# The mathematical modelling of human eyes - a PhD study

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### **Abstract**

We illustrate how a range of fluid and solid mechanics problems relevant to the human eye have been combined in a continuing Ph.D. study. Anterior chamber flow, the solid mechanics of tonometry, the effects of scleral buckle surgery and the mechanics of retinal detachment are all discussed. Finally, a number of other eye problems that are amenable to a theoretical mechanics treatment are proposed.

#### Introduction

he main objective of this article is to illustrate one of the areas that typifies the sort of interdisciplinary research that many of today's mathematics Ph.D students are engaged in. When confronted with the fact that a three-year Ph.D. is taking place on "The Mathematics of Eyes", many people's first reaction is that the work must either have something to do with optimising the manufacture of spectacles, or perhaps consist of analysing the optics of the human eye. Both these guesses are wrong and, as we hope to illustrate below, understanding many of the functions and possible defects of the human eye turns out to be a matter of applying traditional theoretical fluid and solid mechanics.

As the reader will gather from the descriptions below, some of the problems that are discussed should still be regarded partially as "work in progress". This accurately reflects one of the key features of many interdisciplinary problems, namely that they can never really be regarded as being "solved" Typically, whenever headway is made with the original problem, new questions are prompted and new complicating effects are introduced.

Of necessity, many of the clinical and mathematical details of the problems that are discussed below have had to be omitted. Our aim is more to provide the reader with an example of the sort

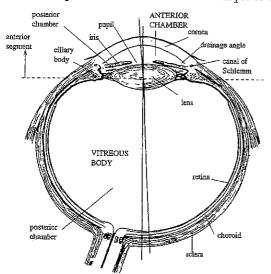


Figure 1: Schematic diagram of the major regions and components of a human eve

of cross-disciplinary research that is now becoming not only desirable, but essential at the mathematics/life sciences interface. In order to understand this article some basic knowledge of the eye and its main mechanisms is necessary. Figure 1 shows the most important regions and components of a normal human eye; for further information, the reader is referred to [3], which contains a wealth of detailed information, and (for the non-squeamish) [8] which contains excellent colour pictures of a vast range of abnormal eye conditions

## Flow in the anterior chamber

The anterior chamber (AC) of the eye comprises the region between the iris and the pupil aperture, and the inner surface of the cornea. Aqueous humour (a fluid with very similar properties to water that is usually referred to simply as "aqueous") flows from the ciliary body past the front of the lens and behind the back of the iris, through the pupil aperture and into the AC. Eventually, the aqueous in the AC exits through the drainage angle via the trabecular meshwork into the canal of Schlemm before flowing away.

It has long been agreed amongst ophthalmologists that non-trivial fluid flow patterns may be present in the AC. Under normal conditions the aqueous flow is essentially invisible, but if the flow is "seeded" with marker particles, a circulating flow is often observed This flow appears to have mainly vertical streamlines, falls at the front of the chamber and rises at the rear. In some eye conditions such "marker particles" are naturally present. For example, a blow in the eye from a squash ball can lead to the presence of red blood cells in the AC, infection can lead to the presence of white blood cells, and a number of temporary and hereditary conditions can seed the aqueous with pigment particles from the back surface of the iris.

What causes these flows? It has long been conjectured that, since the temperature at the back of the AC is close to normal body temperature (37°C) and (at least the outer face of) the cornea is at ambient temperature (typically around 10-20°C colder), the flow is caused by buoyancy effects. The fact that the AC is "long and thin" and a typical flow speed is small makes this problem an ideal one for the application of thin-layer lubrication theory. Under the assumptions that (a) the flow through the pupil aperture is small compared to that produced by buoyancy effcts, (b) the aspect ratio  $\varepsilon = h_0 / L$  (where  $h_0$  is a typical corneal height and L is a typical AC diameter) is small, (c) the buoyancy may be modelled using the standard Boussinesq assumption and (d) the non-dimensional parameters  $\varepsilon^2 Re$  and  $Re Pr \varepsilon^2$ Re = LU/v, L and U being a typical length and speed respectively and v the kinematic viscosity of the aqueous, and  $Pr = \rho_0 v c_n / k$  where  $\rho_0$  is the density of the aqueous at temperature  $T_0$  and  $c_n$  and k are respectively the specific heat and thermal conductivity of the aqueous) are small, the (dimensional) leading order equations are

