Mathematical Statistician and Engineering Applications
ISSN: 2094-0343
2326-9865

"A Mathematical Model of the Oxygen Transport in the Different Layers of Corneal Tissue"

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Article Info
Page Number: 10795-10807
Publication Issue:
Vol. 71 No. 4 (2022)

Article History
Article Received:
15 September 2022
Revised: 25 October 2022
Accepted: 14 November 2022
Publication: 21 December 2022

Abstract
Many authors thought the corneal tissue had three layers (Endothelium, Stroma, and Epithelium). The Bowman's layer and Descemet's membrane are also two additional slice layers of corneal tissue. Analytical modeling can be used to study the corneal tissue in great detail. For healthy eyes, it is incorrect to say that the Bowman's layer and Descemet's Membrane layers do not absorb oxygen. Furthermore, it is false to believe that the cornea's layers consume the same amounts of oxygen. The purpose of this study is to provide a detailed analysis based on Fick's law and Monod Kinematics, allowing us to determine how much oxygen is consumed and how the partial pressure is distributed for each corneal layer.

Keywords: Corneal Tissue, Bowman's Layer, Descemet's Membrane, Consumption, Monod Kinematics

Introduction:

The majority of authors predict that the oxygen consumption and diffusion rate of ocular tissue won't alter. To solve this issue, we used Monod kinematics and mathematical modelling. We discovered countless nonsensical negative oxygen tension values as a result of our analysis. A model that only shows oxygen consumption as a function of oxygen pressure was developed by many authors. Some researchers used sigmodels and linear models to represent oxygen consumption, while others used metabolic models to reflect oxygen consumption in corneal tissue. The cornea is a multilayered tissue made up of five layers: endothelium, bowman's stroma, descemet's membrane, and epithelium.

Measure the flow of oxygen into the corneal tissue as well as the partial pressure of oxygen in the tissue when the cornea's oxygen content decreases. The strength of corneal tissue is determined by the continuous metabolic activity it undergoes. There are three different kinds of corneas: the average, with measurements between 540 and 560 millimetres; the thick, with dimensions between 560 and 600 millimetres; and the extra-thick, with a thickness of more

than 600 millimetres. According to the experiment by Bonanno et al., they used the metabolic model that Chhabra et al. had previously used to get the metabolic constant and determine how much oxygen the retinal layers were consuming.

In the current work, we quantify the numerical rates of oxygen consumption by various layers of corneal tissue and discuss the variation in oxygen consumption rate with corneal layer thickness. In Monod kinematics, Chhabra et al. [8] utilized the metabolic constant k m=2.2 mmHg.

