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ANALYTIC MULTIPLICATIVE SEPARATION AND EXISTENCE INVESTIGATION OF NON-LINEAR OXYGEN TRANSPORT WITH POISEUILLE HEMODYNAMIC FLOW IN A SEMI-GENERALIZED COORDINATE SYSTEM

Keith C. Afas[1], Terry E. Moschandreou[2 §]
[1,2]Department of Applied Mathematics
Western University
London, Ontario, N6A 5B7, CANADA

Abstract: A well known governing nonlinear PDE used to model oxygen transport is formulated in a generalized co-ordinate system where the Laplacian is expressed in metric tensor form. A reduction of the pde to simpler problem, which has never been done before, subject to specific integrability conditions is shown. A specific form of the initial equation to be reduced has been used by Nair and coworkers[1-3] describing the intraluminal problem of oxygen transport in large capillaries or arterioles and more recent work by [4] describing release of ATP in microchannels. In each of these cases, a tube with a central core, rich in red blood cells, and with a thin plasma region near the boundary wall, free of RBCs is considered. A co-ordinate transformation to solve reduced pde in core region is adopted. An extension and modification of the work of Erbe and Wang [5] is derived and existence of positive solutions of an ode obtained in the general formulation is obtained for nonhomogeneous mixed boundary conditions and on general positive interval. Finally a solution method is given to solve a linear equation used by Nair [1-3] in the plasma layer.

Key Words: Lagrange inversion, poiseuille flow, oxygen transport, curvilinear co-ordinates, existence

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[§]Correspondence author

1. Introduction

Nair et al [1-3] have developed a model for intraluminal oxygen in arteriole-size vessels('large capillaries') where the vessel is considered to be embedded in a thin film of silicone rubber in order to match an in vitro experimental system [6-7]. The model takes into account convection of plasma and RBCs in a cell-rich region together with a thin cell-free region of plasma. The model involves four coupled pde describing diffusion of free oxygen in the cell-free layer, in the plasma surrounding RBCs and in RBCs, and diffusion of hemoglobin-bound oxygen in RBCs. Three of these equations are non-linear because of the slope of the oxyhemoglobin dissociation curve. These equations have a term describing the reaction rate, the rate of oxygen dissociation from hemoglobin per unit volume of RBC. Since no hemoglobin escapes from the RBCs the total heme concentration within the RBC remains constant. The convective terms in governing equations have both plasma and RBC velocity profiles together with a radial distribution of hematocrit.

In this paper, we consider the simplified model of Nair et al[1-3], where the system of four pdes are reduced to one non-linear pde[8], and a linear equation by assuming chemical equilibrium within RBC between oxygen and oxyhemoglobin and neglecting intracellular boundary-layer resistances. The governing nonlinear pde is the subject of the present paper. The pde is generalized for a Laplacian expressed in metric tensor form and is reduced to a simpler system of equations with specific integrability conditions for separation of equation. A relatively recent existence theorem due to Erbe et al [5] is extended to nonhomogenous mixed boundary conditions used based on recent studies for the release of adenosine triphosphate in micro channels with arbitrary radial positive interval. [4]. Also a solution method is given to solve a linear equation used by Nair [1-3] in the plasma layer.

2. Governing Equation for Oxygen Transport

The general form of the nonlinear pde for consideration defining oxygen transport in core region with Poiseuille hemodynamic flow is given by Eq. (2.1):

See section (10) Appendix for general derivation of oxygen transport equation, boundary conditions in section(10.2) of the Appendix and Figure (5) showing the geometry of the problem

$$\left[v_p(1-H_T)+v_{RBC}H_T\frac{K_{RBC}}{K_p}\left(1+\frac{[Hb_T]}{K_{RBC}}\frac{dSO_2}{dPO_2}\right)\right]\frac{\partial PO_2}{\partial z}$$

$$= D_p \nabla^2 PO_2. \quad (2.1)$$

There is a core region of blood flow with RBCs and plasma and a cell-free region with only plasma flowing. In the plasma region near wall of medium, the governing equation is as in Eq.(2.1), without the second term in the square brackets. We will first solve Eq.(2.1) in the general case for the core area.The geometry of the problem occurs in a tube or a channel [4] , and the Laplacian will be generalized below. The blood plasma velocity is v_p and v_{RBC} is the velocity of RBCs with plasma in the cell-rich region. The velocity of the RBCs is lower due to the slip between plasma and RBCs. The distribution of RBCs is such that hematocrit is higher at the center of the fluid container or medium and lower near the wall. The term $\frac{dSO_2}{dPO_2}$ is the slope of the oxyhemoglobin dissociation curve and is a highly nonlinear function of oxygen tension PO_2 [1-3]. The dissociation curve is approximated by the Hill equation[4], where N is an empirical constant and P_{50} is the oxygen tension that yields 50 percent oxygen saturation. $[Hb_T]$ is the total heme concentration which is equal to four times the hemoglobin concentration due to their being four heme groups on each hemoglobin molecule. D_p is the oxygen diffusion coefficient in plasma and has units of $\mu m^2/s$ and K_{RBC}, K_p are the solubilities of O_2 in the RBCs and plasma, respectively, and have units of $M/mmHg$. The values of respective parameters are taken from Table 1 in [4].

It is found that by dividing, expanding, and factoring constants, utilizing the fact that $v_{RBC} = (1 - slp)v_p$, one obtains:

$$\left[v_p \frac{1-H_T}{D_p} + v_{RBC} \frac{H_T}{D_p} \frac{K_{RBC}}{K_p} \left(1 + \frac{[Hb_T]}{K_{RBC}} \frac{dSO_2}{dPO_2}\right)\right] \frac{\partial PO_2}{\partial z} = \nabla^2 PO_2, \quad (2.2)$$

$$\left[\frac{1-H_T}{D_p} + \frac{v_{RBC}}{v_p} \frac{H_T}{D_p} \frac{K_{RBC}}{K_p} \left(1 + \frac{[Hb_T]}{K_{RBC}} \frac{dSO_2}{dPO_2}\right)\right] \frac{\partial PO_2}{\partial z} = \frac{1}{v_p} \nabla^2 PO_2, \quad (2.3)$$

$$\left[\frac{1-H_T}{D_p} + (1-slp) \frac{H_T}{D_p} \frac{K_{RBC}}{K_p} \left(1 + \frac{[Hb_T]}{K_{RBC}} \frac{dSO_2}{dPO_2}\right)\right] \frac{\partial PO_2}{\partial z} = \frac{1}{v_p} \nabla^2 PO_2, \quad (2.4)$$

$$\left[\left(\frac{1-H_T}{D_p} + (1-slp) \frac{H_T}{D_p} \frac{K_{RBC}}{K_p}\right) + \left((1-slp) \frac{H_T}{D_p} \frac{[Hb_T]}{K_p} \frac{dSO_2}{dPO_2}\right)\right] \frac{\partial PO_2}{\partial z} = \frac{1}{v_p} \nabla^2 PO_2. \quad (2.5)$$

The resultant equation may be simplified by allowing some definitions:

$$const = \frac{1-H_T}{D_p} + (1-slp) \frac{H_T}{D_p} \frac{K_{RBC}}{K_p} \approx 3.631(10)^{-4} \frac{s}{\mu m^2} \quad (2.6)$$

$$coeff = (1 - slp)\frac{H_T}{D_p}\frac{[Hb_T]}{K_p} \approx 3.686(10)^{-1}\frac{smmHg}{\mu m^2}. \tag{2.7}$$

This substitution yields:

$$\left(const + coeff\frac{dSO_2}{dPO_2}\right)\frac{\partial PO_2}{\partial z} = \frac{1}{v_p}\nabla^2 PO_2. \tag{2.8}$$

We may permit the definition of

$$\Sigma(PO_2) = const + coeff\frac{dSO_2}{dPO_2},$$

allowing for a transformation of the PDE into a kind of non-linear heat equation,

$$\Sigma(PO_2)\frac{\partial PO_2}{\partial z} = \frac{1}{v_p}\nabla^2 PO_2. \tag{2.9}$$

3. Semi-Generalized Coordinate Representation and Separation

We then establish that

$$PO_2 = PO_2(\vec{r}), \tag{3.1}$$

and allow a kind of "Decomposition Substitution" allowing the tri-dimensionality of PO_2 to be expressed as one longitudinal coordinate, z, and a bi-dimensional generalized set of coordinates, q^i, defined on the wire cross section i.e. (q^1, q^2), (r, θ), (x, y)

$$\Sigma(PO_2(\vec{r})) = P(q^i)L(z), \tag{3.2}$$

$$PL\frac{\partial}{\partial z}\Sigma^{-1}(PL) = \frac{1}{v_p}\nabla^2\Sigma^{-1}(PL). \tag{3.3}$$

Let $\hat{\hat{g}}_{\mu\nu}$ be the metric tensor of the coordinate system composed of q^i. We know that to express the laplacian of an arbitrary function, $f(\vec{q})$ in terms of the metric tensor in curvilinear coordinates, the following form emerges:

$$\nabla^2 f(\vec{q}) = \sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial f}{\partial q^i}\right). \tag{3.4}$$