$$-\frac{p_x}{\rho_0} + vu_{zz} + g(1 - \alpha(T - T_0)) = 0, \quad -\frac{p_y}{\rho_0} + vv_{zz} = 0, \quad p_z = 0, \quad (1)$$

$$u_x + v_y + w_z = 0, \quad T_{zz} = 0.$$
 (2)

with u = v = w on z = 0 and on the cornea z = h(x, y),  $T = T_1 \sim 37^{\circ}$  C on z = 0 and  $T = T_0 \sim 20^{\circ}$ C on z = h(x, y) Here p denotes pressure, T temperature, z is the coordinate normal to the iris and x and y are the coordinates in the plane of the iris, the aqueous velocity is q = (u, v, w), g is the acceleration due to gravity,  $\alpha$  is the coefficient of linear thermal expansion of the aqueous and subscripts denote differentiation. In the simplest case, (1)–(2) may easily be solved to yield

$$u = -\frac{(T_1 - T_0)g\alpha z}{12\nu h}(2z - h)(z - h)$$

$$v = 0$$

$$w = -\frac{(T_1 - T_0)g\alpha z^2 h_x}{24\nu h^2}(z^2 - h^2)$$

$$T = T_1 + \frac{z}{h}(T_0 - T_1)$$

$$p = p_a + (x + a)g\rho_0 \left[1 - \frac{\alpha(T_1 - T_0)}{2}\right]$$

The flow is thus essentially two-dimensional: typical streamlines are shown in the left-hand diagram of figure 3. When realistic parameters are used, we find that the flow takes about 18 seconds to perform one complete circuit of the AC.

The fluid flow is thus determined, but what of the aforementioned blood cells or pigment particles that may be present in the flow? From a medical point of view, it is crucial to know what influence the flow has on the final resting place of any particles that may be present. This is because an agglomeration of red blood cells can cause a hyphema to form, white blood cells can clump together to form keratic precipitates that ultimately may form a hypopyon, and pigment particles may lead to the formation of a Krukenburg spindle (see figure 2). Each of these

conditions may block the trabecular meshwork, leading to a potentially dangerous increase in AC pressure

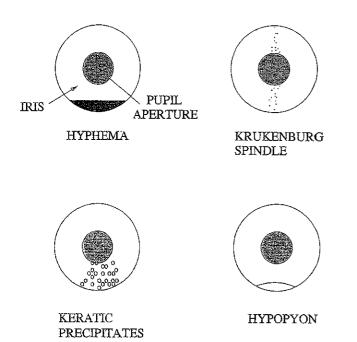
Now that the flow is known, it is relatively easy to include the effects of particles in the analysis. We simply assume that the particles obey a convection-diffusion equation with boundary conditions that reflect their nature (white blood cells tend to be sticky and adhere to each other; red blood cells do not) The solution of the equation for the particles is a routine numerical matter and allows hyphema, hypopyon and Krukenburg spindle predictions to be made. The right-hand diagram of figure 2 shows model predictions of a hyphema, the greyscale contours indicating red blood cell concentration. Using this model, many practical predictions may be made: for example, if even only a few percent of particles cannot leave via the trabecular meshwork then some sort of problem is almost certain to occur. One may also show that a hyphema of a certain size may be dissipated by applying a cold patch to the eye to increase the temperature difference and therefore the strength of the buoyancy-driven flow

Finally, the problem may be studied when flow through the pupil aperture becomes important. In the absence of such flow, the streamlines are essentially two-dimensional, as shown in the left-hand diagram of figure 3. When the flow through the pupil aperture is included, however, a much more complicated picture emerges. The right-hand diagram of figure 3 shows a perspective picture of the flow, and, though fully three-dimensional flows are notoriously hard to display on a printed page, gives some idea of the highly developed topology of the flow

For full details of this work and a discussion of many other aspects of AC flow, see [2].

