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MATHEMATICAL MODELLING OF FLOW IN SCHLEMM'S CANAL AND ITS INFLUENCE ON PRIMARY OPEN ANGLE GLAUCOMA

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Abstract. POAG (Primary Open Angle Glaucoma) is a major cause of blindness. This normally occurs when the IOP (intraocular pressure) increases. High pressure can be caused by an imbalance in the production and drainage of fluid (aqueous humour, AH) in the eye. AH is continually being produced but sometimes cannot be drained because of improperly functioning drainage channels (trabecular meshwork, TM). A mathematical model is presented for the flow of AH through the TM and into the SC (canal of Schlemm) and to couple this flow in order to predict changes in IOP. The governing equations have been developed by using the lubrication theory limit of the Navier-Stokes equations. To close the model, Friedenwald's law has been used to predict changes of IOP. Several different cases have been examined in the model, relating AH flow to changes in IOP for various submodels: (i) the permeability, k in Darcy's law may be either constant or not constant; (ii) the TM may be deformable so that the general theory of a beam under axial load is applicable - a number of different subcases where either θ or λ, may be either large or small have been considered. However only the subcase θ is small has been discussed in this study by assuming the permeability, k is constant and the TM is deformable. This subcase has been solved by using the regular perturbation method. The results show that the IOP rises continually when θ is small and may cause blindness.

Keywords: *POAG, Lubrication theory flow, Friedenwald's law, Darcy's law, Beam bending theory*

1. POAG in Human Eyes

The human eye is a truly amazing organ. It gives us the sense of sight, allowing us to learn more about our surroundings than we can with any of the other four senses. Most people would probably agree that sight is the sense that they value more than all the rest. Each part of the eye has its own special function but if only one of these parts is damaged or injured, this may lead to blindness.

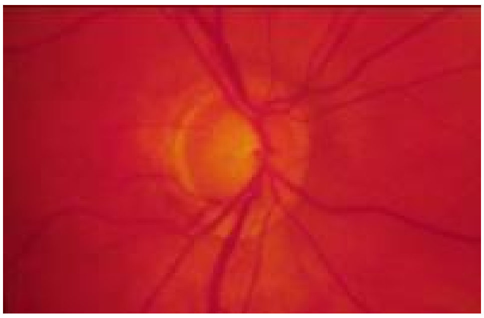

Figure 1. Glaucomatous Optic Nerve Damage. This figure was extracted from [14].

One common cause of blindness is glaucoma. Glaucoma is an eye condition where the optic nerve at the back of the eye is damaged (see Figure 1). In most cases, the damage to the optic nerve is due to an increased pressure within the eye. The several different types of glaucoma include, primary open angle glaucoma (POAG), acute angle closure glaucoma, secondary glaucoma and congenital glaucoma. The most common type is primary open angle glaucoma (also called chronic glaucoma) ([13]). In [13] it was noted that POAG affects about 1 percent of the population over 40 and more than 10 percent over 80. POAG most often occurs when the intraocular pressure (IOP) increases. The cause of this high pressure is generally accepted to be an imbalance in the production and drainage of fluid in the eye (aqueous humour, AH). The channels that normally drain the fluid from inside the eye do not function properly. Though fluid is continually being produced, it cannot be drained because of the improperly functioning drainage channels (trabecular meshwork, TM). This results in an increased amount of fluid inside the eye, thereby raising the pressure (see Figure 2).

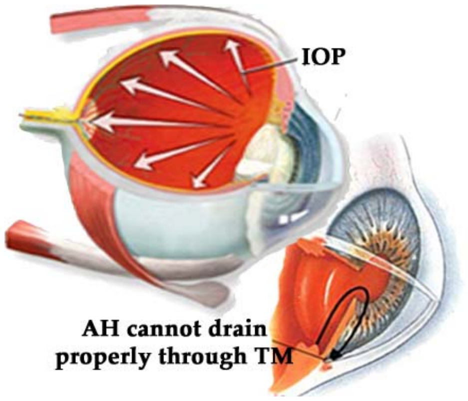

Figure 2. Mechanism for Intraocular Pressure (IOP) increases in Human Eyes. This figure was reproduced from [15].