Allowing this definition of $\nabla^2\Sigma^{-1}(PL)$, we find that by utilizing the chain and product rule, the following equation may be decomposed significantly:

$$PL\frac{\partial}{\partial z}\Sigma^{-1}(PL) = \frac{1}{v_p}\sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial}{\partial q^i}\Sigma^{-1}(PL)\right),$$

$$
\begin{aligned}
PL\frac{\partial(PL)}{\partial z}\frac{\partial}{\partial(PL)}\Sigma^{-1}(PL) =& \frac{1}{v_p}\sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\frac{\partial}{\partial q^i} \\
&\times\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial(PL)}{\partial q^i}\frac{\partial}{\partial(PL)}\Sigma^{-1}(PL)\right) \\
P^2L\frac{dL}{dz}\frac{d\Sigma^{-1}}{d(PL)} =& \frac{1}{v_p}\sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\frac{\partial}{\partial q^i}\left(\frac{L\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{d\Sigma^{-1}}{d(PL)}\right) \\
P^2L\frac{dL}{dz}\frac{d\Sigma^{-1}}{d(PL)} =& \frac{L}{v_p}\sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{d\Sigma^{-1}}{d(PL)}\right) \\
P^2\frac{dL}{dz}\frac{d\Sigma^{-1}}{d(PL)} =& \frac{1}{v_p\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\sum_i \frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{d\Sigma^{-1}}{d(PL)}\right) \\
P^2\frac{dL}{dz}\frac{d\Sigma^{-1}}{d(PL)} =& \frac{1}{v_p\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\sum_i \left[\frac{d\Sigma^{-1}}{d(PL)}\frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\right)\right. \\
&\left.+\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{\partial}{\partial q^i}\frac{d\Sigma^{-1}}{d(PL)}\right] \\
P^2\frac{dL}{dz}v_p\frac{d\Sigma^{-1}}{d(PL)} =& \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\sum_i \left[\frac{d\Sigma^{-1}}{d(PL)}\frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\right)\right. \\
&\left.+\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{\partial}{\partial q^i}\frac{d\Sigma^{-1}}{d(PL)}\right] \\
P^2\frac{dL}{dz}v_p\frac{d\Sigma^{-1}}{d(PL)} =& \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\sum_i \frac{d\Sigma^{-1}}{d(PL)}\frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\right) \\
&+\frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\sum_i \frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{\partial}{\partial q^i}\frac{d\Sigma^{-1}}{d(PL)} \\
P^2\frac{dL}{dz}v_p\frac{d\Sigma^{-1}}{d(PL)} =& \frac{d\Sigma^{-1}}{d(PL)}\sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\right) \\
&+\sum_i \frac{1}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{\partial}{\partial q^i}\frac{d\Sigma^{-1}}{d(PL)}.
\end{aligned}
\tag{3.5}
$$

Noticing the first term on the right side of Eq.(3.5), a reverse definition of the metric tensor expression to the laplacian, may be utilized, to greatly simplify notation:

$$P^2\frac{dL}{dz}v_p\frac{d\Sigma^{-1}}{d(PL)} = \frac{d\Sigma^{-1}}{d(PL)}\nabla^2 P + \sum_i \frac{1}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{\partial}{\partial q^i}\frac{d\Sigma^{-1}}{d(PL)}. \tag{3.6}$$

Grouping terms on both sides, we may isolate and separate the equation:

$$\left(P^2\frac{dL}{dz}v_p - \nabla^2 P\right)\frac{d\Sigma^{-1}}{d(PL)} = \sum_i \frac{1}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\frac{\partial(PL)}{\partial q^i}\frac{\partial}{\partial(PL)}\frac{d\Sigma^{-1}}{d(PL)}$$

$$\left(P^2\frac{dL}{dz}v_p - \nabla^2 P\right)\frac{d\Sigma^{-1}}{d(PL)} = \sum_i \frac{1}{\hat{\hat{g}}_{ii}}L\left(\frac{\partial P}{\partial q^i}\right)^2\frac{d^2\Sigma^{-1}}{d(PL)^2}$$

$$\left(P^2\frac{dL}{dz}v_p - \nabla^2 P\right)\frac{d\Sigma^{-1}}{d(PL)} = L\frac{d^2\Sigma^{-1}}{d(PL)^2}\sum_i \frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial P}{\partial q^i}\right)^2$$

$$\left(P^2\frac{dL}{dz}v_p - \nabla^2 P\right)\left[L\sum_i \frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial P}{\partial q^i}\right)^2\right]^{-1} = \left(\frac{d\Sigma^{-1}}{d(PL)}\right)^{-1}\frac{d^2\Sigma^{-1}}{d(PL)^2} = \mathbb{S}_1$$

$$\left(P^2\frac{dL}{dz}v_p - \nabla^2 P\right)\left[L\sum_i \frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial P}{\partial q^i}\right)^2\right]^{-1} = \left(\frac{d\Sigma^{-1}}{d(PL)}\right)^{-1}\frac{d^2\Sigma^{-1}}{d(PL)^2} = \mathbb{S}_1$$

It follows that $\Sigma^{-1}(PL) = C_1 + C_2 e^{S_1 PL}$ from which we can solve for PL as a function of oxygen tension PO_2. For $\mathbb{S}_1 = 0$, according to the Lagrange Inversion Theorem (see [11]), the form of Σ^{-1} would be:

$$PO_2 = P_0 + \frac{PL - \Sigma(P_0)}{\Sigma'(P_0)} \tag{3.7}$$

Considering $\mathbb{S}_1 = 0$, it follows that the differential equations become:

$$P^2\frac{dL}{dz}v_p - \nabla^2 P = 0, L \neq 0, \sum_i \frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial P}{\partial q^i}\right)^2 \neq 0 \ \ \&$$

$$\left(\frac{d\Sigma^{-1}}{d(PL)}\right)^{-1}\frac{d^2\Sigma^{-1}}{d(PL)^2} = \mathbb{S}_1 = 0, \frac{d\Sigma^{-1}}{d(PL)} \neq 0.$$

Ignoring all the differential equations and conditions except the laplacian equation, we obtain

$$P^2\frac{dL}{dz}v_p - \nabla^2 P = 0$$

$$
\begin{aligned}
&P^2 \frac{dL}{dz} v_p = \nabla^2 P \\
&\frac{dL}{dz} = \frac{1}{P^2 v_p} \nabla^2 P = -\mathbb{S}_2^2 \\
&\frac{dL}{dz} = -\mathbb{S}_2^2, \nabla^2 P = -\mathbb{S}_2^2 v_p P^2
\end{aligned}
$$

$$
\frac{dL}{dz} + \mathbb{S}_2^2 = 0, \nabla^2 P + \mathbb{S}_2^2 v_p P^2 = 0 \tag{3.8}
$$

Combining all conditions into one set of equations:

$$
\nabla^2 P + \mathbb{S}_2^2 v_p P^2 = 0, \quad \sum_i \frac{1}{\hat{\hat{g}}_{ii}} \left(\frac{\partial P}{\partial q^i} \right)^2 \neq 0 \tag{3.9}
$$

$$
\frac{dL}{dz} + \mathbb{S}_2^2 = 0, \quad L \neq 0 \tag{3.10}
$$

$$
\frac{d^2 \Sigma^{-1}}{d(PL)^2} = \mathbb{S}_1 = 0, \quad \frac{d\Sigma^{-1}}{d(PL)} \neq 0 \tag{3.11}
$$

Next, recalling that

$$
\left(P^2 \frac{dL}{dz} v_p - \nabla^2 P \right) \left[L \sum_i \frac{1}{\hat{\hat{g}}_{ii}} \left(\frac{\partial P}{\partial q^i} \right)^2 \right]^{-1} = \left(\frac{d\Sigma^{-1}}{d(PL)} \right)^{-1} \frac{d^2 \Sigma^{-1}}{d(PL)^2} = \mathbb{S}_1. \tag{3.12}
$$

We consider the general case, where $\mathbb{S}_1 \neq 0$ and attempt a general solution of Eq. (3.12) .

Multiplying Eq.(3.12) by L and setting $Q(q^i, z) = PL = \Sigma(PO_2)$ we obtain the following reformulation of Eq.(3.12) in terms of Q.

$$
Q(q^i, z) \frac{\partial Q(q^i, z)}{\partial z} v_p - \nabla^2 Q(q^i, z) = \mathbb{S}_1 \sum_i \frac{1}{\hat{\hat{g}}_{ii}} \left(\frac{\partial Q(q^i, z)}{\partial q^i} \right)^2 \tag{3.13}
$$

Let the function $Q = \zeta(\sigma)$ and substitute into Eq.(3.13).

$$
v_p \zeta \frac{\partial \zeta}{\partial z} - \sum_i \frac{1}{\delta} \frac{\partial}{\partial q^i} \left(\frac{\delta}{\hat{\hat{g}}_{ii}} \frac{\partial \zeta}{\partial q^i} \right) = \mathbb{S}_1 \sum_i \frac{1}{\hat{\hat{g}}_{ii}} \left(\frac{\partial \zeta}{\partial q^i} \right)^2 \tag{3.14}
$$