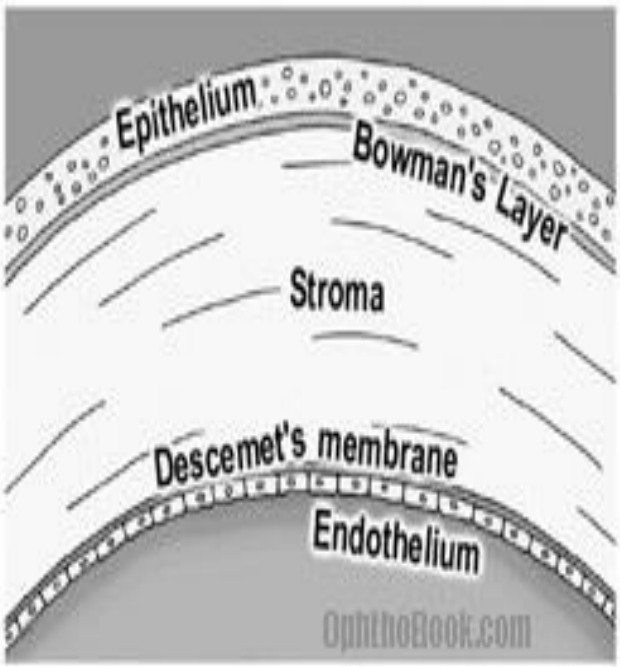

Fig: (1) Schematic Diagram of Corneal Tissue

A key component to ensure physiology is the pace at which corneal tissue uses oxygen. In the human corneal tissue, we discovered an expression for oxygen pressure. Since we are unable to directly quantify the rate of oxygen consumption, some well-known writers [9,10] have developed mathematical models to predict the time-dependent consumption and diffusivity. As a parameter in the Monod Kinematics and graph between Q* vs. PO_2, where k_m stands for the metabolic or Monod kinematics constant. To illustrate the relationship between oxygen consumption and oxygen tension, place a tear in the cornea at the necessary interface. We calculate the oxygen consumption rate of each layer of corneal tissue from the expression of oxygen tension. The current model has five layers and the parameter values are listed in the table (1).

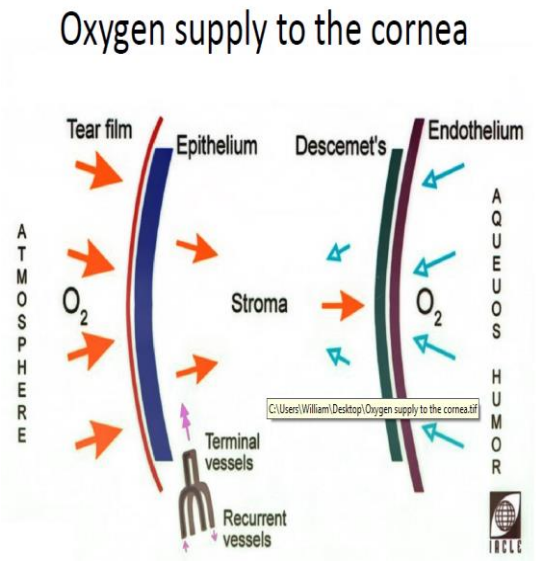

Fig:2 Diagram of oxygen supply to cornea

Epithelium cells have a 7–10 year lifespan. When crystalline enzymes that are intracytoplasmic like those found in lens epithelial cells are present at maximum quantities, this layer is crucial in maintaining optical transparency. The superficial cells, basal cells, and wing cells are three different types of cells that make up the five to six epithelial layer divisions. This layer created small light cells and high dark cells. The epithelial layer is 50 m thick.

The Bowman's membrane, which is composed of collagen and proteoglycans, will now be discussed. It is commonly believed that the Bowman's layer is not a genuine layer and that it diminishes for diseased eyes because it has no regeneration properties and is located directly anterior to Stroma, but recent study suggests otherwise we only collect sound eyes. This layer is crucial to how the cornea is shaped. This layer cannot renew when the eye is injured, which is how we got a dent. Now it is the turn of the stroma, which creates the cornea as a major structural component. Because it is a translucent, colorless layer. Fusion of extracellular matrix and stromal fibres.

Descemet's membrane has a 7μ thickness. It begins in the uterus at the eight-week stage. Endothelial layer continuously secretes it. As people age, this layer becomes thicker. It is an elastic layer that curls up before being cut. The single-layered, five-micron-thick endothelium is composed of cells. It is metabolically active and hexagonal. Endothelial pumps are used to control the water content. When viewed from the side of the posterior chamber, it is monolayer and seems like a mosaic made of a comb of honey.

Material and Methods:

The corneal tissue is assumed in the current metabolic model to initially consist of five layers, as shown in Figure 3. Epithelium is a outer most layer, and Endothelium is the inner most layer of corneal tissue. Rest of all layers situated between outer and innermost layer.

The corneal layers in corneal tissue provide oxygen transfer through

$$D_j \frac{\partial^2 c_0}{\partial x^2} - Q(x) = \frac{\partial c_0}{\partial t} - - - - - - - - (1)$$

Where $j = 1,2,3,4,5$

$c_0 -$ Concentartion of oxygen

And by Henry law we have

$$c_0 = P_0 * k - - - - - - - - - - - - - - (2)$$

Using 2 , equation (1) become

$$D_j \frac{\partial^2 P_0}{\partial x^2} - \frac{Q(x,t)}{k} = \frac{1}{k}\frac{\partial P_0}{\partial t} - - - - - - - - (3)$$