In Western countries, POAG is leading the cause of blindness. It affects approximately 66 million people from all countries around the world [2]. According to [10], POAG can affect anyone, but commonly it will affect people who have a family history of glaucoma, short sight, or diabetes. A number of researchers have studied the problem of POAG (see, for example [7], [11], [2] and [1]). It seems that they mostly understand what happens in POAG. They agree that the component of abnormality that causes the fluid (aqueous humour, AH) not to be drained, (so that the amount of fluid inside the eye slowly increases and thereby raises the intraocular pressure (IOP)) is blockage of the trabecular meshwork (TM).

In many previous studies (see [8], [7], [11] and, [1]) it was shown that, if the IOP increases, then the wall of the SC collapses dramatically. "The collapse of the canal caused by elevated IOP offers resistance to the aqueous flow through it [1]". [8] modelled AH flow in the SC and assumed the inner wall of canal to be a rigid wall. [7] improved the model, making it more realistic by treating the inner wall of canal as a porous and elastic wall, and proposed that "the TM is a series of linear springs that allow the inner wall of canal to deform in proportion to the local pressure drop across it". [11] developed a mathematical model of AH flow through the TM and into the SC by observing the effects that influenced the collapse of the wall. [1] extended this study by considering the inner wall of canal to be both resilient and elastic.

Most of the studies, [8], [7], [11] and, [1] have focused on the flow of AH through the TM and into the SC before it exists at a collector channel. However they did not consider that the flows involved can be assumed as lubrication theory flows [9]. Though, the final fluid dynamics equations that are given below in Section 2.3 are very similar to those in [1], not only is extra coupling now added to determine the IOP, but the equations are interpreted in a full lubrication theory context. This contrasts with [1], where the flow was assumed to be a fluid flow through a narrow elliptical and circular channel. Our approach lends itself much more easily to generalization. A previous study, [3] modelled the flow of AH from the AC through the TM and into the SC and coupled this flow to predict changes in IOP. However, [3] only examined simple modelling cases where $h(x) \equiv h_{\circ}$ and $w_h(x) \equiv \alpha < 0$ were both constant, and only considered the case where flow through the TM was determined by Darcy's law. In this current study, we extend the work of [3] in order to predict changes in IOP, by considering the permeability, *k* in Darcy's law to be either constant or not constant and further assuming that the TM is deformable by applying the general theory of a beam under axial load. Therefore this is the aim in our current study.

2. Governing Equations

2.1 Fluid Modelling

A two-dimensional paradigm problem of flow through the TM into the SC in order to predict changes of IOP is shown in Figure 3. In this problem we assume that the SC typically has half-length, *L* between a symmetry axis and a collector channel; $L = 600\mu m$, an undeformed depth, $h_{\circ} = 25\mu m$ and breadth, $B = 300\mu m$ (all the parameter values are obtained from [7]). The aspect ratio $\delta = h_{\circ}/L$ is thus about 0.04. Using the values from [7], the density, $\rho = 1003 kg/m^3$ and from [16], the dynamic viscosity, $\mu = 0.75\times10^{-3}\,\mathrm{Pa}\,s$, thus we obtain the Reynolds number is $\mathrm{Re} = (\rho UL/\mu) \sim 4$ and the reduced Reynolds number, $\delta^2\,\mathrm{Re} \sim 0.0064$. By using the lubrication theory limit of the Navier-Stokes equations ([9]), we develop the governing equations of this problem (see Figure 3 for nomenclature). These are:

$$p_x = \mu u_{zz} \text{ , } p_z = 0 \text{ , } u_x + w_z = 0 \quad \left(x \in [0, L], 0 \le z \le h(x) \right) \tag{2.1}$$

with the boundary conditions

$$u(x,0) = w(x,0) = 0, u(x,h(x)) = 0, \quad w(x,h(x)) = w_h(x),$$
$$p_x(0,z) = 0, \quad p(L,z) = p_{\text{out}}. \tag{2.2}$$

