Modeling the Partial Pressure of Oxygen in the Lens of the Eye

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Abstract - A simple transient mathematical model for the distribution of partial pressure of oxygen in the lens of the eye has been developed. The model considers the eye lens as spherical in shape bounded by concentric spherical shell of epithelium. The model takes into account the transport of oxygen by diffusion and consumption of oxygen is assumed to follow the Michaelis- Menten's kinetics. The partial differential equation governing the partial pressure of oxygen has been solved by using implicit Crank-Nicholson's iteration scheme. The computational results of the model have been presented by graphs and effects of model parameters have been shown through the graphs and discussed.

***Keywords*: Opacification; spherical lens; differentiating fibre; oxygen diffusion.**

I. INTRODUCTION

Opacification of the lens nucleus is a major cause of blindness and is thought to result from oxidation of key cellular components [10]. The marked increase in oxygen consumption that occur when the lens is exposed to increase the oxygen is likely to result in the production of the higher levels of reactive oxygen species and may provide a link between elevated oxygen levels and the risk of nuclear cataract [5]. An increase in oxygen concentration is thought to be responsible for cataract formation [7]. Thus, the knowledge of oxygen concentration and distribution within the lens is of considerable interest clinically. Few polarographic and optode measurements report oxygen partial pressure from 1 mmHg in the cat lens posterior cortex and nucleus [10] to 10-22 mmHg in the rabbit lens [4] and 0.8-4.0 mmHg in the human anterior cortex [5]. These data indicate that to protect against age- related nuclear cataract formation, oxygen concentration in the lens has to be maintained at very low level.

Eaton [7] and Harding [9] have suggested that partial pressure of oxygen through out the lens is low, if not zero. In vivo, the lens is situated in a relatively low oxygen environment and partial pressure of oxygen could be higher in the core of aged lens. Eaton [7] suggested that the effective exclusion of oxygen from the centre of lens could be one mechanism by which cell in this region preserve their transparency over a prolong period. This hypothesis is supported by the interesting observation that nuclear develop in a remarkable high proportion of patients following hyperbaric therapy [8]. Thus, long-term preservation of lens clarity may depend on the maintenance of hypoxia in the lens nucleus [10].

The lens consists of a mass closely packed fibres cells bounded anteriorly by an epithelial monolayer and enveloped by thick basement membrane, the lens capsule. Fibres cells are continuously produced from the adult lens contains two kinds of fibres cells: those located in the lens core, which are mature and do not contain organelles, and those located in the lens outer layers, which are not yet mature and contains organelles (including mitochondria). The lens contains two populations of fibres cells: an outer layer of differentiating fibres (DF) and a core of mature fibres (MF). The relevant difference between MF and DF is that the DF contains mitochondria, which consume oxygen, whereas the MF has no organelles. The schematic diagram of the lens of the eye is shown in figure (1).

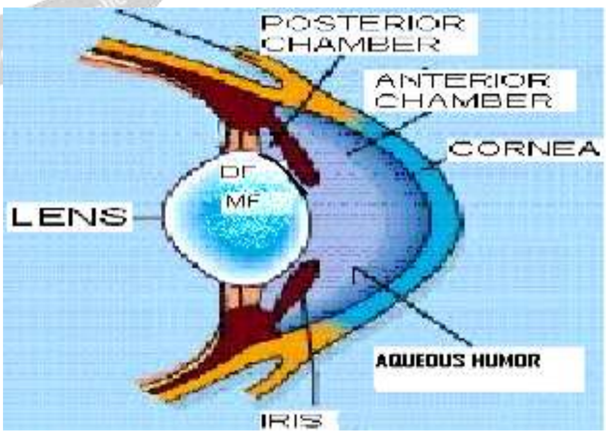

Figure (1). Diagrame of eye showing inter-relationship between lens, cornea, posterior and anterior chambers [8].

In order to prolong the lens transparency and to get nuclear cataract delayed as long as possible there is a need to investigate physiological factors affecting the oxygen diffusion, consumption, and oxidation processes within the lens. A mathematical analysis of oxygen diffusion and

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consumption in the lens may contribute to the knowledge of regulation of tissue oxygen in the lens and quantitative understanding achieved through the analysis may facilitate the design of new therapeutic procedures. McNutty *et al.* [10] developed a simple steady-state diffusion-consumption model for the partial pressure of oxygen in the lens and used it to calculate time constants for oxygen consumption in various regions of the lens and oxygen diffusion coefficient. This model may be generalized and some more relevant predictions can be made.