## The mathematics of tonometry

If you have ever had to visit the eye unit of a hospital for treatment, then you will know that almost invariably the consultant begins your examination by measuring your intraocular pressure (IOP). A normal IOP lies in the range 12–20 mmHg (the units are not SI, but are always used by ophthalmologists; 1mmHg =



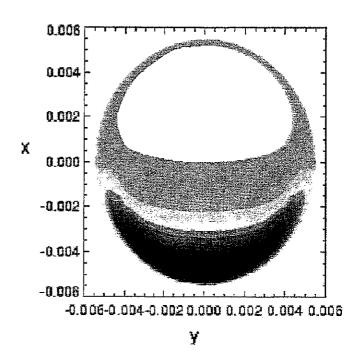
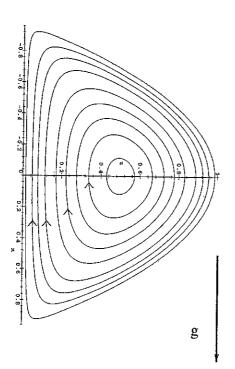


Figure 2: (Left) Schematic diagrams of a hyphema, a Krukenburg spindle, keratic precipitates and a hypopyon. (Right) Hyphema prediction from anterior chamber flow model



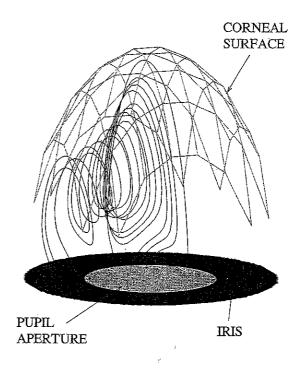


Figure 3: (Left) Flow streamlines (seen from the side of the eye) when no pupil aperture flow is present. (Right) Perspective view of three-dimensional flow field when flow through the pupil aperture is non-negligible

133.322 Pascals). The pressure inside a normal eye is therefore about 1.02 atmospheres. An abnormally high IOP of about 25 mmHg or greater indicates the presence of glaucoma, a sign that something is wrong: an IOP of 50mm or above normally leads fairly rapidly to permanent blindness. Two sorts of glaucoma are identified: in angle-closure glaucoma the iris is pushed against the surface of the corneal/scleral junction. This blocks the canal of Schlemm, the main out flow route for aqueous. The consequent rise in IOP is rapid and painful. In open-angle glaucoma either a slowly-increasing aqueous production rate or a developing flow resistance in the aqueous outflow pathway causes a slow rise in IOP, which may nevertheless still lead to blindness.

Measurements of a patient's IOP are so routinely required that a simple, non-traumatic and non-invasive way of taking the necessary reading must be used. Although many different instruments may be employed (full descriptions are given in [3]), the Goldmann applanation tonometer (and its hand-held relatives the Clement-Clark Perkins or Kowa tonometer) is generally regarded as being one the most accurate and reliable devices. In crude terms, a Goldmann tonometer resembles a hammer with a sprung handle. After a topical anaesthetic has been used to numb the eye (this stings very badly for about one second – such a short time that afterwards you wonder whether it ever really stung at all) the "hammer head" of the tonometer is used to compress the AC until a given surface area A of the cornea is attened ("applanated"). To give a final IOP reading, the "Imbert-Fick" principle ([4], [7]) is now invoked. This states that the applied to nometer force W is related to the IOP  $P_{{\it IOP}}$  by

$$W = P_{IOP}A, (3)$$

where W is measured in units of 0 1 of a gram force (so that a force of about 1.6g will be required for applanation in a normal person),  $P_{IOP}$  is measured in mmHg and A = 7.35mm<sup>2</sup> (so that the diameter of the applanated region is 3.06mm)

Why does this work? The honest answer is that nobody really knows, The Imbert-Fick principle was established over a century ago, and is not the result of any detailed mathematical calculation or engineering principle. The particular units used in (3) are obviously the result of some "correlation" process that has been refined over the years, but still begs a number of questions over what range of IOPs is (3) valid? How accurate is it? What limitations does it have? (see, for example [11]) Finally, and most importantly, does (3) still apply when exceptional circumstances pertain? (see, for example the section on scleral buckles below).

The problem is an obvious candidate for mathematical modelling: we assume that the eye is a linearly elastic hollow sphere and attempt to determine the relationship between the applanating force and the internal pressure. The equations of equilibrium that

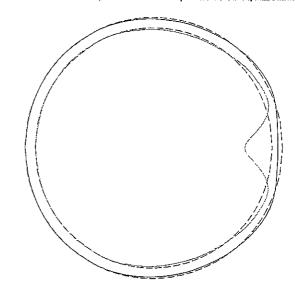


Figure 4: The effect of tonometry on the inner and outer walls of the eye (broken line: undeformed inner and outer eye surfaces)

must be solved for the stresses  $\sigma_{ij}$  are, in the obvious spherical polar coordinates  $(r, \theta, \phi)$ ,

$$\frac{\partial}{\partial r}\sigma_{rr} + \frac{1}{r}\frac{\partial}{\partial r}\sigma_{r\theta} + \frac{1}{r}\left[2\sigma_{rr} - \sigma_{\theta\theta} - \sigma_{\phi\phi} + \sigma_{r\phi}\cot\theta\right] = F_{r} \tag{4}$$

$$\frac{\partial}{\partial r}\sigma_{r\theta} + \frac{1}{r}\frac{\partial}{\partial \theta}\sigma_{\theta\theta} + \frac{1}{r}\left[3\sigma_{r\theta} + (\sigma_{\theta\theta} - \sigma_{\phi\phi})\cot\theta\right] = F_{\theta}$$
 (5)