We can rewrite pde as follows:

$$v_p\zeta\frac{d\zeta}{d\sigma}\frac{\partial\sigma}{\partial z}-\sum_i\frac{1}{\delta}\frac{\partial}{\partial q^i}(\frac{\delta}{\hat{\hat{g}}_{ii}}\frac{d\zeta}{d\sigma}\frac{\partial\sigma}{\partial q^i})=\mathbb{S}_1\sum_i\frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{d\zeta}{d\sigma}\frac{\partial\sigma}{\partial q^i}\right)^2, \tag{3.15}$$

$$v_p\zeta\frac{d\zeta}{d\sigma}\frac{\partial\sigma}{\partial z}-\frac{1}{\delta}\sum_i[\frac{\delta}{\hat{\hat{g}}_{ii}}\frac{\partial\sigma}{\partial q^i}\frac{\partial}{\partial q^i}(\frac{d\zeta}{d\sigma})+\frac{d\zeta}{d\sigma}\frac{\partial}{\partial q^i}(\frac{\delta}{\hat{\hat{g}}_{ii}}\frac{\partial\sigma}{\partial q^i})]$$
$$=\mathbb{S}_1\left(\frac{d\zeta}{d\sigma}\right)^2\sum_i\frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial\sigma}{\partial q^i}\right)^2, \tag{3.16}$$

$$v_p\zeta\frac{d\zeta}{d\sigma}\frac{\partial\sigma}{\partial z}-\frac{1}{\delta}\sum_i[\frac{\delta}{g_{ii}}\frac{\partial\sigma}{\partial q^i}\frac{\partial\sigma}{\partial q^i}\frac{d^2\zeta}{d\sigma^2}+\frac{d\zeta}{d\sigma}\frac{\partial}{\partial q^i}(\frac{\delta}{\hat{\hat{g}}_{ii}}\frac{\partial\sigma}{\partial q^i})]$$
$$=\mathbb{S}_1\left(\frac{d\zeta}{d\sigma}\right)^2\sum_i\frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial\sigma}{\partial q^i}\right)^2, \tag{3.17}$$

$$v_p\zeta\frac{d\zeta}{d\sigma}\frac{\partial\sigma}{\partial z}-\frac{d^2\zeta}{d\sigma^2}\sum_i\frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial\sigma}{\partial q^i}\right)^2-\frac{1}{\delta}\frac{d\zeta}{d\sigma}\sum_i\frac{\partial}{\partial q^i}(\frac{\delta}{\hat{\hat{g}}_{ii}}\frac{\partial\sigma}{\partial q^i})$$
$$=\mathbb{S}_1\left(\frac{d\zeta}{d\sigma}\right)^2\sum_i\frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial\sigma}{\partial q^i}\right)^2, \tag{3.18}$$

$$v_p\zeta\frac{d\zeta}{d\sigma}\frac{\partial\sigma}{\partial z}-\frac{d\zeta}{d\sigma}\nabla^2\sigma=\left(\frac{d^2\zeta}{d\sigma^2}+\mathbb{S}_1\left(\frac{d\zeta}{d\sigma}\right)^2\right)\sum_i\frac{1}{\hat{\hat{g}}_{ii}}\left(\frac{\partial\sigma}{\partial q^i}\right)^2. \tag{3.19}$$

Setting the right hand side of Eq.(3.19) to zero, we obtain the following pde

$$v_p\zeta\frac{d\zeta}{d\sigma}\frac{\partial\sigma}{\partial z}-\frac{d\zeta}{d\sigma}\nabla^2\sigma=0. \tag{3.20}$$

This equation is not known to have exact solutions as is, since the equation is highly nonlinear due to solution of ζ being a logarithmic function.

We can however expand the log function in ζ in terms of $\sigma(y,z)$ and consider a couple of terms in the Maclaurin series .Up to first order we obtain using a cartesian coordinate representation for σ, where $v_p=c-dy^2$ for constants c and d which will be determined later.

$$\left(c-dy^2\right)\left(\frac{\ln\left(C2\,\mathbb{S}_1\right)}{\mathbb{S}_1}+\frac{C1\,\sigma\left(y,z\right)}{C2\,\mathbb{S}_1}\right)\frac{\partial}{\partial z}\sigma\left(y,z\right)-\frac{\partial^2}{\partial y^2}\sigma\left(y,z\right)=0, \tag{3.21}$$

where $C1$ and $C2$ are arbitrary constants in the solution of ζ, and $C2$ is large enough to truncate series. A generalized separable solution linear in z is:

$$\sigma(y,z)=\frac{C2\mathbb{S}_1}{C1}[\phi(y)z+\psi(y)-ln(C2\mathbb{S}_1)/\mathbb{S}_1], \tag{3.22}$$

where the functions $\phi(y)$ and $\psi(y)$ are determined by the system of ode:

$$\frac{1}{c-dy^2}\phi''(y)-\phi^2(y)=0, \tag{3.23}$$

$$\frac{1}{c-dy^2}\psi''(y)-\phi(y)\psi(y)=0. \tag{3.24}$$

The first equation Eq.(3.23) can be solved independently of the second Eq.(3.24). Equation (3.24) has a particular solution $\psi(y)=\phi(y)$. Therefore a general solution [12] can be given as follows:

$$\psi(y)=C_1\phi(y)+C_2\phi(y)\int\frac{dy}{\phi^2(y)}. \tag{3.25}$$

We consider an existence theorem in section 6 for Eq.(3.23) and a coordinate transformation method for it's solution as is the case with the more general equation Eq.(3.8), in section 5.

Equation (3.23) has a solution [13] as follows:

Consider the transformation $y=\kappa(z)$, $\phi=w\sqrt{a\kappa'(z)}$, substituting into Eq. (3.23) gives:

$$w''(z)+\left[\frac{1}{2}\frac{\kappa'''(z)}{\kappa'(z)}-\frac{3}{4}\left(\frac{\kappa''(z)}{\kappa'(z)}\right)^2\right]w(z)$$
$$+a^{-2}(a\kappa'(z))^{3/2}(c-d\kappa(z)^2)w(z)^2a\kappa'(z)=0 \tag{3.26}$$

The sign of the parameter a must coincide with that of the derivative of $\kappa'(z)$.

In 9.Appendix specific values are considered as a test example for the solution of Eq.(3.26).

4. Specific Co-ordinate System: Cartesian Co-ordinates

Analyzing Eq.(3.8), we briefly examine the case, separation, and existence of a solution in the classic bi-dimensional rectangular co-ordinates: (x,y). Under such a co-ordinate system, the metric tensor can be shown to be:

$$\hat{\hat{g}}_{\mu\nu}(Rect.)=\begin{pmatrix}1 & 0\\ 0 & 1\end{pmatrix} \tag{4.1}$$

Assuming no PO_2 saturation variation horizontally, the laplacian becomes a partial second derivative with respect to the vertical co-ordinate, and so Eq.(3.8) becomes:

$$\frac{\partial^2 P}{\partial y^2} + \mathbb{S}_2^2 v_p P^2 = 0, \frac{\partial P}{\partial y} \neq 0 \tag{4.2}$$

Allowing $P(x, y) = X(x)Y(y)$, Eq.(4.2) may be further developed:

$$X\frac{d^2Y}{dy^2} + \mathbb{S}_2^2 v_p X^2 Y^2 = 0, X \neq 0 \text{ and } \frac{dY}{dy} \neq 0 \tag{4.3}$$

We see that the equation may be factored to show

$$X\left(\frac{d^2Y}{dy^2} + \mathbb{S}_2^2 v_p X Y^2\right) = 0$$

But we know from the first inequality in Eq.(4.3) that $X \neq 0$ so then:

$$\frac{d^2Y}{dy^2} + \mathbb{S}_2^2 v_p X Y^2 = 0, X \neq 0 and \frac{dY}{dy} \neq 0 \tag{4.4}$$

Co-ordinate-separating the first equation, allowing $-\mathbb{S}_3^2$ to be the separation constant yields:

$$\frac{1}{\mathbb{S}_2^2 v_p Y^2}\frac{d^2Y}{dy^2} = -X = -\mathbb{S}_3^2, X \neq 0 and \frac{dY}{dy} \neq 0 \tag{4.5}$$

We obtain, as expected, that $X(x)$ is a non-zero constant. The $Y(y)$ equation, defining $\mathbb{S}_2\mathbb{S}_3 = \mathbb{S}_4$ is obtained as:

$$\frac{d^2Y}{dy^2} + \mathbb{S}_4^2 v_p Y^2 = 0 \tag{4.6}$$

The plasma velocity function, $v_p(y)$ has the general form of $v_p = \sigma_i^2 - \mu_i^2 y^2$ where the index, i, indicates whether v_p is taken in the channel sleeve or channel area. According to this form, Eq.(4.6) may be rewritten in the final explicit form, along with the inequality condition:

$$\frac{d^2Y}{dy^2} + \mathbb{S}_4^2 \cdot (\sigma_i^2 - \mu_i^2 y^2) \cdot Y^2 = 0, \frac{dY}{dy} \neq 0 \tag{4.7}$$

An existence of positive solutions to Eq.(4.7) subject to mixed boundary conditions will be given in section 6.

5. Laplacian Formulation and Solution in Transformed Co-ordinate System

In addition, we also consider the concept of a co-ordinate system which may formulate the Laplacian of Eq.(3.8) in such a way such that the equation may be solvable. By decomposing the Laplacian curvilinearly, components of the metric tensor may be obtained as PDE's and may yield the form of the co-ordinate transform. We proceed by starting at Eq.(3.8) allowing the Laplacian to be decomposed:

$$\begin{aligned}\nabla^2 P + \mathbb{S}_2^2 \upsilon_p P^2 =& 0\\ \sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}} \frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}} \frac{\partial P}{\partial q^i}\right) + \mathbb{S}_2^2 \upsilon_p P^2 =& 0\\ \sum_i \frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}} \frac{\partial P}{\partial q^i}\right) + \left(\prod_i \sqrt{\hat{\hat{g}}_{ii}}\right) \mathbb{S}_2^2 \upsilon_p P^2 =& 0.\end{aligned}$$

