 90^\circ$ for the arrangement with $\varepsilon=0.53$. Whereas, for the arrangement with $\varepsilon=0.40$ the P_{O_2} values increased through the front end of the fiber. The profiles at $L=1.00$ showed that, the maximum variation was 32 mmHg on the $\varepsilon=0.53$ profile, whereas it was only 3 mmHg for the $\varepsilon=0.40$ profile. The maximum value, which was seen through the rear end of the fiber, was 730 mmHg for the arrangement with $\varepsilon=0.53$. However, it was very close to the inner wall P_{O_2} value (760 mmHg) for the arrangement with $\varepsilon=0.40$.

The Sh-Sc-Re, dimensionless number, plots were utilized to further analyze the averaged mass transfer efficiencies of the selected fibers, as illustrated in Figure 10. For both of the arrangements, the Sh-Sc^{1/3} curves increased with the increase of Re. Higher values were observed for the fibers at $L=0.00$. Values lowered through the end of the bundle region. At the entrance of the fiber region ($L=0.00$), $\varepsilon=0.40$ curve was higher than that of $\varepsilon=0.53$, and the separation increased with high Re conditions. At $L=0.25$, the curves crossed each other on Re=3.0 condition. At the exit of the fiber region ($L=1.00$), the Sh-Sc^{1/3} value of $\varepsilon=0.53$ arrangement was higher than the one of $\varepsilon=0.40$ at low Re conditions, and getting closer to each other for higher Re conditions.

The overall mass transfer performance of the arrangements was compared with the variation of oxygen transfer rates as a function of blood flow rate, as shown in Figure 11. Note that, the mass transfer rates were calculated based on the inlet and exit P_{O_2} and S_{O_2} levels. For both of the arrangements, the mass transfer rates increased with the increase of flow rate. There was a slight increase in the oxygen transfer rate for the fiber bundle with a lower void fraction under these blood flow rates.

The oxygen saturation predictions from the arrangement with $\varepsilon=0.53$ were compared with the experimental results. Figure 15 shows the predicted oxygen saturation along the fiber bundle region and the experimentally obtained data from the benchmark device. The oxygen transfer rate across a transverse cross-section area of the benchmark device was also calculated and compared to the experimental values. The oxygen transfer rate, $\dot{m}_{O_2}$, was calculated with the oxygen partial pressures (P_{O_2}) and saturations (S_{O_2}) at the inlet and the locations along the flow direction in the fiber bundle using Equation 11. The experimental $\dot{m}_{O_2}$ values were obtained by utilizing the measured P_{O_2} and S_{O_2} values from the benchmark device. The predicted oxygen partial pressures and saturations were the averaged fluid values on the corresponding axial positions.

The S_{O_2} values increased from 66.5% to almost full saturation through the exit of the fiber region. A general agreement was observed between the predicted and measured S_{O_2} values for the lower Reynolds number condition. However, the model showed an over-prediction at $L=0.125$ for both high and low Re conditions. Additionally, the predictions at the higher Reynolds number condition were slightly more than the measurements at $0.375 \leq L \leq 0.75$. On the other hand, at the locations $L>0.75$, the numerical and experimental profiles were in agreement with full saturation for both cases.

The $\dot{m}_{O_2}$ increased from 0 to 13 ml/min along the fiber for Re=2, and from 0 to 30 ml/min for Re=5 conditions. As similarly observed in the oxygen saturation plot, the experimental $\dot{m}_{O_2}$ values were lower than the predictions at $L=0.125$. For the higher Reynolds number case, the predictions were found to be more than the measurements at $0.50 \leq L \leq 0.75$. However, after that position, there was a better agreement between the experimental and numerical values.

4. Discussion

We developed a “two region” modeling approach to link the blood flow to the oxygen transfer from the lumen of fiber to the blood in the hollow fiber bundles with consideration of the oxygen diffusion process through the fiber wall. This approach was applied to 2-D single-fiber and multi-fiber geometries.

Based on the single fiber calculations, the predicted oxygen distribution on the fiber surface with the “two region” model exhibited a strong variation along the outer fiber surface. These variations were more pronounced for the higher Reynolds number conditions. These observations may indicate the significance of the fiber wall resistance in the gas transfer to the blood flowing around the fiber. The vortex formation affected the P_{O_2} profiles at the outer fiber surface which may create a low gas transfer region.