Here L denotes the length between a symmetry axis and a collector channel, p is the pressure, $\bar{q} = (u(x,z), w(x,z))$ is the fluid velocity, w_h is the flow speed through the TM, and $p_{out} \sim 9\text{mmHg}$ ([7]) is the pressure at a collector channel. We note that [3] also developed the governing equations (2.1) and the boundary conditions (2.2) that are shown above.

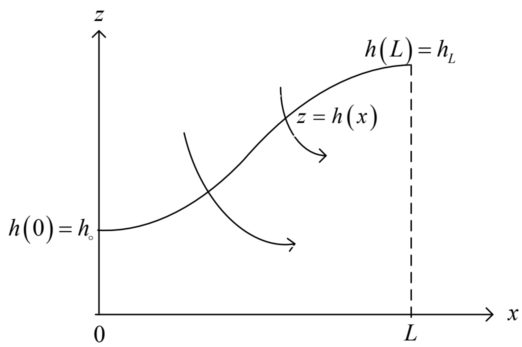

Figure 3. Schematic diagram of flow through the TM into the SC

2.2 Friedenwald's Law

To close the model, we must relate the IOP to the eye's AH production and removal. [6] stated that measurements of the ocular rigidity of the sclera, choroid or retina portion of the eye have traditionally been expressed in term of 'Friedenwald's law' rather than using a traditional linear elasticity approach involving Young's modulus and Poisson's ratio. We use Friedenwald's law to predict changes of IOP (see [3]). [5] stated that the volume and IOP of a human eye are related. Friedenwald's law stated that p_1 and p_2 (two IOPs) are related to respective ocular volumes V_1 and V_2 (measured in μl) via

$$K(V_1 - V_2) = \log_{10} p_1 - \log_{10} p_2$$
$$\Rightarrow \quad p_1 = p_2 \exp\left(K(V_1 - V_2)\ln 10\right).$$

We denote normal conditions using a subscript *n* and altered conditions using a subscript *i*. We therefore find that,

$$p_i = p_n \exp\left(\tilde{K}(V_i - V_n)\right).$$

Here $K \sim 0.025/\mu l$ is a known constant. $\tilde{K} = K \ln 10 \sim 5.75646 \times 10^7 / \text{m}^3$. If we differentiate the equation above with respect to t now we get

$$\frac{dp_i}{dt} = \tilde{K} p_n \exp\left[\tilde{K}(V_i - V_n)\right](\dot{V}_i - \dot{V}_n) \quad \Rightarrow \quad \frac{dp_i}{dt} = \tilde{K} p_i (\dot{V}_i - \dot{V}_n),$$

$$\therefore \quad \frac{dp_i}{dt} = \tilde{K} p_i (\dot{V}_{in} - \dot{V}_{out}) \tag{2.3}$$

where $\dot{V}_i = \dot{V}_{in} (\sim 3.3321 \times 10^{-11} m^3 / \text{sec})$ and $\dot{V}_n = \dot{V}_{out} (\text{m}^3 / \text{sec})$ denote the respective total amounts of fluid flowing in and out of the eye.