In order to decompose this further, we allow the sum to be expanded. However, issues arise when attempting to define q^i. We allow q^i to be (ξ_1, ξ_2). According to this definition, we allow the general co-ordinate transformation to deviate from the Cartesian Laplacian by the transformation: $x = f(\xi_1, \xi_2), y = g(\xi_1, \xi_2)$. We also assume a separation by: $P(\xi_1, \xi_2) = \Xi_1(\xi_1)\Xi_2(\xi_2)$

$$\frac{\partial}{\partial \xi_1}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{11}} \frac{d\Xi_1}{d\xi_1}\Xi_2\right) + \frac{\partial}{\partial \xi_2}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{22}} \Xi_1 \frac{d\Xi_2}{d\xi_2}\right) + \left(\prod_i \sqrt{\hat{\hat{g}}_{ii}}\right) \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2^2 = 0$$

$$\Xi_2 \frac{\partial}{\partial \xi_1}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{11}} \frac{d\Xi_1}{d\xi_1}\right) + \Xi_1 \frac{\partial}{\partial \xi_2}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{22}} \frac{d\Xi_2}{d\xi_2}\right) + \left(\prod_i \sqrt{\hat{\hat{g}}_{ii}}\right) \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2^2 = 0$$

$$\Xi_2 \frac{\partial}{\partial \xi_1}\left(\sqrt{\frac{\hat{\hat{g}}_{22}}{\hat{\hat{g}}_{11}}} \frac{d\Xi_1}{d\xi_1}\right) + \Xi_1 \frac{\partial}{\partial \xi_2}\left(\sqrt{\frac{\hat{\hat{g}}_{11}}{\hat{\hat{g}}_{22}}} \frac{d\Xi_2}{d\xi_2}\right) + \left(\prod_i \sqrt{\hat{\hat{g}}_{ii}}\right) \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2^2 = 0,$$

$$\gamma = \frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{11}}$$

$$\Xi_2 \frac{\partial}{\partial \xi_1}\left(\gamma \frac{d\Xi_1}{d\xi_1}\right) + \Xi_1 \frac{\partial}{\partial \xi_2}\left(\frac{1}{\gamma} \frac{d\Xi_2}{d\xi_2}\right) + \left(\prod_i \sqrt{\hat{\hat{g}}_{ii}}\right) \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2^2 = 0.$$

In the attempt to obtain a family of co-ordinate systems reducing Eq.(3.8) to a solvable ODE we make the assumption that:

$$\frac{\partial}{\partial \xi_2}\left(\frac{1}{\gamma} \frac{d\Xi_2}{d\xi_2}\right) = 0 \tag{5.1}$$

In this assumption, we may advance breaking the equation down:

$$\Xi_2 \frac{\partial}{\partial \xi_1}\left(\gamma \frac{d\Xi_1}{d\xi_1}\right) + \left(\prod_i \sqrt{\hat{\hat{g}}_{ii}}\right) \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2^2 = 0$$

$$\frac{\partial}{\partial \xi_1}\left(\gamma \frac{d\Xi_1}{d\xi_1}\right) + \left(\prod_i \sqrt{\hat{\hat{g}}_{ii}}\right) \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2 = 0$$

$$\gamma \frac{d^2\Xi_1}{d\xi_1^2} + \frac{\partial \gamma}{\partial \xi_1}\frac{d\Xi_1}{d\xi_1} + \left(\prod_i \sqrt{\hat{\hat{g}}_{ii}}\right) \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2 = 0$$

$$\frac{d^2\Xi_1}{d\xi_1^2} + \frac{1}{\gamma}\frac{\partial \gamma}{\partial \xi_1}\frac{d\Xi_1}{d\xi_1} + \frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\gamma} \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2 = 0, \gamma = \frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{11}}$$

$$\frac{d^2\Xi_1}{d\xi_1^2} + \left(\frac{1}{\gamma}\frac{\partial \gamma}{\partial \xi_1}\right)\frac{d\Xi_1}{d\xi_1} + \hat{\hat{g}}_{11} \mathbb{S}_2^2 \upsilon_p \Xi_1^2 \Xi_2 = 0$$

We define:

$$\mu = \frac{1}{\gamma}\frac{\partial \gamma}{\partial \xi_1} \qquad \nu = \hat{\hat{g}}_{11} \mathbb{S}_2^2 \upsilon_p \tag{5.2}$$

to obtain:

$$\frac{d^2\Xi_1}{d\xi_1^2} + \mu \frac{d\Xi_1}{d\xi_1} + \nu \Xi_1^2 \Xi_2 = 0 \tag{5.3}$$

Allowing $\mu = 0$, we obtain an equation which can be separated autonomously

$$\frac{d^2\Xi_1}{d\xi_1^2} + \nu \Xi_1^2 \Xi_2 = 0 \rightarrow \Xi_2 = \mathbb{S}_3^2$$

$$\frac{d^2\Xi_1}{d\xi_1^2} + \nu \mathbb{S}_3^2 \Xi_1^2 = 0 \tag{5.4}$$

Permitting $\mu = 0$: also allows

$$\frac{\partial \gamma}{\partial \xi_1} = \frac{\partial}{\partial \xi_1}\sqrt{\frac{\hat{\hat{g}}_{22}}{\hat{\hat{g}}_{11}}} = 0 \qquad \rightarrow \qquad \frac{\partial}{\partial \xi_1}\frac{\hat{\hat{g}}_{22}}{\hat{\hat{g}}_{11}} = 0 \tag{5.5}$$

In addition, conditions of obtaining Eq.(5.4) were developed which take the form of conditions on the metric tensor. To progress further, the metric tensor of such a general transformation must be developed. In general, for the transformation, $x = f(\xi_1, \xi_2), y = g(\xi_1, \xi_2)$, the metric tensor is:

$$\hat{\hat{g}}_{\mu\nu} = \begin{pmatrix} \left(\frac{\partial f}{\partial \xi_1}\right)^2 + \left(\frac{\partial g}{\partial \xi_1}\right)^2 & \frac{\partial f}{\partial \xi_1}\frac{\partial f}{\partial \xi_2} + \frac{\partial g}{\partial \xi_1}\frac{\partial g}{\partial \xi_2} \\ \frac{\partial f}{\partial \xi_1}\frac{\partial f}{\partial \xi_2} + \frac{\partial g}{\partial \xi_1}\frac{\partial g}{\partial \xi_2} & \left(\frac{\partial f}{\partial \xi_2}\right)^2 + \left(\frac{\partial g}{\partial \xi_2}\right)^2 \end{pmatrix} \tag{5.6}$$

Knowing Eq.(5.2), this defines the metric tensor component $\hat{\hat{g}}_{11}$. Also, Laplacian operators must operate on orthogonal co-ordinate systems. For any n-dimensional orthogonal co-ordinate system, the metric tensor will be always composed of only diagonal components. Knowing this we must also define:

$$\hat{\hat{g}}_{12} = \hat{\hat{g}}_{21} = 0. \tag{5.7}$$

One may then create the following sytem of PDEs relating the above conditions of the components of the metric tensor:

$$\left(\frac{\partial f}{\partial \xi_1}\right)^2 + \left(\frac{\partial g}{\partial \xi_1}\right)^2 = \frac{\nu}{\mathbb{S}_2^2 v_p} \tag{5.8}$$

$$\frac{\partial f}{\partial \xi_1}\frac{\partial f}{\partial \xi_2} + \frac{\partial g}{\partial \xi_1}\frac{\partial g}{\partial \xi_2} = 0 \tag{5.9}$$

Solving the above, it can be easily verified that the solution is:

$$x = F_1(\xi_2) + F_2(\xi_2)\int \frac{1}{\sqrt{v_p}} d\xi_1 \tag{5.10}$$

$$y = \int \frac{\mathbb{S}_2 F_2(\xi_2)}{\sqrt{\nu - (\mathbb{S}_2 F_2(\xi_2))^2}} \frac{\partial x}{\partial \xi_2} d\xi_2 \tag{5.11}$$

where F_1 & F_2 are arbitrary differentiable functions. We allow the assumption that $F_1(\xi_2) = 0$, so that the transformation can be entirely multiplicative. Allowing this simplification allows Eq.(5.10) & Eq.(5.11) to be rewritten as:

$$x = F_2(\xi_2)\int \frac{1}{\sqrt{v_p}} d\xi_1 \tag{5.12}$$

$$y = -\frac{1}{\mathbb{S}_2}\sqrt{\nu - (\mathbb{S}_2 F_2(\xi_2))^2}\int \frac{1}{\sqrt{v_p}} d\xi_1 \tag{5.13}$$

Allowing this form, we compute the following metric tensor:

$$\hat{\hat{g}}_{\mu\nu} = \begin{pmatrix} \frac{\nu}{\mathbb{S}_2^2 v_p} & 0 \\ 0 & \left(\frac{dF}{d\xi_2}\int \frac{1}{\sqrt{v_p}}\right)^2 \left(1 + \frac{\mathbb{S}_2 F_2}{\nu (\mathbb{S}_2 F_2)^2}\right) \end{pmatrix} \tag{5.14}$$

We now observe Eq.(5.5). In order for Eq.(5.5) to be satisfied, we first compute $\frac{\hat{\hat{g}}_{22}}{\hat{\hat{g}}_{11}}$.