In (4) and (5), it has been assumed that the problem is axisymmetric (so that everything is independent of the azimuthal angle  $\phi$  and  $\sigma_{r\phi} = \sigma_{\theta\phi} = 0$ ), while the quantities F, and  $F_{\theta}$  denote the equilibrating forces that must be applied to resist the tonometer pressure.

Although the existence of an Airy stress function for linear elastic problems in rectangular Cartesian or cylindrical polar coordinates is relatively well-known (see, for example [10]), it appears to be much less commonly appreciated that a related "Love stress function" exists for three-dimensional axisymmetric elasticity problems. Briefly, if  $\chi$  is an arbitrary biharmonic function, then the homogeneous forms of (4) and (5) are identically satisfied if

$$u_r = \frac{2(1 - v^2)}{E} \cos \theta \nabla^2 \chi - \left(\frac{1 + v}{E}\right) \frac{\partial}{\partial r} \left(\cos \theta \frac{\partial}{\partial r} - \frac{\sin \theta}{r} \frac{\partial}{\partial \theta}\right) \chi \tag{6}$$

$$\sigma_{rr} = \left( (2 - \nu) \cos \theta \frac{\partial}{\partial r} - \frac{\nu \sin \theta}{r} \frac{\partial}{\partial \theta} \right) \nabla^{2} \chi$$

$$- \frac{\partial^{2}}{\partial r^{2}} \left( \cos \theta \frac{\partial}{\partial r} - \frac{\sin \theta}{r} \frac{\partial}{\partial \theta} \right) \chi$$
(7)

where E and v are Young's modulus and Poisson's ratio respectively and the other displacement  $u_{\theta}$  and the remaining non-zero stresses  $\sigma_{\theta\theta}$ ,  $\sigma_{r\theta}$  and  $\sigma_{\phi\phi}$  are given by similarly horrible expressions to (6) and (7) (for full details, see [9]). The general form of a biharmonic function in spherical polars that we now require is given by

$$\chi(r,\theta) = \sum_{n=0}^{\infty} (A_n r^{-n-1} + B_n r^{-n+1} + C_n r^n + D_n r^{n+2}) P_n(\cos\theta).$$
 (8)

where  $A_n$ ,  $B_n$ ,  $C_n$  and  $D_n$  are arbitrary constants and  $P_n(\cos \theta)$  is the *n*th Legendre polynomial. We now have to decide what boundary conditions must be applied. For simplicity, we shall assume here that on the inner wall of the eye r = b we have

 $\sigma_{rr}(b,\theta) = -p_{at} - p_{IOP}$ ,  $\sigma_{r\theta}(b,\theta) = 0$  (where  $p_{at}$  denotes atmospheric pressure), while on the eye surface r = a we have  $\sigma_{rr}(a,\theta) = -G(\theta)$ ,  $\sigma_{r\theta}(a,\theta) = 0$ , where, for the tonometer problem,

$$G(\theta) = \begin{cases} p_{at} + K & (0 \le \theta < \alpha) \\ p_{at} & (\alpha \le \theta \le \pi) \end{cases}$$

Here  $\alpha$  is the tonometer head half-angle and K is the stress exerted by the tonometer on the eye. It now "only remains" to substitute (8) into the definitions for the stresses, and apply the boundary conditions to determine the unknown coefficients. Needless to say, this proves to be a long job. Use of a symbolic algebra program such as MAPLE simplifies matters greatly, and shows eventually, that, though the equations for  $A_n$ ,  $B_n$ ,  $C_n$  and  $D_n$  are coupled, they can be solved without too much trouble to recover the solution. Figure 4 shows a typical displacement profile of the inner and outer walls of the eye, and it may be shown that for IOPs of up to about 20 mmHg the Imbert-Fick principle is indeed valid, though for higher IOPs it becomes increasingly unreliable.