2.3 Fluid Flow / IOP Equations

The governing equations can now be solved by integrating equation (2.1) and substituting the boundary conditions (2.2) in order to get the fluid velocity, u. We find that

$$u = \frac{p_x}{2\mu}(z^2 - hz). \tag{2.4}$$

We now differentiate equation (2.4) with respect to x and substitute into equation (2.1), yielding

$$w_z = \frac{1}{2\mu} p_x h_x z + \frac{1}{2\mu} p_{xx} \left(hz - z^2 \right).$$

We now solve the equation above by using the boundary conditions (2.2), therefore we get the equation of fluid velocity w,

$$w = \frac{p_{xx}}{2\mu} \left(\frac{hz^2}{2} - \frac{z^3}{3} \right) + \frac{1}{4\mu} p_x h_x z^2. \tag{2.5}$$

From equation (2.5) we may find that the pressure $p(x)$ satisfies

$$w_h(x) = \left[\frac{p_x h^3}{12\mu} \right]_x \quad \left(p(L) = p_{out}, p_x(0) = 0 \right), \tag{2.6}$$

where $w_h(x)$ and $h(x)$ are unknown functions of x which should be determined. The volumetric flow rate, $\dot{V}_C\left(m^3/s\right)$ in this problem from a single collector channel is given by

$$\dot{V}_C = \int_0^{h(L)} B\, u\big|_{x=L}\, dz. \tag{2.7}$$

Substituting equation (2.4) into equation (2.7), we find that

$$\dot{V}_C = -\left.\frac{Bp_x h^3}{12\mu}\right|_{x=L}. \tag{2.8}$$

Generally, the total number of collector channels, N is about 30 ([4]) and so that the total amounts of fluid flowing out of the eye is $\dot{V}_{out} = N\dot{V}_C$. Therefore, the IOP, $p_i(t)$ may now be determined by equation (2.3) with $p_i(0) = p_{i\circ}$. Note that the modelling that has so far taken place is identical to that contained in [3].

3. Results and Discussion

Each of the cases studied in this problem requires a good understanding of the causes and consequences that potentially cause POAG, and different mathematical techniques from analytical to numerical methods. Due to the fact that higher order equations cannot normally be solved analytically, MAPLE was be used to solve these following cases. Many different cases have been examined relating AH flow to changes in IOP for various submodels. Example include,

Case - The permeability, *k* in Darcy's law is constant and the TM is deformable

First we consider the case of flow through TM determined by Darcy's law so that $\overline{q} \propto \overline{\nabla} p$ [9]. We assume that,

$$w_h(x) = -\frac{k}{d\mu}\left(p_i - p\right) \tag{3.1}$$

where d is the width of the TM and the permeability *k* (dimensions m^2) is constant. The permeability *k* has been measured from the TM resistance, R_T (dimensions $kgs^{-1}m^{-4}$), $R_T = \mu d/kBL$ (see [3]). Then we apply the general theory of a beam under axial load. We use a simple model of beam bending, namely Bernoulli-Euler theory. This theory is applicable in this problem because the bending of the beam is small enough so that the elastic reaction force that the beam opposes to the bending force is proportional to the deflection ([12]). We assume that the beam is of length *L* and is located between symmetry axis and the collector channel (see Figure 3). The equilibrium position of the beam is described by a function *h(x)* and is determined by the balance between the elastic forces in the beam and the loads (the IOP in the AC) acting on it. We can now formulate an equation that links the displacement *h(x)* directly to the distributed load which is the different pressure in the AC and SC, thereby obtaining

$$EI\frac{d^4 h}{dx^4} = p - p_i \tag{3.2}$$

where *E* is the modulus of elasticity and *I* is the moment of inertia. Equation (3.2) is a fourth order linear equation. In order to find the solution, we must have appropriate boundary conditions that describe the constraint imposed by the hinges. In this problem, we assume that the beam has a clamped end. Therefore the boundary conditions are

$$h_x(0) = 0, h_{xxx}(0) = 0, h(L) = h_L, h_x(L) = 0. \tag{3.3}$$

Here we assume that the flow through the TM is determined by Darcy's law where *k* is constant. *h(x)* is no longer constant since the TM is deformable and satisfies the beam equation (3.2) and also the boundary conditions (3.3). We now equate equation (3.1) with equation (2.6), yielding

$$\left[\frac{p_x h^3}{12\mu}\right]_x = -\frac{k}{d\mu}\left(p_i - p\right). \tag{3.4}$$