Keeping in mind that $v_p(\xi_1)$ is a fully defined function, we find that in order for Eq.(5.5) to be satisfied, $F_2(\xi_2)$ must be a constant. According to this, the resultant co-ordinate may projected on the cartesian plane appears as in Figure 1. In this way, isolating for F_2 in Eq.(5.13), and substituting into Eq.(5.14), we obtain:

$$y = -\frac{1}{\mathbb{S}_2}\sqrt{\nu - \left(\frac{\mathbb{S}_2 x}{\int \frac{1}{\sqrt{v_p}} d\xi_1}\right)^2} \int \frac{1}{\sqrt{v_p}} d\xi_1 \tag{5.15}$$

Isolating for the integral, we obtain:

$$\int \frac{1}{\sqrt{v_p}} d\xi_1 = \frac{|\mathbb{S}_2|}{\sqrt{\nu}}\sqrt{x^2 - (\mathbb{S}_2 y)^2} \tag{5.16}$$

Obtaining $v_p(\xi_1)$ from[4], the function has a general parabolic form with constant depending on erythrocyte regions. They may be indexed as μ_i & σ_i,
to obtain the general form of:

$$v_p(\xi_1) = \sigma_i^2 - \mu_i^2 \xi_1^2 \tag{5.17}$$

According to this form, the integral has the form:

$$\int \frac{1}{\sqrt{v_p}} d\xi_1 = \frac{1}{\mu_i} sin^{-1}\left(\frac{\mu_i \xi_1}{\sigma_i}\right) \tag{5.18}$$

Therefore, utilizing Eq.(5.17), we may solve for ξ_1 to obtain the inverse transformation:

$$\xi_1 = \frac{\sigma_i}{\mu_i} sin\left(\frac{\mu_i |\mathbb{S}_2|}{\sqrt{\nu}}\sqrt{x^2 - (\mathbb{S}_2 y)^2}\right) \tag{5.19}$$

Once Eq.(5.4) is solved, Eq.(5.19) will be used to transform the solution back into cartesian co-ordinates.

6. Existence Results for Rectangular Co-ordinates Formulation

In this section we shall consider the boundary value problem(BVP)

$$\frac{d^2 R}{dy^2} + \mathbb{S}_4^2 \cdot (c - dy^2) \cdot f(R) = 0, \quad 0 < y < a \tag{6.1}$$

$$\alpha R(0) = 0 \tag{6.2}$$

$$\gamma R(a) + \delta R'(a) = \frac{\delta_2 \gamma}{\alpha}(a\gamma + \delta) \tag{6.3}$$

It is assumed that:

$\alpha, \gamma, \delta, c, d$ are positive real numbers and $W = \alpha\delta > 0,\ f(R) = R^2,\ \mathbb{S}_4^2 = 1,$

$\delta_2 \in R^+$). The boundary condition in Eq.(6.3) arises in a recent problem in oxygen transport and release of ATP in microchannels [4] , where an oxygen permeable membrane at the wall of channel is used to decrease the hemoglobin oxygen saturation of erythrocytes flowing through the channel.

The above BVP has at least one positive solution using the fixed point theorem in [9-10]:

Theorem 1. *Let E be a Banach space, and let $C \subset E$ be a cone in E. Assume Ω_1, Ω_2 are open subsets of E with $0 \in \Omega_1, \overline{\Omega_1} \subset \Omega_2$ and let*

$$A : C \cap (\overline{\Omega_2} \setminus \Omega_1) \to C$$

be a compact operator such that either

$$(i)\|AR\| \le \|R\|, R \in C \cap \partial(\Omega_1), and \|AR\| \ge \|R\|, R \in C \cap \partial\Omega_2; or$$

$$(ii)\|AR\| \ge \|R\|, R \in C \cap \partial(\Omega_1), and \|AR\| \le \|R\|, R \in C \cap \partial\Omega_2.$$

Then A has a fixed point in $C \cap (\overline{\Omega_2} \setminus \Omega_1)$.

Theorem 2. *The BVP (6.1)-(6.3) has at least one positive solution.*

Proof. The BVP (6.1)-(6.3) has a solution $R = R(y)$ iff R satisfies the following fixed point equation:

$$R(y) = \int_0^a G(y,s)(c - ds^2)R(s)^2 ds + \delta_2\gamma y/\alpha = AR(y),$$

$\delta_2, \in R$ and positive. (6.4)

Let $\delta_0(y) = \delta_2\gamma y/\alpha$.

The function of two variables $G(y,s)$ denotes the Green's function for the homogeneous BVP given as follows:

$$\frac{d^2 R}{dy^2} = 0 \tag{6.5}$$

$$\alpha R(0) = 0 \tag{6.6}$$

$$\gamma R(a) + \delta R'(a) = 0 \tag{6.7}$$

and is explicitly given by $G(y,s) =$

$$\begin{cases} \frac{1}{W}(\gamma(a-y)+\delta)(\alpha s) & 0 \le s \le y \le a \\ \frac{1}{W}(\alpha y)(\gamma(a-s)+\delta) & 0 \le y \le s \le a \end{cases} \tag{6.8}$$

The function $f(R) = R^2$ is continuous on the positive reals and satisfies $M_1 \le f(R)G(y,s) \le M_2$, for $y, s \in [0,a]$,where $0 < M_1 < M_2$ are two constants.

In addition it is assumed that the following inequality is true

$$\delta_0(y) + M_2 \int_0^a (c - ds^2)ds < l, \text{ for } l \in (0,\infty). \tag{6.9}$$

Since $\delta_0(y), > 0$, then $A(R(y)) > 0$ for all $y \in [0,a]$.

There is a $\zeta \in (0,1)$ and for $0 < x < a$ such that

$$min_{y\in[x,a]}(AR)(y) = (AR)(x) = \int_0^a G(x,s)(c-ds^2)R(s)^2 ds + \delta_0(y)$$

$$\ge M_1(\int_0^a (c-ds^2)ds + \delta_0(y)) \ge \zeta \|AR\| \tag{6.10}$$

$$\zeta = \frac{M_1(\int_0^x (c-ds^2)ds + \delta_0(y)}{M_2(\int_0^a (c-ds^2)ds + \delta_0(y)} \tag{6.11}$$

Consider the cone in the set of positive continuous functions on $[0,a]$:

$$C = \{R : R(y) \ge 0, min_{y\in[x,a][}R(y) \ge \zeta\|R\|\}, \tag{6.12}$$

where$\|R\| = sup_{[0,a]}\|R(y)\|$.

Now $G(y,s) \le G(s,s), \quad 0 \le s \le y \le a$, so if $R \in C$, then

$$AR(y) = \int_0^a G(y,s)(c-ds^2)R(s)^2 ds + \delta_0(y) \le \int_0^a G(s,s)(c-ds^2)R(s)^2 ds + \delta_0(y) \tag{6.13}$$

$$\|AR\| \le \int_0^a G(s,s)(c-ds^2)R(s)^2 ds + \delta_0(y). \tag{6.14}$$

Lemma 1. *For $y \in [x,a]$, $s \ge y$*

$$\frac{G(y,s)}{G(s,s)} \ge \zeta. \tag{6.15}$$

Proof.

$$\begin{aligned} M_2\int_0^a (c-dy^2)dy+\delta_0(y) &\geq \int_0^a G(y,s)R^2(c-dy^2)dy+\delta_0(y)\\ &\geq \int_0^x G(y,s)R^2(c-dy^2)dy+\delta_0(y)\\ &\geq M_1\int_0^x (c-dy^2)dy+\delta_0(y),\\ G(y,s)M_2\int_0^a (c-dy^2)dy+\delta_0(y) &\geq G(y,s)M_1\int_0^x (c-dy^2)dy+\delta_0(y)\\ &\geq G(s,s)M_1\int_0^x (c-dy^2)dy+\delta_0(y), \end{aligned}$$

for $s \geq y$, then $G(y,s) \geq G(s,s)$. □

Now, if $R \in C$,

$$\begin{aligned} min_{[x,a]}AR(y) &= min_{[x,a]}\int_0^a G(y,s)(c-ds^2)R(s)^2ds+\delta_0(y)\\ &\geq \zeta\int_0^a G(s,s)(c-ds^2)R(s)^2ds+\delta_0(y) \geq \zeta\|AR\|. \end{aligned} \quad (6.16)$$

Therefore, $AC \subset C$, and thus $A : C \to C$, is compact. The function $f(R) = R^2$ is continuous and thus $R^2+\delta_0(y) \leq \delta R+\delta_0(y)\;\; for\;\; 0 < \|R\| \leq \epsilon$, where $\delta > 0$ satisfies

$$\delta\int_0^a G(s,s)(c-ds^2)ds \leq 1. \quad (6.17)$$

Thus, if $R \in C$ and $\|R\| = \epsilon$, then from previous equation(6.13) and (6.17)

$$AR(y) \leq \int_0^a G(s,s)(c-ds^2)R^2(s) \leq \|R\|, \quad 0 \leq y \leq a. \quad (6.18)$$

Letting

$$\Omega_1 = \{R \in E : \|R\| < \epsilon\} \quad (6.19)$$

Thus we have

$$\|AR\| \leq \|R\|, \quad R \in C \cap \partial\Omega_1. \quad (6.20)$$

Since limit of R^2 is ∞, there exists $\epsilon_1 > 0$ such that $R^2+\delta_0(y) \geq \delta_1 R+\delta_0(y)$, $\|R\| \geq \epsilon_1$, where $\delta_1 > 0$ satisfies

$$\zeta\delta_1\int_x^a G(a/2,s)(c-ds^2)ds \geq 1 \quad (6.21)$$

Let $\epsilon_2 = max\{2\epsilon, \epsilon_1/\zeta\}$ and $\Omega_2 = \{R \in E : \|R\| < \epsilon_2\}$.

Then $R \in C$ and $\|R\| = \epsilon_2$ implies

$$min_{[x,a]} R(y) \geq \zeta \|R\| \geq \epsilon_1 \tag{6.22}$$

and

$$\begin{aligned} AR(a/2) &= \int_0^a G(a/2,s)(c-ds^2)R^2(s)ds \geq \int_x^a G(a/2,s)(c-ds^2)R^2(s)ds \\ &\geq \delta_1 \int_x^a G(a/2,s)(c-ds^2)R(s)ds \geq \delta_1\zeta\|R\| \int_x^a G(a/2,s)(c-ds^2)ds \\ &\geq \|R\|. \end{aligned} \tag{6.23}$$

Hence, $\|AR\| \geq \|R\|$ for $R \in C \cap \partial\Omega_2$.