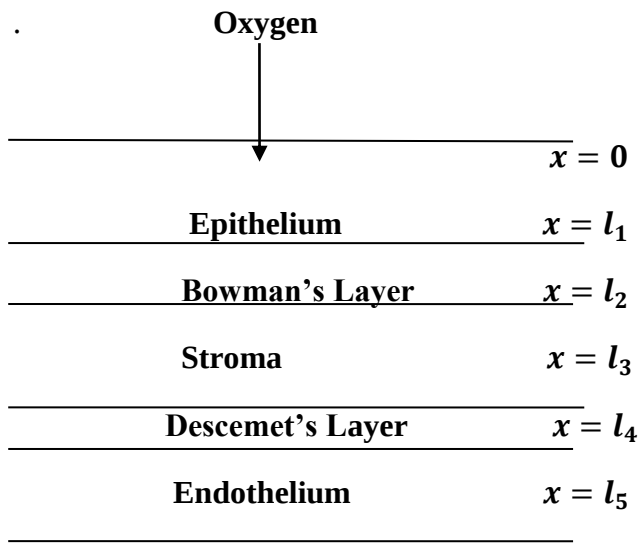

Figure:3**:** Schematic Diagram of oxygen transport in Corneal Tissue.

$$Q(x,t) = \alpha * Q^* P_0 - - - - - - - - - - (4)$$

$$where\ \alpha = \frac{P_0(a + P^*)}{P^*(a + P_0)}$$

Using (4), 3rd become

$$D_j \frac{\partial^2 P_0}{\partial x^2} - \frac{\alpha P_0 Q^*(x)}{k} = \frac{1}{k}\frac{\partial P_0}{\partial t} - - - - - (5)$$

$$\frac{D_j}{P_0 \alpha}\frac{\partial^2 P_0}{\partial x^2} - \frac{Q^*(x)}{k} = \frac{1}{\alpha P_0 k}\frac{\partial P_0}{\partial t} - - - - (6)$$

Equation (6) solvable by separation method

$$\frac{1}{\alpha P_0 \mathrm{k}}\frac{\partial \mathrm{P_0}}{\partial \mathrm{t}} = -\mathrm{m}$$

$$\frac{\partial \mathrm{P_0}}{P_0\,\partial \mathrm{t}} = -\mathrm{m}\alpha\mathrm{k} - - - - - - - - - - (7)$$

The solution of (7) is proposed by following relation

$$\frac{P_0(t) - S_{O_2}}{I_{O_2} - S_{O_2}} = e^{-\mathrm{m}\alpha\mathrm{kt}}$$

$$then\ P_0(t) = S_{O_2} + e^{-\mathrm{m}\alpha\mathrm{kt}}(I_{O_2} - S_{O_2})$$

Or $P_0(t) = S_{O_2}\left(1 - e^{-\mathrm{m}\alpha\mathrm{kt}}\right) + e^{-\mathrm{m}\alpha\mathrm{kt}}\left(I_{O_2}\right)$— (8)

$S_{O_2} -$ Stationary value of given oxygen tension for corneal layer

$I_{O_2} -$ Initial Partial Pressure

$\alpha -$ Consumption coefficient of oxygen

$m - \frac{1}{\tau}$

$k -$ Oxygen diffusion constant

$t -$ Time

Equation (8) matched with the experimental conditions of Bonano etal. data.

Now we shall consider the two cases

(i) At initial $\mathrm{t} = 0$ then $\mathrm{P_0(t)} = \mathrm{I_{O_2}}$

(ii) At last $\mathrm{t} = \infty$ then $\mathrm{P_0(t)} = \mathrm{S_{O_2}}$

Now again we solved the

$$\frac{\mathrm{D_j}}{P_0\alpha}\frac{\partial^2 \mathrm{P_0}}{\partial \mathrm{x}^2} - \frac{\mathrm{Q^*(x)}}{\mathrm{k}} = -\mathrm{m} - - - - - - (9)$$