We now rearrange equation (3.2) and we find that

$$p = p_i + EI\, h_{xxxx}. \tag{3.5}$$

Then we differentiate equation (3.5) with respect to x, now we get that

$$p_x = EI\, h_{xxxxx}. \tag{3.6}$$

We now substitute equations (3.5) and (3.6) into equation (3.4) and therefore we may obtain the governing equation for this case. Thence it is given by

$$\left(h^3 h_{xxxxx}\right)_x = \theta h_{xxxx} \quad ; \quad \theta = 12k/d \tag{3.7}$$

with boundary conditions,

$$h_x(0)=0,\, h_{xxx}(0)=0,\, h_{xxxxx}(0)=0,\, h(1)=1,\, h_x(1)=0,\, h_{xxxx}(1)=\lambda \ \left(\lambda<0, \lambda=\frac{L^4}{h_L}\left(\frac{p_{out}-p_i}{EI}\right)\right). \tag{3.8}$$

We have examined a number of different subcases where either θ or λ, may be either large or small. However in this study, for brevity, we only discuss the subcase where $\theta \ll 1$.

$\theta \ll 1$

The governing equation (3.7) can now be solved by using regular perturbation method where we assume that

$$h(x) = h_\circ(x) + \theta h_1(x) + \ldots \quad . \tag{3.9}$$

We now substitute equation (3.9) into equation (3.7) and boundary conditions (3.8), here we get that

$$\left[\left(h_\circ(x)+\theta h_1(x)+\ldots\right)^3\left(h_\circ(x)+\theta h_1(x)+\ldots\right)_{xxxxx}\right]_x = \theta\left(h_\circ(x)+\theta h_1(x)+\ldots\right)_{xxxx} \tag{3.10}$$

with boundary conditions

$$\begin{aligned}&\left(h_\circ\right)_x(0)+\theta\left(h_1\right)_x(0)+\ldots=0,\ \left(h_\circ\right)_{xxx}(0)+\theta\left(h_1\right)_{xxx}(0)+\ldots=0,\ \left(h_\circ\right)_{xxxxx}(0)+\theta\left(h_1\right)_{xxxxx}(0)+\ldots=0,\\ &\left(h_\circ\right)(1)+\theta\left(h_1\right)(1)+\ldots=1,\ \left(h_\circ\right)_x(1)+\theta\left(h_1\right)_x(1)+\ldots=0,\ \left(h_\circ\right)_{xxxx}(1)+\theta\left(h_1\right)_{xxxx}(1)+\ldots=\lambda.\end{aligned} \tag{3.11}$$

From equation (3.10) and the boundary conditions (3.11), we examine the governing equation at leading order,

$$\left[\left(h_\circ(x)\right)^3\left(h_\circ(x)\right)_{xxxxx}\right]_x = 0.$$

We now find that either

$$\left(h_\circ(x)\right)^3 = 0 \quad \Rightarrow \quad h_\circ(x) = 0$$

(this equation can be ignored because it does not satisfy the boundary conditions (3.11)) or

$$\left(h_\circ(x)\right)_{xxxxx} = 0.$$

If we integrate the above equation five times with respect to x, we may get that

$$h_\circ(x) = \frac{1}{24}C_1x^4 + \frac{1}{6}C_2x^3 + \frac{1}{2}C_3x^2 + C_4x + C_5. \tag{3.12}$$

Thus we substitute the boundary conditions (3.11) at $x = 0$ into equation (3.12), we may obtain that

$$C_2 = 0, \quad C_4 = 0.$$

We now rewrite equation (3.11) by substituting the values above, yielding

$$h_\circ(x) = \frac{1}{24}C_1x^4 + \frac{1}{2}C_3x^2 + C_5. \tag{3.13}$$

Then we substitute the boundary conditions (3.11) at $x = 1$ into equation (3.12), we may find that

$$C_1 = \lambda, \quad C_3 = -\frac{\lambda}{6}, \quad C_5 = 1 + \frac{\lambda}{24}.$$