Of course, one may argue that the wrong problem has been solved Since the tonometer is designed to function by producing the correct degree of applanation, it seems much more logical to specify the normal displacement under the tonometer rather than the stress. It turns out that this mixed boundary value problem is a lot more interesting from a mathematical point of view, and leads to coupled integral equations for the unknown stresses and displacements. These may also be solved, though space does not permit a full explanation of the methods that must be employed.

# The modelling of scleral buckles

Retinal detachment (RD) is a time-critical eye emergency that typically affects about 1 in 10–20 thousand of the population and usually presents in patients aged 40–70. The condition occurs when the retina (the light-sensitive component of the eye) detaches from the choroid. Initial symptoms commonly include a "flashing light" sensation, followed by a shadow in the peripheral vision field. If ignored, this may spread until complete blindness rapidly ensues.

RD was first recognised in the early 18th century by de Saint-Yves, but clinical diagnosis was impossible until the invention of the ophthalmoscope in 1851 The condition still condemned the

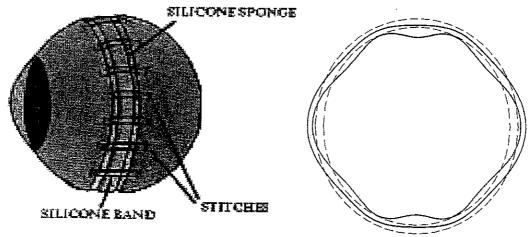


Figure 5: (Left) Scleral buckling of an eye with rhegmatogenous retinal detachment. (Right) Displacements calculated using mathematical model (broken line: undeformed inner and outer eye surfaces)

sufferer to certain blindness until the 1920s when Jules Gonin, MD, pioneered the first successful treatment in Switzerland

The most common modern way to treat RD is by scleral buckling surgery. Under general or local anaesthetic, the surgeon stitches a scleral buckle to the outside of the eye (see figure 5) The operation is normally quick and simple and no overnight hospitalisation is required; the buckle normally remains permanently in place.

The scleral buckle "buckles" the sclera towards the middle of the eye. This decreases the traction on the retina, allowing retinal tears to settle against the wall of the eye, and prevents fluid from entering and worsening the detachment. Simultaneously, the retina may be scarred using cryopexy (extreme cold), laser light (photocoagulation) or heat (diathermy) to hold it in place until it reattaches to the choroid.

Scleral buckling enjoys an 80–90% success rate for rhegmatogenous detachments (i.e. those caused by a retinal hole, break, or tear), but is rarely successful for "traction" detachments caused by the tugging of scar tissue.

Once the mathematical machinery for the tonometry problem of the previous Section has been set up, a number of other medically important problems related to scleral buckles may easily be tackled. For example

- Scleral buckling distorts the shape of the eye what effect does this have upon the focal length?
- How accurate is a Goldmann tonometer when a scleral buckle is present? Should any changes to the Imbert-Fick principle be made?
- One difficulty with buckling surgery is that choroidal detachments may develop one or two days after surgery, and increase in size. Can the seriousness of a choroidal detachment be predicted from the details of the buckling process?

Space constraints preclude all but the briefest discussion of these questions, but it is clear that the focal length of a buckled eye may be determined simply by changing the boundary conditions (3) to

$$G(\theta) = \begin{cases} p_{at} & (0 \le \theta < \pi/2 - \alpha) \\ p_{at} + S & (\pi/2 - \alpha \le \theta \le \pi/2 + \alpha) \\ p_{at} & (\pi/2 + \alpha < \theta \le \pi) \end{cases}$$

where S is the pressure exerted by the scleral buckle. The right-hand diagram of figure (5) shows typical model results for buckling displacement: the model may also be used to relate scleral buckle force to change in focal length.

# The mechanics of retinal detachment

A treatment for RD has been discussed in the previous Section; it is interesting to ask, however, exactly how and why RD happens in the first place. Like cancer, RD has many causes, many cures and its treatment contains many possible pitfalls. One common cause of the condition, however, is the tendency of the vitreous humour near to the centre of the posterior segment of the eye to solidify as a patient ages. This solidification can drag the retina away from the choroid. A small tear forms, mobile vitreous humour flows into the tear from the extremities of the posterior segment and the retina is peeled away from the choroid like a strip of sticky tape being pulled off.