Therefore by theorem 1, it follows that A has a fixed point and $G(y,s) > 0$ implies $R(y) > 0$ for $0 < y < a$. □

7. Plasma Region Differential Equation Separation

Considering a region where there are no red blood cells, then one may assume that the oxygen-dissociation curve is constant. In this case, the equation is reduced to a linear equation:

$$\left(\frac{1-H_T}{D_p} + (1-slp)\frac{H_T}{D_p}\frac{K_{RBC}}{K_p}\right) v_p \frac{\partial PO_2}{\partial z} = \nabla^2 PO_2. \tag{7.1}$$

Allowing us to define a constant, we reduce Eq.(7.1) to:

$$\kappa v_p \frac{\partial PO_2}{\partial z} = \nabla^2 PO_2, \text{ where } \kappa = \frac{1-H_T}{D_p} + (1-slp)\frac{H_T}{D_p}\frac{K_{RBC}}{K_p}. \tag{7.2}$$

We allow an elementary separation of PO_2 into a planar component, P (defined on the cross section of the channel), and a longitudinal component, $L(z)$:

$$\kappa v_p \frac{\partial}{\partial z}(PL) = \nabla^2(PL), \tag{7.3}$$

$$\kappa v_p \frac{\partial}{\partial z}(PL) = \sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}} \frac{\partial}{\partial q^i} \left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}} \frac{\partial (PL)}{\partial q^i} \right)$$

$$\begin{aligned}
\kappa v_p P\frac{dL}{dz} =& L\sum_i \frac{1}{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}\frac{\partial}{\partial q^i}\left(\frac{\prod_i \sqrt{\hat{\hat{g}}_{ii}}}{\hat{\hat{g}}_{ii}}\frac{\partial P}{\partial q^i}\right)\\
\kappa v_p P\frac{dL}{dz} =& L\nabla^2 P\\
\frac{1}{L}\frac{dL}{dz} =& \frac{1}{\kappa v_p P}\nabla^2 P = \mathbb{S}_1
\end{aligned}$$

$$\frac{dL}{dz} = \mathbb{S}_1 L, \nabla^2 P = \mathbb{S}_1 \kappa v_p P \tag{7.4}$$

It is worth noting that for Eq.(7.4), the $L(z)$ equation has an elementary linearly superimposed exponential solution:

$$L(z) = \sum_k c_{L1(k)} e^{\mathbb{S}_{1k} L}. \tag{7.5}$$

7.1. Cell Free Separation under Cartesian Coordinates

Assuming cartesian coordinates, we attempt a multiplicative separation of the following equation, allowing $P(x, y) = X(x)Y(y)$:

$$\begin{aligned}
&\nabla^2(XY) = \mathbb{S}_1 \kappa v_p(y) XY\\
&\frac{\partial(XY)}{\partial x^2} + \frac{\partial(XY)}{\partial y^2} = \mathbb{S}_1 \kappa v_p XY\\
&Y\frac{d^2X}{dx^2} + X\frac{d^2Y}{dy^2} = \mathbb{S}_1 \kappa v_p XY\\
&Y\frac{d^2X}{dx^2} = \left(\mathbb{S}_1 \kappa v_p Y - \frac{d^2Y}{dy^2}\right) X\\
&\frac{1}{X}\frac{d^2X}{dx^2} = \frac{1}{Y}\left(\mathbb{S}_1 \kappa v_p Y - \frac{d^2Y}{dy^2}\right) = -\mathbb{S}_2^2\\
&\frac{d^2X}{dx^2} = -\mathbb{S}_2^2 X \;\;\&\;\; \mathbb{S}_1 \kappa v_p Y - \frac{d^2Y}{dy^2} = -\mathbb{S}_2^2 Y
\end{aligned}$$

$$\frac{d^2X}{dx^2} + \mathbb{S}_2^2 X = 0 \;\;\&\;\; \frac{d^2Y}{dy^2} - \left(\mathbb{S}_1 \kappa v_p + \mathbb{S}_2^2\right) Y = 0. \tag{7.6}$$

It can be observed that the first equation of Eq.(7.6) is a classic trigonometric differential eigenvalue equation with a classic solution of:

$$X(x) = \sum_k \Big[c_{X1(k)} \cos(\mathbb{S}_{2k} x) + c_{X2(k)} \sin(\mathbb{S}_{2k} x)\Big], \quad \mathbb{S}_2 \in \mathbb{R}. \tag{7.7}$$

The second equation follows a more interesting behaviour. It is a classical linear, non-autonomous, homogeneous, second order, ordinary differential equation. This one, due to the $v_p(y)$ function being inherently parabolic (See Appendix 10.4), admits parabolic cylinder functions as its solutions. Allowing the velocity function to be represented as $v_p(y) = \sigma - \mu y^2$, and defining the cylinder functions as the two independent solutions ($U(\alpha, x)$ and $V(\alpha, x)$) of the differential equation:

$$\frac{d^2U}{dx^2} = \left(\frac{1}{4}x^2 + \alpha\right) U(x), \tag{7.8}$$

arguments and coefficients of the equation are as such, obtained from Eq.(7.6):

$$\begin{aligned}
\frac{d^2Y}{dy^2} &= \left(\mathbb{S}_1 \kappa v_p + \mathbb{S}_2^2\right) Y \\
\frac{d^2Y}{dy^2} &= \left[\mathbb{S}_1 \kappa(\sigma - \mu y^2) + \mathbb{S}_2^2\right] Y \\
\frac{d^2Y}{dy^2} &= \left[(-\mathbb{S}_1 \kappa \mu) y^2 + (\mathbb{S}_2^2 + \mathbb{S}_1 \kappa \sigma)\right] Y, \quad \xi = \gamma y \\
\gamma^2 \frac{d^2Y}{d\xi^2} &= \left[\left(\frac{-\mathbb{S}_1 \kappa \mu}{\gamma}\right)^2 \xi^2 + (\mathbb{S}_2^2 + \mathbb{S}_1 \kappa \sigma)\right] Y \\
\frac{d^2Y}{d\xi^2} &= \left[\left(\frac{-\mathbb{S}_1 \kappa \mu}{\gamma^2}\right)^2 \xi^2 + \frac{\mathbb{S}_2^2 + \mathbb{S}_1 \kappa \sigma}{\gamma^2}\right] Y.
\end{aligned}$$

Allowing the separation such that,

$$\left(\frac{-\mathbb{S}_1 \kappa \mu}{\gamma^2}\right)^2 = \frac{1}{4}$$

we obtain γ, and obtain the parabolic cylinder α co-efficient:

$$\gamma = \pm\sqrt{\pm 2\mathbb{S}_1 \kappa \mu}, \quad \alpha = \pm\frac{\mathbb{S}_2^2 + \mathbb{S}_1 \kappa \sigma}{2\mathbb{S}_1 \kappa \mu} \tag{7.9}$$

So the full solution would be:

$$Y(y) = \sum_k \left[c_{Y1(k)} U\left(\alpha_k, \gamma_k y\right) + c_{Y2(k)} V\left(\alpha_k, \gamma_k y\right)\right], \tag{7.10}$$

where:

$$\alpha_k = \pm\frac{\mathbb{S}_{2k}^2 + \mathbb{S}_{1k} \kappa \sigma}{2\mathbb{S}_{1k} \kappa \mu}, \quad \gamma_k = \pm\sqrt{\pm 2\mathbb{S}_{1k} \kappa \mu}. \tag{7.11}$$

Uniting all three equations together, [Eq.(7.5), Eq.(7.7), and Eq.(7.10)], we may obtain the full multiplicative solution for $PO_2(x,y,z)$, and allow a linear transformation of $PO_2(x,y,z)$ as the final solution.

8. Conclusion

A well known governing nonlinear pde used to model oxygen transport was formulated in a generalized co-ordinate system where the Laplacian is expressed in metric tensor form. A reduction of the pde to simpler problem subject to specific integrability conditions has been shown. An attempt to obtain a family of coordinate systems reducing the governing equations to a solvable ODE has been considered.As a consequence it has been shown that the governing nonlinear pde can be reduced and solved. An extension and modification of the work of Erbe and Wang [5] is derived and existence of positive solutions of an ode obtained in the general formulation is obtained for nonhomogeneous mixed boundary conditions and on general positive interval. A general solution method is given for the plasma layer which is necessary in order to match the core and plasma region solutions. Future work will provide greater insight into this for more general boundary conditions.