It was demonstrated with the correlation between Sh, Sc, and Re that, as compared to the current model the traditional approach over predicted by a factor of two. The significance of this observation is that, the mass transfer efficiencies can be over estimated with the traditional approach. The mentioned observation looks especially noticeable for the higher flow conditions, and may also be associated with the over predictions of the Sherwood numbers observed with the traditional approach [22].

It was also demonstrated that the oxygen distribution on the fiber surface was strongly affected by the presence of the surrounding fibers. As the simulations of a single fiber were compared to those of the simple multi-fiber configurations (Fig. 6a), an increase in P_{O_2} levels were noticed at $\theta=90^\circ$. This peak corresponded to the decreased velocity in the flow field, resulted from the opening between two fiber layers positioned above (or below) the central fiber layer. Within the structure of the staggered array used in this geometry, the presence of the surrounding fibers created a squeezed creeping flow around the central fiber, and the flow field was relaxed through the above mentioned opening. It is also noticed that there was a drop in P_{O_2} at $\theta=120^\circ$ which also corresponded to the increased flow velocity at the narrow flow path between the neighboring fibers.

To evaluate different fiber arrangements with the current approach, we conducted a parametric analysis. This parametric analysis was based on the local and overall evaluation of the effects of different bundle arrangements on the mass transfer performance. We have utilized Sh-Sc-Re correlation, mass transfer rates, and P_{O_2} and mass transfer coefficient profiles for the local and/or overall analysis.

We have generated two different arrangements to create the bundle void fractions of 0.53 and 0.40. In simple multi-fiber model, we densely packed the same sized fibers for the $\epsilon=0.40$ arrangement, which resulted in a 15% higher total membrane surface area than that of the $\epsilon=0.53$ arrangement. In the mini oxygenator multi-fiber model, the arrangement with $\epsilon=0.53$ was used to create the model of the device that we used in the experiments. However, the one with a void fraction of 0.40 was created as a theoretical mini oxygenator arrangement with larger diameter fibers while keeping the wall thickness and the mass transfer area same for both arrangements.

The mass transfer rate-blood flow rate plots revealed that, higher overall mass transfer performances were noticed for the lower void fraction arrangement. Although at lower flow conditions the mass transfer rates for the arrangement with $\epsilon=0.40$ were only slightly higher than that of the arrangement with $\epsilon=0.53$. However at higher flow rates the denser configuration looked more favorable. This was similarly observed in regards to configurations with different void fractions and same total mass transfer area [23]. Our

observations may indicate the significance of the packing density on the mass transfer performance for the arrangements with or without same mass transfer areas.

The local mass transfer capabilities may be evaluated with the mass transfer coefficient profiles, as shown in Figure 9. In the figure frequent oscillatory peaks were noticed for both arrangements. The location and the size of these peaks may also be associated with the P_{O_2} profiles. The peaks in the mass transfer coefficient plots occurred based on the variations in the concentration gradients that were utilized in the mass transfer coefficient calculations. Therefore, changes in the slope of the P_{O_2} profiles led to the variation in concentration gradients, and ultimately the peaks in the mass transfer coefficient profiles occurred. The degree of these slope changes determined the size of the peaks. For this reason, at the front end of the fibers ($0^\circ \leq \theta \leq 30^\circ$) there were less K variations for $\varepsilon=0.53$, and bigger oscillations for $\varepsilon=0.40$. The higher variations in the P_{O_2} values resulted in larger local mass transfer coefficients, that showed higher mass transfer in these locations.

The shapes on the P_{O_2} profiles (Fig 9b) were the consequences of the fiber arrangements. As can be seen, the second part of the profiles ($\theta \geq 90^\circ$) were qualitatively similar to each other for both arrangements. However, the first parts were different. At the front end of the fibers lower P_{O_2} values were seen for $\varepsilon=0.53$ arrangement, whereas higher values were noticed for $\varepsilon=0.40$ arrangement. As a result of the higher packing density of $\varepsilon=0.40$ arrangement, and corresponding flow advection, the front surface P_{O_2} values were influenced from the previous fiber, and therefore higher P_{O_2} values were seen there.