After the values of C_1, C_3 and C_5 have been got, thus we rewrite equation (3.13), yielding

$$h_\circ(x) = \frac{\lambda}{24}x^4 + \frac{\lambda}{12}x^2 + \frac{\lambda}{24} + 1. \tag{3.14}$$

We now substitute equation (3.14) into equation (3.9), thus we obtain

$$h_\circ(x) = \frac{\lambda}{24}x^4 + \frac{\lambda}{12}x^2 + \frac{\lambda}{24} + 1 + O(\theta). \tag{3.15}$$

Equation (3.15) may now be plotted (see Figure 4) in order to examine the deformation of the TM when θ is less that one. Here we assume that $\lambda = -1$. Figure 4 shows the deformation of the TM when θ is small. Three different curves shown in Figure 4 have been measured for different values of θ. It shows that when the value of θ decreases, then *h(x)* becomes much less deformed.

Then we may find the volumetric flow rate, $\dot{V}_c$ is equal to zero at leading order, by substituting the equations (3.6) and (3.15) into equation (2.8). This is because when we differentiate equation (3.15) five times with respect to x, we may find that $\left(h_\circ(x)\right)_{xxxx} = 0$ at leading order. Thus $p(x)$ (in equation (3.6)) becomes zero.
Therefore the total amount of fluid flowing out of the eye, $\dot{V}_{out}$

$$\dot{V}_{out} = N\dot{V}_c \quad \Rightarrow \quad \dot{V}_{out} = N\left(0 + O(\theta)\right) \tag{3.16}$$

is very small. This means that the amount of AH flowing across TM is also negligible. Thus the IOP, $p_i(t)$ may now be determined by substituting equation (3.16) into equation (2.3), therefore the total change in IOP is

$$\frac{dp_i}{dt} = \tilde{K}p_i\dot{V}_{in} + O(\theta) \quad ; \quad p_i(0) = p_{io} \, .$$

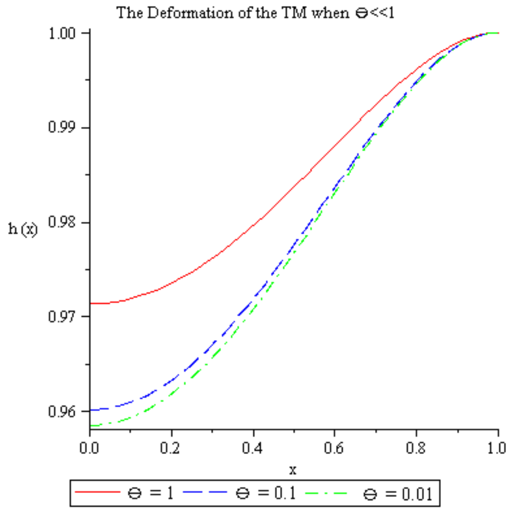

Figure 4. The deformation of the TM at λ = -1 for different values of θ

Thence the IOP rises continually at leading order and there is nothing to stop it. Note that, though we could find $h_1(x)$ in this problem there is no point in doing so because when θ is small, we can see by just looking at the $h_\circ(x)$ terms, the IOP rises dramatically and blindness will inevitably result.

4. Conclusions and Further Work

In this study, we sought to model the flow of AH through the TM and into the SC, and to couple this flow to the pressure in the AC in order to predict changes in IOP. We have discussed the particular subcase where θ is small where we assume the permeability, k is constant and the TM is deformable, and this subcase has been solved by using the regular perturbation method. Many other possible cases can be considered for other different values of θ and λ. These will be dealt with in a further study.

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