9. Appendix

9.1. Test Example for Equation (3.26) in the Porous Membrane Region of Channel

Choosing $\kappa(z) = \frac{z^3}{6}$ and $a = 1\times 10^{-10}$ in Eq.(3.26) and noting that Eq.(3.26) is a quadratic equation in the unknown $w(z)$, we can solve an equation to find the roots and express it in terms of the unknown function $w(z)$ as follows, where the $a^2 w(z)^2$ term has been dropped since it is very small by choice of a:

$$4\,z^{-4} - 5.0000000000\times 10^{-11}\,z^5\sqrt{2}\left(c - 1/36\,dz^6\right)\left(\frac{\partial^2 w}{\partial z^2}\right)$$
$$= 4\,z^{-4} - 5.0000000000\times 10^{-11}\,z^3\sqrt{2}\left(c - 1/36\,dz^6\right)w. \quad (9.1)$$

Eq.(9.1) has solution:

$$w(z) = \_C11\; z^{1/2+(1/2)\sqrt{5}} + \_C12\; z^{(-1/2)\sqrt{5}+1/2}. \quad (9.2)$$

Recalling the transformation ϕ for Eq.(3.26), the factor $\sqrt{a}$ defines the function ϕ in terms of new constants as follows,

$$\phi = \left(\_C1\ z^{1/2+(1/2)\sqrt{5}} + \_C2\ z^{(-1/2)\sqrt{5}+1/2}\right) z\sqrt{2} \tag{9.3}$$

In terms of y, recalling the first transformation $y = \kappa(z)$ for Eq.(3.26),

$$\phi(y) = \_C1\ \left(\sqrt[3]{6}\sqrt[3]{y}\right)^{1/2+(1/2)\sqrt{5}} \sqrt[3]{6}\sqrt[3]{y}\sqrt{2} \tag{9.4}$$

where the constant $\_C2$ is taken to be zero at $y = 0$ since w is undefined at 0.

$$\psi(y) = C1\ \phi(y) + C2\ \phi(y) \int (\phi(y))^{-2}\, dy \tag{9.5}$$

resulting in:

$$\begin{aligned}\psi(y) =& 1/2\ C1\ \_C1\ \left(\sqrt[3]{6}\sqrt[3]{y}\right)^{1/2+1/2\sqrt{5}} \sqrt[3]{6}\sqrt[3]{y}\sqrt{2} \\ &- 1/10\, \frac{C2\ 6^{2/3} y^{2/3}\sqrt{2}\sqrt{5}}{\_C1\ \left(\sqrt[3]{6}\sqrt[3]{y}\right)^{1/2+1/2\sqrt{5}}}\end{aligned} \tag{9.6}$$

$$G = \left(\sqrt[3]{6}\sqrt[3]{y}\right)^{1/2+0.5\sqrt{5}} \tag{9.7}$$

Setting $z = 7005$ microns for approximately near to the inlet of the permeable membrane region, we have the following definition in relation to Eq.(3.22)

$$\begin{aligned}H = -S1 \Bigg[& (7005\,\_C1 + 1/2\ C1\ \_C1)\sqrt{2}\sqrt[3]{6}\sqrt[3]{y}\left(\sqrt[3]{6}\sqrt[3]{y}\right)^{1/2+0.5\sqrt{5}} \\ & - 1/10\, \frac{\sqrt{5}\sqrt{2}6^{2/3} y^{2/3}\, C2}{\_C1\ \left(\sqrt[3]{6}\sqrt[3]{y}\right)^{1/2+0.5\sqrt{5}}}\Bigg].\end{aligned} \tag{9.8}$$

Expanding and then simplifying we obtain:

$$\begin{aligned}H =& -47314.97458\, S1\, y^{\frac{2181694989}{2500000000}}\,\_C1 - 3.377228736\, S1\, y^{\frac{2181694989}{2500000000}}\,\_C1\ C1 \\ &+ 0.3972608581\, S1\, y^{\frac{1909830059}{15000000000}}\, C2\,\_C1^{-1}.\end{aligned} \tag{9.9}$$

The PO_2 is equal to the following

$$PO_2 = C9\ \mathrm{e}^{H} + C10. \tag{9.10}$$

Taking the natural logarithm of PO_2 and then differentiating with respect to y and setting y near zero(as close as we like but not equal to zero), the constant $C2$ may be determined. For example setting $y = 1 \times 10^{-9}$, $C2 = 0.1598341110\,\_C1^2 + 0.00001140857324\,\_C1^2 C1$. Next we substitute $C2$ into Eq.(9.9) and can solve for $C1$ for derivative of PO_2 set to zero, for $y = 1 \times 10^{-9}$. The value $C1 = -23467.97346$ was determined using Maple. As a result Eq. (9.9) depends only on two constants $\_C1, C9$ as $S1 = -0.0002170376282$ is given. The constants C9, $\_C1$ and C10 are arbitrary constants of integration. The constant C10 was chosen to be 150 representing the Dirichlet condition at $y = 0$ and C9 was determined by matching the derivatives in cell rich and no cell regions at $y = 49$ microns. The $PO2$ has been written in compact form from several unknown constants down to two constants $\_C1$ and $C9$. It is worthy to note that the expressions used for the matching of core to no cell region and no flux at zero gave two equations in two unknowns in terms of exponential function. It was only possible to solve by truncating the series at arbitrary number of terms and solve unknowns with Maple. In any case for arbitrarily large number of terms(n=30 in this test example) only one of the 30 roots given were real, the rest being complex valued. The values$\{C9 = -0.9046675381, _C1 = -0.02210756925\}$ In the vicinity of the inlet to permeable membrane at $y = 0$ we set the flux to be small and positive wheras further downstream in the membrane area at $y = 0$ the flux was of the same magnitude but negative.The Robin condition was used in the no cell region and is shown below.

The Neumann and Robin condition used in [4] is:

$$\frac{\partial PO_2}{\partial y}(0) = 0, \tag{9.11}$$

$$-7.85PO_2(50) + PO_2'(50) = 78.5. \tag{9.12}$$

Incorporating the boundary conditions we obtain the solutions plotted in Figure 1, 2, 3 and 4. Note that in Fig.(4) we have used nearly a no flux condition at the wall of channel at y=50 microns as in [4]. The results also resemble those in [4] where a numerical solution was obtained in the channel.

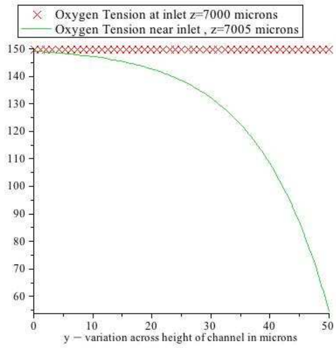


Figure 1: Oxygen tension PO_2 versus channel height in microns at inlet and at axial distance z=7005 microns

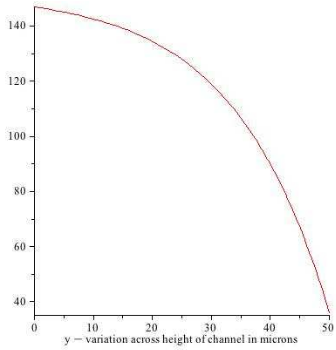


Figure 2: Oxygen tension PO_2 versus channel height in microns at axial distance z=7256.3 microns

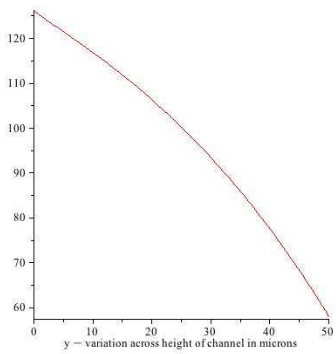


Figure 3: Oxygen tension PO_2 versus channel height in microns at axial distance z=7500 microns

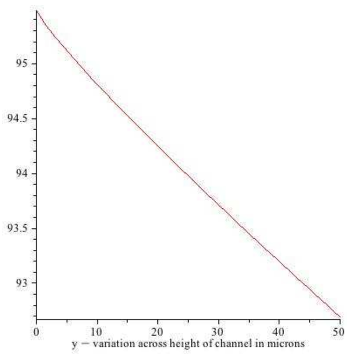


Figure 4: Oxygen tension PO_2 versus channel height in microns at axial distance z=8500 microns

10. Appendix

10.1. Derivation of Cell Free and Core Region Oxygen Transport PDEs

We start off by considering a general flux transport integral equation. We begin by assuming that total net change of mass in a volume, Ω, is total change of mass created in Ω plus the flux of mass entering the boundary of Ω, $\partial\Omega$.

Describing this in a surface integral equation, we have:

$$\frac{dm_{O_2}}{dt} + \oiint_{\partial\Omega} \vec{j}_{O_2} \cdot d\vec{S} = \Sigma_{O_2}, \tag{10.1}$$

where m_{O_2} is the mass of oxygen in grams, and $\frac{d}{dt}m_{O_2}$is the created change of O_2 in g/s.

We define $\vec{j}_{O_2}$ to be the flux of O_2 into the closed boundary (measured in $g/(\mu m^2 \cdot s)$) and allow Σ_{O_2} to be the constant net change of O_2 in the boundary, measured in g/s. To obtain a differential form, we first define that the mass of O_2 is the volume integral of the density of O_2, ρ_{O_2}. Also we assume that Σ_{O_2} is the volume integral of a density constant, σ_{O_2}. Therefore we simplify the equation to obtain a differential form:

$$\frac{d}{dt}\iiint_{\Omega} \rho_{O_2} dV + \oiint_{\partial\Omega} \vec{j}_{O_2} \cdot d\vec{S} = \iiint_{\Omega} \sigma_{O_2} dV.$$

Using Liebniz's Integral Rule on the first term and the Divergence Theorem on the second term, we obtain:

$$\iiint_{\Omega} \frac{\partial \rho_{O_2}}{\partial t} dV + \iiint_{\Omega} \vec{\nabla} \cdot \vec{j}_{O_2} dV = \iiint_{\Omega} \sigma_{O_2} dV.$$

Unifying all the expressions under one volume integral, we obtain:

$$\iiint_{\Omega} \left(\frac{\partial \rho_{O_2}}{\partial t} + \vec{\nabla} \cdot \vec{j}_{O_2} - \sigma_{O_2} \right) dV = 0$$

If the volume integral of an expression over a volume is zero, then the expression in that domain must be identical to 0. So:

$$\frac{\partial \rho_{O_2}}{\partial t} + \vec{\nabla} \cdot \vec{j}_{O_2} - \sigma_{O_2} = 0 \tag{10.2}$$

