Research statement

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1 Introduction

Biomechanics is the study of the functioning of biological systems from the mechanical point of view. Mechanics is heavily involved in several body processes, as well as in the generation of many pathological states. Solid and fluid mechanicists have been studying various aspects of the human body for centuries, the most obvious examples being the study of the musculoskeletal system and blood flow in the arteries. Remarkably, mechanics is also intrinsically bound up in the functioning of and in many pathologies of the eye, because the eye is mostly constituted by fluids, which are contained within a solid shell. For this reason biomechanical researchers have progressively been devoting increasing attention to this organ. Relevant examples are works on the mechanics of the cornea, the flow of the aqueous humour, and the pathogenesysis of glaucoma. This interest is witnessed by some recent reviews that have appeard in biomechanics and fluid mechanics journals (Siggers and Ethier, 2012; Braun, 2012; Ethier et al., 2004).

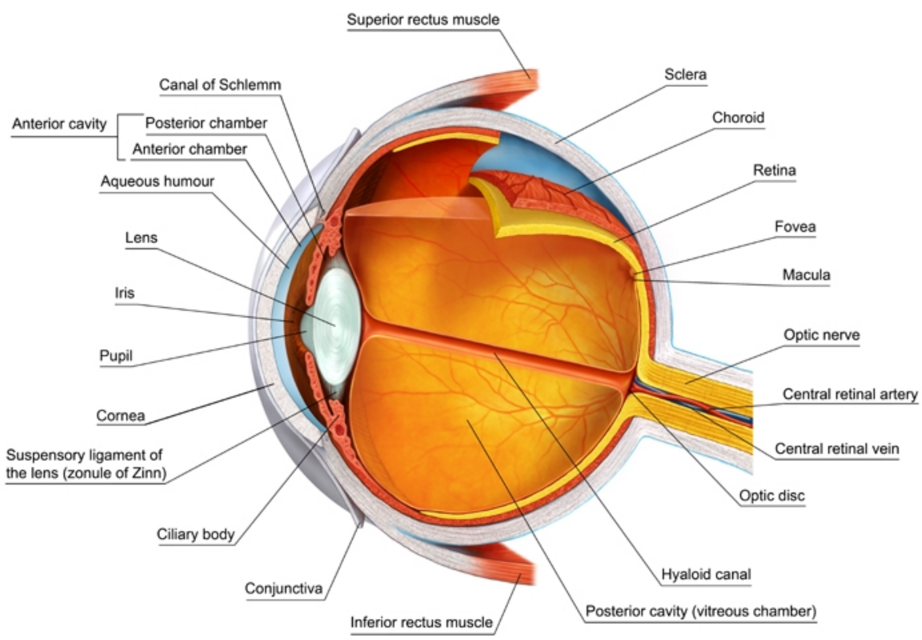

Figure 1: Eye anatomy

The proposed project is focused on fluid mechanic processes occurring in the vitreous chamber. This is the largest chamber of the eye, it is delimited anteriorly by the lens and posteriorly by the retina, the light sensitive layer lining the inner surface of the eye, and it is filled by the vitreous humour. In healthy young subjects, the vitreous is a gel-like material with inhomogeneous viscoelastic properties. With advancing age, vitreous liquefaction commonly occurs, which consists of a disintegration of the gel structure, leading to the formation of liquid gaps in the vitreous body. In various pathological conditions, and in particular to treat retinal detachment (RD), the vitreous is surgically removed from the eye and replaced with tamponade fluids (vitrectomy), typically silicone oils. The vitreous has the important mechanical functions of

- supporting the retina in contact with the outer layers of the eye,
- acting as a diffusion barrier for molecule and heat transport between the anterior and the posterior segments of the eye.

It is well accepted that mechanics plays a fundamental role in the mechanisms leading to RD, which occurs in about 12 out of 100,000 people and is among the most frequent causes of blindness in Western countries. Mechanics is also involved in the success of surgical procedures adopted to treat RD. Finally, mechanics is relevant to predict the efficiency of drug delivery to the retina by intravitreal injections. For these reasons, there are many recent papers on the biomechanics of the vitreous humour. However, our understanding is still limited and non-systematic, providing the motivation for this project. We envisage that the research will provide physically-based, practical indications to clinicians, both to identify risk factors of developing a RD and to optimise surgical interventions for RD treatment. From the mathematical point of view, the study of vitreous motion is a very fascinating problem, which is amenable to analytical treatment, owing to the (almost) spherical shape of the vitreous chamber.

Possible problems of great clinical relevance that can be tackled during the PhD research are listed below.

1. Study of the dynamics of the vitreous humour induced by eye rotations, accounting for the complex and inhomogeneous characteristics of the vitreous. This is important as, during eye rotations, the vitreous exerts stresses on the retina that are known to be the main cause of retinal breaks and eventually retinal detachments.
2. After a surgical procedure called vitrectomy the vitreous is replaced by tamponade fluids. Vitrectomy is one of the main surgical tools to treat retinal detachments. Since the fluids employed are immiscible with water, typically a film of aqueous forms between the retina and the oil. This is likely to affect the mechanical stresses transmitted by the tamponande fluid to the retina. Also, in some circumstances the interface between the tamponade fluid and the aqueous turns out to be unstable and emulsification occurs.