Equation (9) May be written as

$$\frac{\partial^2 \mathrm{P_{0_i}}}{\partial \mathrm{x}^2} - \frac{\mathrm{P_{0_i}}\alpha}{\mathrm{D_j}}\frac{\mathrm{Q^*(x)}}{\mathrm{k}} + \mathrm{m}\,\mathrm{P_{0_i}}\alpha = 0\ )$$

$$\mathrm{or}\frac{\partial^2 \mathrm{P_{0_i}}}{\partial \mathrm{x}^2} - \frac{\mathrm{P_{0_i}}\alpha}{\mathrm{D_j k}}\left(\mathrm{Q^*(x)} - \mathrm{mD_j k}\right) = 0 - - - - - - - (10)$$

$\mathrm{Q^*(x)} \gg \mathrm{mD_j k}$ then

$$\frac{\partial^2 \mathrm{P_{0_i}}}{\partial \mathrm{x}^2} - \frac{\alpha}{\mathrm{D_j k}}\mathrm{Q^*(x)P_{0_i}} = 0 - - - -(11)$$

To calculate the numerical value of $P_{0_i}(x)$, we took the different numerical values of $Q^*(x)$ for corneal tissue.

In the current study we assume that the rate of oxygen consumption remains constant throughout the various layers, the solution of equation 11 is given by $P_{0_i}(x) = c_1 e^{-\sqrt{\frac{\alpha Q^*}{D_i k}}x} + c_2 e^{\sqrt{\frac{\alpha Q^*}{D_i k}}x} - -(12)$

With boundary conditions

$P_0(0) = P_c$

$$P_{o_1}(l_1) = P_{o_2}(l_1) and D_2 k_2 \left(\frac{\partial P_{o_2}}{\partial x}\right)_{x=l_1} = D_1 k_1 \left(\frac{\partial P_{o_1}}{\partial x}\right)_{x=l_1} - (a)$$

$$P_{o_3}(l_2) = P_{o_2}(l_2) and D_3 k_3 \left(\frac{\partial P_{o_3}}{\partial x}\right)_{x=l_2} = D_2 k_2 \left(\frac{\partial P_{o_2}}{\partial x}\right)_{x=l_2} - (b)$$

$$P_{o_4}(l_3) = P_{o_3}(l_3) and D_4 k_4 \left(\frac{\partial P_{o_4}}{\partial x}\right)_{x=l_3} = D_3 k_3 \left(\frac{\partial P_{o_3}}{\partial x}\right)_{x=l_3} - (c)$$

$$P_{o_5}(l_4) = P_{o_3}(l_4) and D_5 k_5 \left(\frac{\partial P_{o_5}}{\partial x}\right)_{x=l_4} = D_4 k_4 \left(\frac{\partial P_{o_4}}{\partial x}\right)_{x=l_4} - (d)$$

$$P_{o_5}(l_5) = P_e - - - - - - - - - - - - (e)$$

By using boundary conditions, we can get the solution of equation (12) we can obtain the values of oxygen tension for different layers.

Also the oxygen tension at each site of the corneal tissue determines the solution to equation (11). The value of Q*(x) can be calculated using the following postulates since the solution of (11) also depends on the consumption of the corneal layers.

- Oxygen tension remains constant for different layers.
- Described by metabolic model, this is also known as Monod Kinematics.

By applying the above mentioned boundary conditions, we can see that the solution of equation (11) displays the oxygen partial pressure and fluxes. Many publications used the values of 24.1 mmHg for oxygen tension and 61.5 mmHg for partial pressure for the epithelial layer. It is based on how transmissible various corneal layers are.

- $p(x = 0) = P_o = 24.2$ mmHg
- $\left(p(x = l_i) = p_{xl_i}\right)_{i=(1,2,3,4,5)}$
  $= \text{epi, Bowman, str, Des, endo}$

Many authors developed mathematical models to study the oxygen distribution with many parameters through corneal tissue under different conditions, almost authors generated one dimensional model.

Monod kinematics will be applicable if we assumed that the cornea's oxygen consumption stays constant. In general, we saw that ocular tissue had the lowest pressure gradient. The corneal surface has the lowest oxygen pressure gradient [1,2,3].