At this point, it is assumed that there is no mass being generated, and so therefore, no creation of O_2 rendering the first term to zero. It is also assumed that chemical equilibrium is established allowing no net change of O_2 implying $\sigma_{O_2} = 0$. So then, the full, governing, vector differential equation, under the stated assumptions is:

$$\vec{\nabla} \cdot \vec{j}_{O_2} = 0$$

Now, a further examination of $\vec{j}_{O_2}$ is conducted. The problem of oxygen transport is conducted imagining that there are two sources of flux in the boundary: advection ($\vec{j}_{Adv}$), and diffusion ($\vec{j}_{Diff}$). Each source of flux is handled by two general equations: a steady state continuity law, and Fick's second law, respectively. In this, it is assumed that since the analysis is steady state, speed of O_2 in its medium (blood & plasma), $\vec{v}_{\ell O_2}$, is steady and constant. So, the equation is continued as :

$$\begin{aligned}\vec{\nabla}\cdot\left(\vec{j}_{Adv}+\vec{j}_{Diff}\right)&=0\\ \vec{\nabla}\cdot\left([O_2]\vec{v}_{\ell O_2}-\vec{\nabla}(D_{\ell O_2}[O_2])\right)&=0\\ \vec{v}_{\ell O_2}\cdot\vec{\nabla}[O_2]-\vec{\nabla}^2\left(D_{\ell O_2}[O_2]\right)&=0\\ \vec{v}_{\ell O_2}\cdot\vec{\nabla}[O_2]-D_{\ell O_2}\vec{\nabla}^2[O_2]&=0,\end{aligned}$$

$$\vec{v}_{\ell O_2}\cdot\vec{\nabla}[O_2]=D_{\ell O_2}\vec{\nabla}^2[O_2]. \tag{10.3}$$

Allowing the coordinate system to be analyzed as one z-axis down the length of the channel, and two other orthogonal coordinates defined on the cross section of the channel, Eq.(10.3) can be reduced. In general, advection is only occuring down the length of the channel (ie. $\vec{v}_{\ell O_2}=v_{\ell O_2}\hat{k}$). Also since the channel is open along the z-axis, there is no diffusion in the z direction. So then the equation can be reduced to the form:

$$v_{\ell O_2}\frac{\partial[O_2]}{\partial z}=D_{\ell O_2}\vec{\nabla}^2_{2d}[O_2]. \tag{10.4}$$

According to ideal gas and fluid laws, it can be demonstrated that pressure and density of a fluid are proportional to each other. Recognizing that the terms are in multiplicative relation, constants of proportionality can cancel out. Letting PO_2 be the partial pressure of O_2, and letting the notation of $\vec{\nabla}^2_{2d}$ be ∇^2, we obtain in general:

$$v_{\ell O_2}\frac{\partial PO_2}{\partial z}=D_{\ell O_2}\nabla^2 PO_2. \tag{10.5}$$

10.1.1. Cell Free

In the case that there are no cells in the region being analyzed, then the model dictates that $v_{\ell O_2}$ be a function of the arguments of PO_2. In fact, since $v_{\ell O_2}$ is invariant on the z-coordinate, $v_{\ell O_2}=v_p(q^i)$, where $v_p(q^i)$ is a parabolic expression of the speed from the center according to Appendix 10.4, Eq.(10.15). Therefore, the model evolves to:

$$v_p\frac{\partial PO_2}{\partial z}=D_p\nabla^2 PO_2. \tag{10.6}$$

Worth noting, since there is a differential operator acting on both of the terms, any linear transformation of PO_2 in the form of $\alpha PO_2 + \beta$ is also a solution to the above equation.

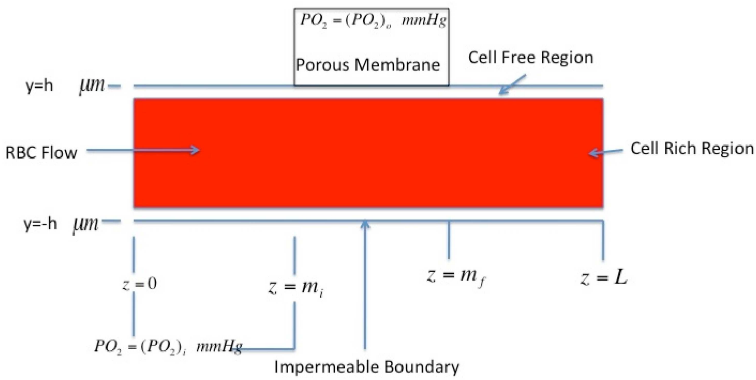
10.1.2. Core Region

In the case the there is the central core region then at this central location there oxygen dissociating to form HbO_2. In which case, the velocity of the O_2 liquid medium depends on the velocity of plasma and also the rate of Oxygen dissociating. So therefore, $v_{\ell O_2} = f\left(v_p(q^i), \frac{dSO_2}{dPO_2}\right)$. Utilizing the definition given in a computational microfluidic model [4], the model evolves to:

$$\left[v_p(1-H_T) + v_{RBC} H_T \frac{K_{RBC}}{K_p}\left(1 + \frac{[Hb_T]}{K_{RBC}}\frac{dSO_2}{dPO_2}\right)\right]\frac{\partial PO_2}{\partial z} = D_p \nabla^2 PO_2. \quad (10.7)$$

10.2. Boundary Conditions

In these equations, the conditions are intuitive. The concept is to consider a channel where there is only a permeable membrane over a certain location and length on the model with an inlet value.



(10.8)

Figure 5: Geometry of micro-channel with permeable membrane centered at top of channel.

As such, we have a collection of conditions (expressed in cartesian coordinates, $PO_2(x, y, z)$ for simplicity. Assuming that variation along the x is minimal, we may express PO_2 as $PO_2(y, z)$.

1. The PO_2 incoming into the permeable membrane must be defined. Assuming it is constant, we have:

$$PO_2(y, m_i) = (PO_2)_i, \forall y \in (-h, h) \tag{10.9}$$

2. Since there will be no permeability anywhere else in the channel except at the membrane, we must also allow no flux in certain areas; namely, before the membrane at the top and bottom membrane, at the bottom of the section containing the membrane (since the membrane is at the top of the channel), and after the membrane:

   (a) <u>Pre-Membrane</u>

$$\left.\frac{\partial PO_2}{\partial y}\right|_{y=\pm h} = 0, \forall z \in (0, m_i) \tag{10.10}$$

   (b) <u>Bottom of Membrane Region</u>

$$\left.\frac{\partial PO_2}{\partial y}\right|_{y=-h} = 0, \forall z \in (m_i, m_f) \tag{10.11}$$

   (c) <u>Post-Membrane</u>

$$\left.\frac{\partial PO_2}{\partial y}\right|_{y=\pm h} = 0, \forall z \in (m_f, L) \tag{10.12}$$

3. The only region not covered by the above three flux equations is the region of PO_2 occupying $z \in (m_i, m_f)$ at $y = h$. That is because this is the region of the membrane. This region is governed by a robin condition specified in [4]. The boundary condition occupies the form as such:

$$\left.\frac{\partial PO_2}{\partial y}\right|_{y=h} = \frac{D_m K_m}{D_p K_p}\left(\frac{(PO_2)_o - PO_2(h, z)}{\tau}\right), \forall z \in (m_i, m_f) \tag{10.13}$$

   where $(PO_2)_o$ is the PO_2 level on the other side of the membrane.

All of these conditions act on the entire system.

10.3. Method of Solution

The system to be solved is in fact two systems: the core and the cell-free region:

1. **Cell Free Region** Utilizing Eq.(10.6), we solve for the PO_2 in the cell free region. This corresponds to $\forall z \in (m_i, m_f)$ and $\forall y \in (-h, -y_i) \cap (y_i, h)$. Using this, we incorporate Eq.(10.9), Eq.(10.11), & Eq.(10.13) as boundary conditions. Therefore, having solutions, we take note of the values and/or set of values for $PO_2(\pm y_i, z)$ & $\left.\frac{\partial PO_2}{\partial y}\right|_{y=\pm y_i}, \forall z \in (m_i, m_f)$. These are used for the core solutions.

2. **Core Region** For the core region, we utilize Eq.(10.7). Solving and obtaining a general solution, we incorporate Eq.(10.9) as a initial condition. This solution is applicable $\forall y \in (-y_i, y_i)$. We also develop four initial conditions, namely, ensuring that the function is relatively smooth with the boundary and the boundary's derivative of the cell free region. This means that $(PO_2)_{Core}(\pm y_i, z) = (PO_2)_{CellFree}(\pm y_i, z), \forall z \in (m_i, m_f)$ and
$$\left.\frac{\partial (PO_2)_{Core}}{\partial y}\right|_{y=\pm y_i} = \left.\frac{\partial (PO_2)_{CellFree}}{\partial y}\right|_{y=\pm y_i}, \forall z \in (m_i, m_f).$$
Utilizing these four conditions, we obtain solutions for both solutions (Cell Free & Core), and glue them in a piecewise fashion. For any regions within
$$\tag{10.14}$$

10.4. Velocity Profile Function

The following velocity profile with all constants appear in [4].

$$v_p(\hat{\mathbf{x}}) = \frac{3(130) \cdot 10^6}{4w\left[h^3 + \left(\frac{\mu_p}{\mu_c} - 1\right) y_i^3\right]} \begin{cases} (h^2 - \hat{\mathbf{x}}^2), & y_i \leq |\hat{\mathbf{x}}| \leq h \\ (h^2 - y_i^2) + \frac{\mu_p}{\mu_c}\left(y_i^2 - \hat{\mathbf{x}}^2\right) & 0 \leq |\hat{\mathbf{x}}| \leq y_i \end{cases} \tag{10.15}$$

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Section 3 up to $\mathbb{S}_1 = 0$ development due to K.C. Afas wheras $\mathbb{S}_1 \neq 0$ development and results due to T.E. Moschandreou.

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