In the next section these two possible research projects are shortly described.

2 Description of the research

2.1 Dynamics of the virteous humour

Understanding the dynamics of the vitreous induced by eye rotations and predicting the stress exerted by the vitreous on the retina is of great practical importance since mechanical stresses on the retina as known to be primarily responsible for the generation of retinal breaks. Theoretical models of vitreous dynamics have been recently developed by Meskauskas et al. (2011, 2012). In these models several aspects were considered:

- motion of a viscoelastic fluid in a sphere;
- eigenvalues and eigenfunctions of the system;
- possibility of resonant excitation of natural frequencies;
- effect of the shape of the vitreous chamber, with particular attention devoted to myopic eye.

The authors found that the vitreous humor within the vitreous chamber has natural frequencies of oscillation that are close to frequencies characteristic of eye rotations. Such frequencies can therefore be resonantly excited by eye movements, possibly leading to very high values of the stress on the retina.

Moreover, the authors found that in myopic eyes, which are typically longer and bigger than normal eyes, the stress level is significantly higher than in emmetropic eyes. This finding provides a feasible explanation for the fact that myopic eyes are at a higher risk of developing of retinal detachment.

In the PhD project the above models can be extended to include inhomogeneity of vitreous viscoelastic properties. In fact, it is known that elastic modulus of the vitreous humor grows towards the wall. In addition to that aging might cause liquefaction. It could be interesting to study how the natural frequencies of the system together with the stress on the retina change according to those properties.

A fully numerical approach can be used. In addition, the problem can be studied analytically through a perturbation approach, by assuming small variations of the mechanical properties of vitreous humor.

2.2 Dynamics of the tamponade fluids in the vitreous chamber

It is known that when the vitreous is replaced by tamponade fluids, which are typically hydrophobic oils, a thin layer of aqueous solution forms between the retina and the oil (at least in some regions). Understanding its effect on the stresses on the retina is of utmost importance to predict the success of the procedure. This problem could be studied both experimentally and theoretically.

There are several problems related to using silicone oils. They are listed below:

- since silicone oils have a lower density then water, this leads to reduced or absent tamponade effect in inferior retinal tears;
- the persistence of silicone oil over long periods leads to life-threatening complications of cataract, glaucoma and keratopathy;
- the emulsification of the oil is possible. There are several factors, that play important role in emulsion formation such as the surface tension, presence of surface-active agents (emulsifiers), viscosity or molecular entanglements.

My work during the MS thesis was related to this problem. We have studied the stability of a stratified fluid over an oscillating flat wall which can be the first step in studying the instability of the oil-water interface and the onset of oil bubble formation. We modeled two layers of different immiscible fluids set in motion by harmonic oscillation of the wall. The upper fluid represents the silicone oil and it is assumed to extend to infinity in the y direction (see fig. 2).

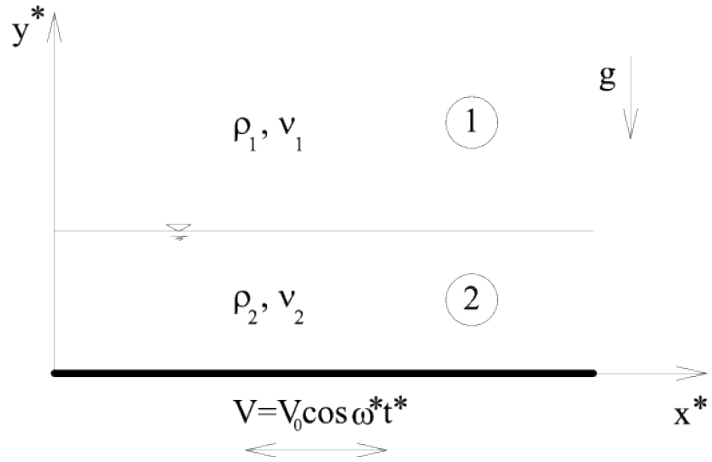

Figure 2: Sketch of the problem

For realistic values of the controlling parameters the frequency of oscillation of the wall is relatively small. This led us to use the quasi-steady approach in order to study the instability of the system.

The eigenvalue problem governing the linear stability of the interface was solved numerically. The results showed us that instability is possible for the certain values of parameters. Also, we concluded that the surface tension has a strong stabilizing effect on short disturbances. The viscosity also slightly influences the stability of the system.

There are several possibilities to the extend this work to make it closer to the real case:

- More realistic geometry; this can be done gradually:
  - including effect of wall curvature;
  - considering a 2D circular model;
  - considering a 3D domain including the effect of gravity.
- Non-modal stability analysis. The motivation for using tools of non-modal analysis is given by the fact that not always the linear stability analysis is in agreement with experimental results. That might happen when the superposition of the decaying modes give rise to a short-term transient growth due to the absence of orthogonality of the eigenfunctions of the system.
- Inclusion of the effect of wall roughness. If the layer of the fluid is very thin then the presence of ripples on the wall might affect greatly stability conditions.

- Use the Floquet theory. This analysis might be applied to the periodic solution where quasi-steady approach cannot be applied;

- Numerical simulations of the fully non-linear equations.

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