Now by Monod Kinematics the consumption of oxygen as the function of partial pressure, this is given by

$$\mathrm{Q}\left(\mathrm{P}_{\mathrm{o_i}}\right) = \frac{\mathrm{Q}^{*}\mathrm{P}_{\mathrm{o_i}}}{\mathrm{k_m} + \mathrm{P}_{\mathrm{o_i}}} - - - -(13)$$

Where $\mathrm{i} = 1,2,3,4,5$

$\mathrm{k_m}$ −Monod dissociation constant

Equation (11) solved by numerically and finally to obtain the result we use the boundary conditions (a-e).

Q is calculated by Fatt etal [4,5,6,7]

$$Q(x_c) = \left[2(P_t - P_c)\frac{Dk_c}{{x_{c_i}}^2}\right] - 2\frac{f_c}{x_c} - (14)$$

Then

$P_t =$ Oxygen tension in the tears.

$P_c =$ Oxygen tension in corneal tissue.

$Dk_c =$ Oxygen permeability of corneal tissue.

$f_c =$ Oxygen flux in corneal tissue.

$x_{c_i} =$ Thickness of corneal layers.

The solution of equation (11) may be determine by using [11], which solvable by numerically by using finite volume approach and obtained the solution by using Matlab software.

Result:

In various studies, the Bowman's layer was not consumed the oxygen these layers do not consume the oxygen when eye is not healthy but for healthy eye it consume the oxygen in very little quantity and also contains a very low oxygen tension, it is clear from figure (7) and figure (4). We used the experimental data which provided by Bonanno et al. , we determine the rate of consumption of oxygen by corneal layers and oxygen tension in whole corneal layers. This model presents the absorption algorithm of o_2 in the cornea and present the relationship between oxygen tension and consumption of oxygen as $\mathrm{Q}\left(\mathrm{P}_{\mathrm{o_i}}\right) = \frac{\mathrm{Q}^{*}\mathrm{P}_{\mathrm{o_i}}}{\mathrm{k_m}+\mathrm{P}_{\mathrm{o_i}}}$. From figure (5) the oxygen tension increase as oxygen stay time increase at the surface of corneal layers. This research is very useful for deep study for different layers of cornea.

Discussion:

We noticed that when oxygen tension is zero, oxygen consumption is also zero, and it is obvious from figure (4) that as oxygen tension increases to saturation limited in accordance with experimental values obtained by Bonano et. al [12,13], the Monod Kinematics equation to show the rate of oxygen consumption is given by equation (13).

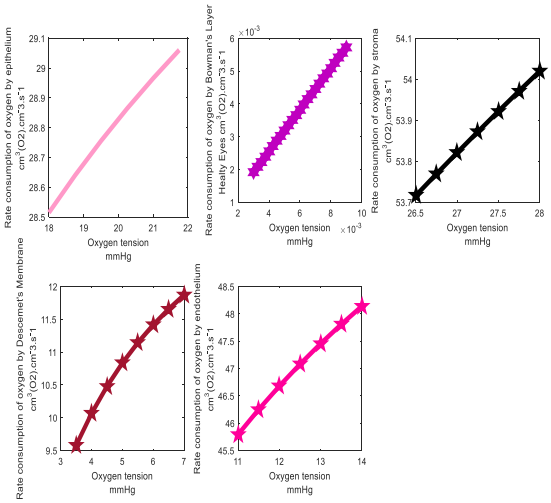

Fig:4: Oxygen tension and corresponding graphical representation of rate of oxygen consumption by different layers

The metabolic activity is lowered and cells respond to obtain oxygen by thickening the corneal layers when the oxygen tension in the various corneal layers is at its lowest. In the current study, we assume that the entire cornea has an oxygen tension of 70 mmHg. The epithelium controls oxygen consumption at maximum pressure, and we assume that the cornea's maximum oxygen tension is 155 mmHg.

According to Monod Kinematics, the cornea's total oxygen consumption is estimated to be between 50 and 60 percent for the epithelium and Bowman's layer and between 33 and 43 percent for the stroma and Descemet's layer.