When $Sh-Sc-Re$ plots were examined, higher $Sh-Sc^{1/3}$ curves were observed for the fibers positioned at the front of the bundle as compared to the others. Therefore, the mass transfer efficiency was higher in the front section which was caused by the higher P_{O_2} gradients noticed there as compared to the other sections (Fig. 9b).

Another observation on $Sh-Sc-Re$ plots was that, the relative efficiency of the arrangements was affected by the location in the bundle and the flow rate. For example, at $L=0.00$, the efficiencies of the arrangements were similar for $Re=1.0$. However, the lower void fraction was favorable for the higher flow rates. At $L=0.25$, the arrangement with a higher void fraction was favorable for $1 \leq Re \leq 3$. Whereas, the lower void fraction arrangement was more efficient at $3 < Re \leq 10$. At the end of the bundle region, on the other hand, $\varepsilon=0.53$ configuration was more efficient in regards to the studied flow conditions.

The local mass transfer coefficient profiles illustrated in Figure 9 can also be related to the $Sh-Sc^{1/3}$ values at $Re=1.0$ presented in Figure 10. Since, dimensionless numbers are representing the mass transfer efficiencies in averaged quantities, the averaged mass transfer coefficients must be in agreement with them. For the $\varepsilon=0.53$ configuration the averaged mass transfer coefficients varied from $2.0E-4$ down to $2.7E-5$, as L increased from 0.00 to 1.00. However, the corresponding values for $\varepsilon=0.40$ varied from $3E-4$ down to $2.1E-6$. In essence, the relative variation of these averaged mass transfer coefficients followed the same order with the $Sh-Sc^{1/3}$ values at $Re=1.0$.

The mass transfer coefficient and P_{O_2} profiles may give an important guidance to the designer in terms of the approach that can be utilized. For the denser packings the traditional approach with the assumptions of uniform oxygen partial pressure on the fiber surface and negligible mass transfer resistance can be selected, as a representative situation on at least $3/4^{th}$ of the bundle region. However, for the less dense packings the traditional approach fails, and the method, as presented in this work, may be a better selection.

The predictions with the “two-region” approach were further compared to the measurements obtained from the device along the fiber area for different operating conditions. For this

purpose $\varepsilon=0.53$ arrangement was utilized. The results were presented in terms of oxygen saturation and transfer rates. For the lower Re condition, the numerical and experimental profiles were in good agreement throughout the fiber region. For the higher Re condition the predictions were mostly above the measured values, although they were aligned through the exit of the fiber region ($L>0.85$). The maximum deviation was observed at $Re=5$ (excluding the data at $L=0.125$) as approximately 5% in oxygen partial pressures and 15% in oxygen transfer rates. Although the measured sharp change in $0.00 \leq L \leq 0.25$ was not precisely predicted, this non-linear behavior was captured, especially for $Re=5.0$, as a change in the slope in both oxygen saturation and transfer rate profiles. Consequently, in regards to the typical conditions for oxygenators ($Re=3-5$, [36]) the current approach appears accurate enough.

5. Limitations of the approach

The oxygen diffusivity was estimated from measurements of oxygen hydraulic permeance reported in the literature using Equation (4). This method was chosen as no data were available for the diffusive permeability in these fibers. Since oxygen permeance, rather than oxygen diffusivity was used, some error may be introduced into the results. While the diffusive resistance of the membrane appears to be significant from the comparison of the single fiber with and without membrane diffusion, this effect may actually be small compared with the diffusive resistance of the stagnant liquid layer adhering to the membrane surface. Although the hydrophobic property for the considered membrane material was mentioned before, the effect of the diffusive resistance of the stagnant liquid layer on the gas transfer in the multi-fiber model has yet to be quantified.

Although it is not directly related with the approach, but related with the way of conducting it, in regards to the viscoelastic nature of the blood, different types of non-Newtonian models may give better agreement with the measurements.

Similarly, as another parameter affecting the conductivity of the approach, the presence of the hollow fibers can be considered as a limiting factor of this application, in terms of the requirement of implanting computational cells into them.