A lubrication theory fluid dynamics model may be constructed to explain the process of RD and subsequent fluid entry In its

simplest form, the displacement h(x, t) of the retina can be shown to satisfy the fourth-order PDE

$$h_t + \frac{\sigma}{\mu} \left( \frac{h^3}{3} h_{xxx} \right)_x = 0 \tag{9}$$

where subscripts denote partial derivatives, t denotes time, x the distance along the choroid, and  $\sigma$  and  $\mu$  denote respectively the "surface tension" of the retina and the dynamic viscosity of the liquid vitreous. Serious mathematical complications immediately present themselves to enable the detachment point to move something sensible must be said about the contact angle. This notoriously difficult matter may be side-stepped by using the engineering correlation known as "Tanner's law" which states that the contact angle  $h_x$  at the detachment point is a (known) power of the speed of the contact point. Unfortunately, it is easy to show that when this condition is imposed, (9) has no solution! A good deal of further technical analysis is required before any conclusions on the causes of RD may be drawn (for fuller details, see [6])

# Up to our eyeballs in problems....

The three years of a standard Ph.D. studentship are nowhere near long enough to investigate the host of theoretical mechanics problems that are associated with eye conditions and functions. Many other interesting modelling problems have recently presented themselves to us including:

- One popular method for repairing RDs involves "spot welding" the retina to the choroid using a small laser The power and duration of the laser pulse that is required to give secure fixing with minimal scarring are well known from experimental studies. If a laser with a much larger beam radius is used, how much power is now required and how is the laser energy distributed in the beam?
- Another popular treatment for RD consists of removing the vitreous humour from the posterior segment (vitrectomy) and replacing it with saline and a gas bubble. The bubble "tamponades" the retina to the choroid until it can reattach itself Increasing numbers of patients fly to the nearest eye unit on commercial flights where the ambient cabin pressure is about 0 8 Atm, but some simple gas dynamics calculations show that if they y home when the gas bubble is still present, a rapid decrease in cabin pressure may cause severe glaucoma. Luckily, a simple ordinary differential equation model may be constructed to predict when air travel is safe.
- How big do blood or pigment particles have to be to block the trabecular meshwork through which the AC drains? (This is a porous medium flow problem: if the particles are too large they cannot enter the meshwork, and if they are too small they will pass through it.) More simply, how does flow through the trabecular meshwork take place? (Pilocarpine, a drug used to lower IOP, forces the ciliary muscles to contract and mechanically stretches the trabecular meshwork, increasing the through flow of aqueous.)
- When a patient's lenses become cloudy (cataracts) they are surgically removed and false lenses made of plastic or silicone are substituted Visually, these function well, but how do they perform mechanically when subjected to high accelerations? (The original form of this question concerned fighter pilots, who may have to use an ejector seat in an emergency)

- How does the tear film rupture in "dry eye" patients? (Dry eye
  is extremely uncomfortable: the reader is challenged to try not
  blinking for 30 seconds.) It turns out that the process involves a
  delicate balance between gravity, surface tension and evaporation. Some two-dimensional asymptotic and numerical calculations (for full details see [1]) give good agreement with
  observed film rupture times, though it is clear that a fully threedimensional study will eventually be required
- When a human cornea is damaged, the cells may regrow in a spiral shape. This is known as "hurricane" or "vortex" keratopathy Why does this happen? Some published studies have suggested that the naturally-occurring potential difference between the front and the back of the eye drives a magnetic field which affects the growth pattern of the iron-doped corneal cells. Although it may easily be shown that the potential difference in question (about 6 mV) is far too small to lead to such effects, hurricane keratosis is still unexplained and awaits the development of a two-dimensional cell transport model to explain it (though see [5]).
- Measurements of the ocular rigidity of the sclera/choroid/ retina portion of the eye (the capsule) have traditionally been expressed in terms of "Friedenwald's law" rather than using the traditional Young's modulus and Poisson's ratio. How is Friedenwald's law related to linear (or possibly nonlinear) elasticity theory?

We have carried out some initial estimates and calculations for most of these problems clearly though there is a great deal of scope for future Postgraduate work.

## **Conclusions**

The human eye is a truly wondrous piece of engineering. A good deal of the science of mathematical medicine involves analysing

the role of a single bodily organ, and as, usual, the more one analyses the eye the more one wonders at the fact that the vast majority of eyes work almost faultlessly for so long and that evolution has provided us with such a cleverly-designed ocular device Though during the course of a Ph.D study we have been able to consider a range of fascinating theoretical mechanics problems, it is evident that much work remains to be done  $\square$ 

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