The present work is concerned with the development of a simple transient mathematical model for the oxygen diffusion-consumption in the eye lens. The lens is modeled as a spherical shell, bounded by an epithelium layer and which comprises two functionally different domains of fibre cells: differentiating fibres (DF) near the surface and mature fibres (MF) located in the central region of the tissue. The model takes into account the transport of oxygen by diffusion and consumption of oxygen is assumed to follow the Michaelis- Menten's kinetics. The partial differential equation governing the partial pressure of oxygen has been solved by using implicit Crank-Nicholson's iteration scheme. The prime objective of the present study is to investigate the effect of model parameters: the Michaelis- Menten's kinetic constant and maximum rate of consumption on the partial pressure of oxygen in the mammalian lens.

II. MATHEMATICAL FORMULATION

The oxygen enters the lens by diffusion from the surrounding humors and crosses many thousand of fibre cell plasma membrane readily. Some of the oxygen is consumed by mitochondria (DF) and non-mitochondrial elements (MF) and the remaining reaches/diffuses readily into the centre of the lens. The illustration of physical model relevant to the present study is shown in figure (2).

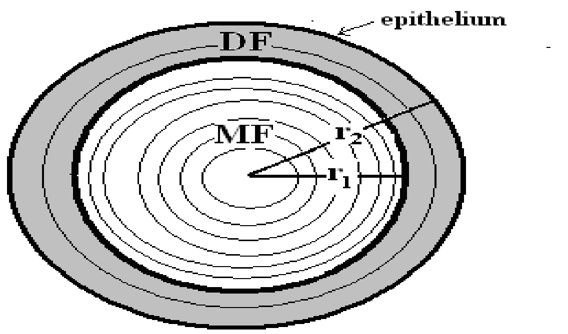

Figure (2) : Schematic diagrame of lens of the eye

The model treats the lens as a sphere with radius r_2. If r is the redial distance from the lens centre, the outer shell of differentiating fibre (DF) is located at $r_1 \le r \le r_2$, where $r_1 = 0.8r_2$ Thus mature fibre (MF) is at $0 \le r \le r_1$. The border between DF and MF is located at a distance r_1 from the centre.

2.1 Governing equation:

The Fick's law of diffusion and Michaelis- Menten's kinetics of consumption result in following P.D.E. describing the partial pressure of oxygen in the lens:

$$\frac{\partial P}{\partial t} = D\left(\frac{\partial^2 P}{\partial r^2} + \frac{2}{r}\frac{\partial P}{\partial r}\right) - \frac{V_{\max} P}{P+K}, \; r > 0 \qquad (1)$$

$$\frac{\partial P}{\partial t} = 3D\left(\frac{\partial^2 P}{\partial r^2}\right) - \frac{V_{\max} P}{P+K}, \qquad r = 0 \qquad (2)$$

where *P* is the partial pressure of oxygen, V_{max} is the maximum rate of consumption, *K* the Michaelis- Menten's Kinetic constant for the reaction and *D* the diffusion coefficient.

2.2 Boundary and Interface conditions:

In order to formulate a physiologically consistent and mathematically tractable model, boundary and interface conditions relevant to present model are described below:

$$P(r_2, t) = P(bath) \qquad (3)$$

$$P(r_1^+) = P(r_1^-), \left(\frac{\partial P}{\partial r}\right)_{r=r_1^+} = \left(\frac{\partial P}{\partial r}\right)_{r=r_1^-}, \quad t \ge 0 \qquad 4(a,b)$$

$$\left(\frac{\partial P}{\partial r}\right)_{r=0} = 0 \qquad (5)$$

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Eq. (3) shows that, the partial pressure of oxygen at the surface of the lens is same as that in the bathing solution. Eq.4 (a,b) represents that, there must be, all times, the continuity of oxygen concentration and flux at the interface between two adjacent layers. Eq. (5) depicts that at the centre of the lens there is no flux.