We also determine the amount of time needed to raise the oxygen tension at the corneal layers' surface. We noted that the starting pressure at x=0 was 24.2 mmHg; this number represents the pace of glycolysis's synthesis of ATP. Additionally, we noticed that the corneal layers are completely oxygenated, as seen in fig (4).

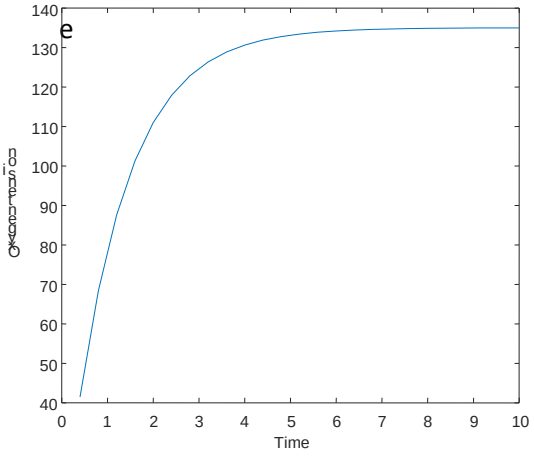

Fig:5, Graphical representation of oxygen tension according to time.

The oxygen tension obtained from fig 5, the oxygen tension profile obtained by equation (8) and we obtained the different values of oxygen tension at different time periods. From figure 5 we conclude that the oxygen tension increased as the time increased. The line shows the numerical solution of corneal tissue for the metabolic model and data was provided by Bonanno etal[13].

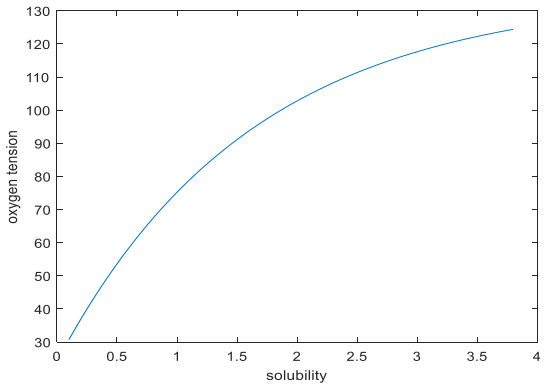

Fig:6 Graphical Representation of change in oxygen tension(mmHg) according to solubility change.

Chhabra et.al took the value $k_m = 2.2$ when pressure is less than 20 mmHg when the pressure (oxygen tension) is greater than 20 mmHg then permeability changed so we found the solubility by using permeability and also found that the oxygen tension is also affected from variation in solubility.

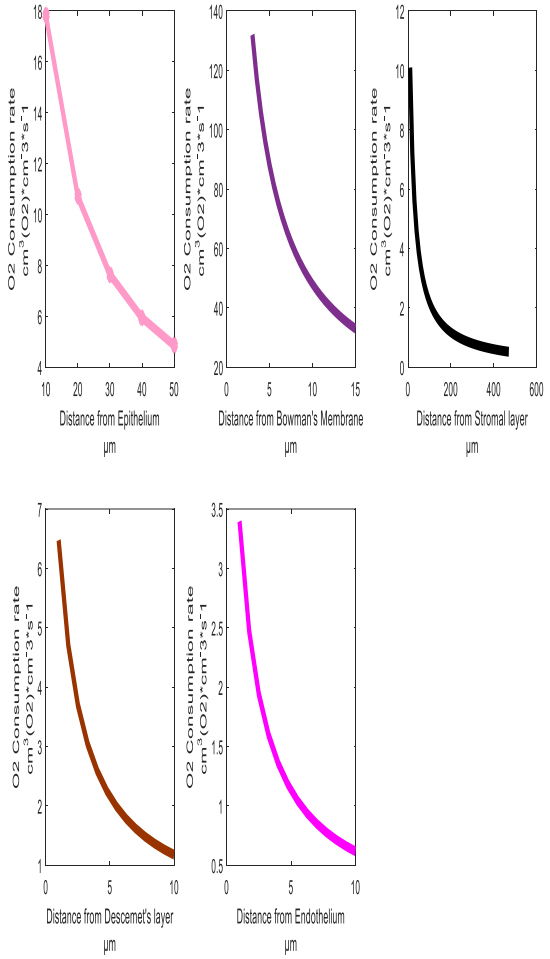

Fig:7 The graphical representation of change in consumption of oxygen according to distance

We deduced from graphical depiction 7 that oxygen consumption initially peaks and subsequently decreases as it moves deeper into the concern layer. In this study, we take into account that the oxygen consumption varies depending on

the layer. Additionally, k_m is 2.2 mmHg, and Table (1) lists the oxygen permeability values for each of the five layers of corneal tissue . And graphical depictions are shown in figure (7).