6. Conclusions

The computational micro-scale model of the hollow fiber membrane was developed with a proposed “two region” modeling approach. An advantage of this approach was to utilize the hollow fibers explicitly to couple the flow field to the oxygen transfer, which was achieved as evidenced by the comparisons with experiments. While there are some commercial implementations of oxygenator models, they are insufficiently reported to enable reproduction of the results. Our model is clearly described, the results validated against experiment, and the limitations explicitly acknowledged. While the model does have some limitations its advantages are: that surface P_{O_2} values are obtained as a result of the calculations; and the oxygen transfer capabilities of fiber arrays with different structures can be evaluated.

It was illustrated that, the current approach can be utilized to predict the mass transfer efficiencies without overestimating. The variation of the P_{O_2} content on the fiber outer surface demonstrated the significance of the fiber resistance on the oxygen transfer. Utilization of this approach was found to be beneficial for the geometries with less packing density, in which the significant P_{O_2} variations observed on the fiber surfaces. It was also noticed that, for the geometries with dense packings, the traditional approach with the underlying assumptions of uniform oxygen partial pressure on the fiber surface and negligible mass transfer resistance, could be applicable.

In the future, the local mass transfer coefficients could be utilized in the continuum models to improve their accuracy. Furthermore, this modeling approach could be extended to evaluate the potential impact of the membrane permeability and thickness with 2-D and/or 3-D models of mini-oxygenators with different types of fiber membranes and fiber arrangements, and to introduce additional complexities such as oxygen/carbon dioxide interaction (the Halden effect). The 3-D application of the current approach may be beneficial to realistically study the effect of different fiber arrangements on obtaining the interstitial flow fields and calculating the gas transfer performances.

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Glossary

Nomenclature

A	membrane surface area in simple multi-fiber model [cm^2]
a	empirical factor in Equation (1) [-]
C_{O_2}	oxygen concentration [$\text{ml O}_2/\text{ml blood}$]
d	transversal distance between the fiber centers [μm]
D	tube outer diameter [μm]
D_b	free oxygen diffusivity in blood [cm^2/s]
D_{eff}	effective oxygen diffusivity [cm^2/s]
D_i	diffusion coefficient in the fiber [cm^2/s]
$\vec{g}$	gravitational force [kg.m/s^2]
h	pore diameter [μm]
Hb	total hemoglobin [g/dl]
$[H_b]$	O_2 binding capacity of blood [ml Hb/ml blood]
J_i	flux through fiber wall [g.cm/s.ml]
K	mass transfer coefficient [m/s]
Km	membrane permeation [$\text{cm}^3/(\text{s.cm}^2.\text{cmHg})$]
l	characteristic length used in Sh and Re [m]
L	normalized fiber bundle length [-]
$\dot{m}_{O_2}$	oxygen transfer rate at 37°C and 1atm [ml/min]
P	pressure [mmHg]
P_{O_2}	oxygen partial pressure [mmHg]
P_0	standard pressure [mmHg]
P_{50}	pressure at half saturation [mmHg]
Q_b	volumetric flow rate of blood [l/min]
S_{O_2}	oxygen saturation x100 [%]

T	temperature [K]
T_0	standard temperature [K]
U	mean inlet velocity [m/s]
x	distance [mm]

Greek letters

α	oxygen solubility in plasma [ml O ₂ /ml plasma/mmHg]
α	exponent in Equation (1) [-]
β	exponent in Equation (1) [-]
ε	bundle void fraction [-]
ε'	fiber porosity [-]
θ	angular location on the fiber surface [degree]
ρ	density of the blood [kg/m ³]
v	velocity [m/s]
τ	tortuosity [-]

Dimensionless numbers

Re	Reynolds number ($Re=lUp/\mu$) [-]
Sc , Schmidt number (Sc	$\mu/\rho D_b$) [-]
Sh , Sherwood number (Sh	Kl/D_b) [-]

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Figure 2.

Figure 3.

Figure 4.

Figure 5.

Figure 6.

Figure 7.

Figure 8.

Figure 9.

Figure 10.

Figure 11.

Figure 12.