2.3 Initial condition:

A study state solution [9] to the governing Eqs. (1)- (2) subject to the boundary and interface conditions (3), 4(a,b), and (5) and the case P<< K, which serves as an initial condition for our transient state problem, is given by:

$$P(r,t=0)=P_1\begin{cases}\dfrac{\lambda_{MF} r_2 \sinh\left(\dfrac{r}{\lambda_{MF}}\right)}{\lambda_{DF} r \cosh\left(\dfrac{r_1}{\lambda_{MF}}\right)}, & 0<r\le r_1\\[2ex] \dfrac{r_2 \sinh\left(\dfrac{r-r_1}{\lambda_{DF}}\right)}{r}+\left(\tanh\left(\dfrac{r_1}{\lambda_{MF}}\right)\right)\dfrac{\lambda_{MF} r_2 \cosh\left(\dfrac{r-r_1}{\lambda_{DF}}\right)}{\lambda_{DF} r}, & r_1<r\le r_2\end{cases} \qquad (6)$$

where P_1 is the common term of the solution of Eqs. (1) – (2) is given by:

$$P_1=\frac{P_{Bath}}{\cosh\left(\dfrac{r_2-r_1}{\lambda_{DF}}\right)\left[\tanh\left(\dfrac{r_2-r_1}{\lambda_{DF}}\right)+\dfrac{\lambda_{MF}}{\lambda_{DF}}\tanh\left(\dfrac{r_1}{\lambda_{MF}}\right)\right]}$$

Here ***λDF*** and ***λMF*** are length constant for DF and MF regions

III. SOLUTION TO THE PROBLEM

Due to the non-linear term in Eqs. (1)- (2) the analytic solution of these equations, subject to boundary, interface and initial conditions (3), 4(a,b), (5) and (6), seems to be formidable task. Hence an implicit finite difference Crank Nicholson iterative scheme [11] has been used to find the numerical solution of non-linear partial differential Eqs. (1)- (2) governing the quasi-steady state distribution of oxygen in the lens. This scheme is unconditionally stable and offers a series of advantages such as its accuracy, versatility and frequent employment in the solution of similar equations. The finite difference approximations of Eqs. (1)- (2), obtained by employing Crank-Nicholson implicit scheme is given by:

$$a_i P_{j-1,k+1}+b_i P_{j,k+1}+c_i P_{j+1,k+1}=f_i\left(P_{j,k}\right) \qquad (7)$$

Where $f_i\left(P_{j,k}\right)$ denote the term corresponding to the equation for location *j* in the grid and is given by:

$$f_i\left(P_{j,k}\right)=\begin{cases}P_{j,k}^{\,2}+\left(K-2\alpha-V_{\max}\Delta t\right)P_{j,k}+(\alpha-\beta)P_{j-1,k}+(\alpha+\beta)P_{j+1,k}, & \text{for } i=1\\ P_{j,k}^{\,2}+\left(K-2\alpha-V_{\max}\Delta t\right)P_{j,k}+(\alpha-\beta)P_{j-1,k}+(\alpha+\beta)P_{j+1,k}, & \text{for } i=2\end{cases}$$

$$a_i=\begin{cases}\left(P_{j,k}+K+2\alpha\right), & \text{for } i=1\\ \left(P_{j,k}+K+6\alpha\right), & \text{for } i=2\end{cases},\quad b_i=\begin{cases}(-\alpha+\beta), & \text{for } i=1\\ -3\alpha, & \text{for } i=2\end{cases},\quad c_i=\begin{cases}-(\alpha+\beta), & \text{for } i=1\\ -3\alpha, & \text{for } i=2\end{cases},$$

$$\alpha=\frac{D\Delta t}{2(\Delta r)^2}\left(P_{j,k}+K\right) \text{ and } \beta=\frac{D\Delta t}{2r_j\Delta r}\left(P_{j,k}+K\right)$$

The finite difference analogues of the boundary and interface conditions are given by:

$$P_{j-1,k+1}=P_{j+1,k+1}, \qquad (8)$$

$$P_{j,k+1}=P(bath) \qquad (9)$$

$$P_{j-2,k+1}-2P_{j,k+1}+P_{j+2,k+1}=-P_{j-2,k}+2P_{j,k}-P_{j+2,k} \qquad (10)$$

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3.1 Solution of Algebraic System:

The implicit iterative scheme given by Eq.(7) is simplified in light of the finite difference analogues of the initial, boundary and interface conditions and the resulting system of algebraic equation written in the trigonal matrix form $AP_{j,k+1} = f\left(P_{j,k}\right)$ was solved by using Thomas algorithm [6].