Table:

Parameter	**Symbol**	**Value**	**Unit**
Stationary value of given oxygen tension for	S_{O_2}	**155**	**mmHg**

corneal layer			
Initial Partial Pressure	I_{O_2}	**24.2**	**mmHg**
Oxygen diffusion constant	k	$\mathbf{1.0268 * 10^{-5}}$	$\boldsymbol{cm^3 of\ o_2 cm^{-3}}$
Constant	τ	> 1	
Oxygen tension in the tears	$P_{t_{Epitheli}}$ $P_{t_{Bowma}}$ $P_{t_{Stroma}}$ $P_{t_{Desceme}}$ $P_{t_{Endothe}}$	**21.1** **16.3** **28** **6.5** **13.5**	**mmHg**
Oxygen tension in corneal tissue	$P_{c_{Epitheli}}$ $P_{c_{Bowma}}$ $P_{c_{Stroma}}$ $P_{c_{Desceme}}$ $P_{c_{Endothe}}$	**14.7** $\mathbf{.003 * 10^{-6}}$ **26.5** **5.2** **12.2**	**mmHg**
Oxygen permeability of corneal tissue	$Dk_{Epithel}$ Dk_{Bowma} Dk_{Stroma} Dk_{Descem} Dk_{Endoth}	**5.3,** **6.18** **86.2** **16.3.** **5.3**	**Barrer** **Barrer** **Barrer** **Barrer** **Barrer**

Thickness of corneal layers.	$x_{Epitheliu}$ x_{Bowman} x_{Stroma} $x_{Descemet}$ $x_{Endothel}$	**50** **15** **478** **10** **4**	**µm** **µm** **µm** **µm** **µm**
Oxygen flux in corneal tissue	$f_{c_{Epi}}$ $f_{c_{Bowman}}$ $f_{c_{Stro}}$ $f_{c_{Descemet}}$ $f_{c_{Endotheli}}$	**1.638** **.01** **3.12** **1.58** **2.964**	**Weber** **Weber** **Weber** **Weber**
Metabolic model Parameter	k_m	**2.2**	**mmHg**

Constants/parameter values needed to calculate oxygen tension in corneal layers and the rate of oxygen consumption

Conclusion:

In this research we present the method to solve the non linear partial differential equation $D_j \frac{\partial^2 P_0}{\partial x^2} - \frac{Q(x,t)}{k} = \frac{1}{k}\frac{\partial P_0}{\partial t}$ for oxygen tension P_0 which depends on time and position. Another method to solve this pde used in Chhabra's work, we used the values km and solubility described in Chhabra's work. We can replicate the results of the experiment for the oxygen tension at the layers of corneal tissue for both open and closed eyes using Monod kinematics,

we only addressed the results for open eyes, where they show the site of maximum oxygen tension at 155mmHg (Open eye at sea level). The rate of oxygen consumption for the epithelium, bowman layer, stroma, Descemet's layer, and endothelium layers was not predicted using the Monod method. Most authors believe that the Bowman's layer does not utilize oxygen, although this is untrue when the eye is healthy, as shown in graph 7. The cornea is sufficiently oxygenated in all five of its layers. Figure 4 shows a similar outcome for oxygen tension for all subjects what I consider in this research is five layers. Furthermore, a key discovery of ours is that oxygen consumption is dependent on oxygen flux, layer depth, and oxygen tension rather than remaining constant.

Acknowledgment:

The reviewers of the original draught of the paper made helpful and insightful remarks, which the authors are quite pleased to acknowledge.

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