3.2 Table (1)

Input parameters for our model:

Constant	Symbol	Numerical value
Partial pressure of oxygen in bathing solution	*P(bath)*	36 mmHg
Michaelis- Menten's Kinetic constant	K	4.834
Diffusion coefficient	D	$3x10^{-5}$ cm^2s^{-1}
Maximum rate of consumption	V_{max}	9.9μl-h^{-1}
Length constant for DF region	λ_{DF}	0.8 mm
Length constant for MF region	λ_{MF}	0.9 mm
Radius of lens	r_2	5.0 mm

These parameter values are supported by [8, 10].

IV. Results and Discussion

The computational results to the model are obtained by using the physiological values of the parameters listed in table (1) and discussed through the graphs:

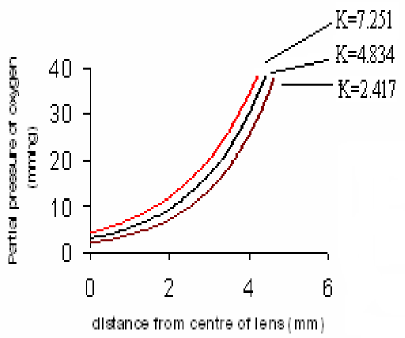

Figure 1. Partial pressure of oxygen profile for different values of Michelis- Menten kinetic at 1 hour

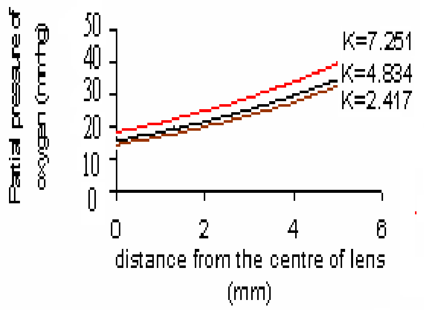

Figure 2. Partial pressure of oxygen profile for different values of Michelis- Menten kinetic at 2 hour

Figure 1. and 2 shows that from centre of lens to outward, the partial pressure of oxygen increases with increase in Michaelis- Menten's Kinetic constant K at different time.

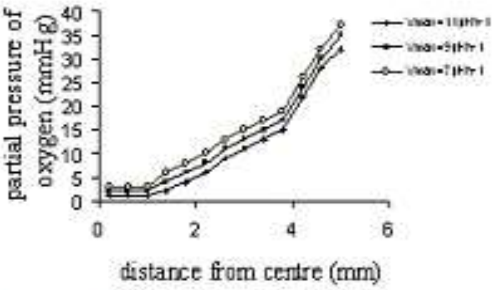

Figure 3. Partial pressure of oxygen profile for different value of maximum rate of consumption at 1 hour.

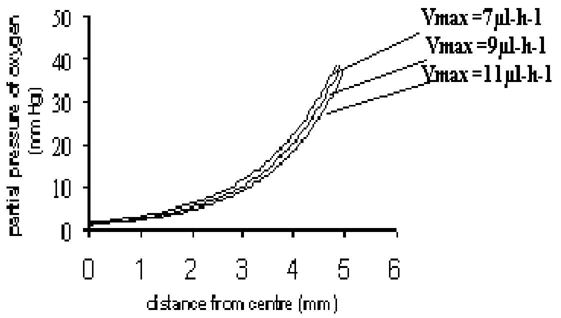

Figure 4. Effect of maximum rate of consumption on pressure distribution along radius at 2 hour

Figure 3 and 4 shows that from centre of lens to outward, the partial pressure of oxygen increases with increase in maximum rate of consumption at different time.

V. Conclusion

These graphs show that partial pressure of oxygen increases with increase of 'K' and decreases with increase of Vmax. Therefore Partial Pressure can be regulate by

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regulating ‘K’. The present mathematical analysis of oxygen diffusion in the lens may contribute to the knowledge of regulation of tissue oxygen in the lens and quantitative understanding achieved through the analysis may facilitate the design of new therapeutic procedures. This analysis may help in regulating the partial pressure of oxygen in the lens.

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