A biomechanical model of the cornea to guide refractive interventions

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Abstract — The planning of refractive surgical interventions is a challenging task. Numerical modelling has been proposed as a solution to support surgical intervention and predict visual acuity. We propose a numerical framework to simulate patient-specific intervention based on corneal topography acquired on the patient. A validation study performed on patients who underwent cataract surgery showed that the model was able to predict the level of astigmatism induced by the intervention. We can conclude that the numerical simulation can become a valuable tool to plan corneal incisions in cataract surgery and other ophthalmo-surgical procedures in order to optimize patients' refractive outcome and visual function.

Keywords: opto-mechanical; personalized finite-element analysis; wavefront.

Models of fluid flow in the vitreous chamber and generation of vitreoretinal tractions

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Abstract — The vitreous cavity is filled by the vitreous humour, which is a substance with viscoelastic properties. Understanding the dynamics of vitreous induced by eye rotations is important because the vitreous exerts tractions on the retina that are associated with the occurrence of retinal detachment. In the talk various mathematical and experimental models of generation of vitreoretinal tractions will be presented and discussed. Both the physiological case and various pathological states will be considered, in particular myopia, posterior vitreous detachment and vitreoschisis.

Keywords: vitreoretinal tractions; vitreoschisis; posterior vitreous detachment; myopia.

Towards a full model for ocular biomechanics, fluid dynamics and hemodynamics

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Abstract — This contribution presents an ongoing work to implement a patient-specific mathematical virtual simulator for the eye. The aim is to create a multiscale and multiphysics model for the description of ocular biomechanics, fluid dynamics and hemodynamics. This instrument may serve to illustrate and estimate some clinically relevant parameters and predict their spatial and temporal evolution adopting forward-looking numerical techniques.

Keywords: ocular virtual simulator; hybridisable discontinuous Galerkin method; multiphysics; multiscale.

Nano-structure and mechanical changes in sclera following proteoglycan depletion

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Abstract — The mechanical properties of ocular tissues such as the sclera have a major impact on healthy function of the eye, and are governed by the properties and composition of the microstructural components. For example, biomechanical degradation associated with myopia occurs alongside a reduction of proteoglycans. In this study, the role of proteoglycan degradation on the nano-mechanical properties of the porcine sclera is explored. In vitro enzymatic degradation of proteoglycans was conducted with α-amylase and chondroitinase ABC enzymes. Collagen fibril morphology and nanomechanical stiffness was

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measured with atomic force microscopy (AFM). The elastic modulus of the tissue was reduced in all enzyme treated samples relative to controls. In addition, collagen fibril organisation was disrupted by proteoglycan depletion. Our data demonstrate that proteoglycans play an important role in determining not only the mechanical properties at these length scales but also collagen fibril arrangement.

Keywords: proteoglycan depletion; collagen structure; scleral mechanical properties.

Clinical assessment of intraocular pressure: A whole eye dynamic model

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Abstract — The aim of this work is to provide a quantitative description of how geometrical and material properties of ocular tissues and fluids influence intraocular pressure (IOP).

Keywords: intraocular pressure; glaucoma management; mathematical modelling; sensitivity analysis.

Ultrastructural and nanomechanical changes of the cornea following enzymatic degradation

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Abstract — Understanding of the ultrastructure and nano-mechanical behaviour of the cornea is important for a number of ocular disorders. In this study, atomic force microscopy (AFM) was used to determine nano-scale changes in the porcine cornea following enzymatic degradation. Different concentrations of amylase were used to degrade the cornea. Following enzyme treatment a reduction in nano-stiffness along with a disrupted collagen topography in the stroma was observed. This study highlights the interplay between mechanical properties and collagen organisation in the healthy cornea.

Keywords: corneal biomechanics; amylase; keratoconus.

Multiscale modeling and simulation of neurovascular coupling in the retina

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Abstract — The role of nitric oxide (NO), usually considered as a potent vasodilator, in regulating retinal neurovascular coupling is still elusive. Measurements of flicker light-induced functional hyperemia in humans show that an increase of NO levels reduces vasodilation. This evidence has lead to conjecture that such increase may be responsible for suppressing flickerevoked vasodilation in diabetic retinopathy. In this paper, we propose a mathematical model to theoretically investigate the effect of an increase of neural NO (nNO) on the vasodilation of retinal arterioles. Simulation results indicate that nNO increase may (1) significantly affect vasoconstrictive agent production by glial cells; and (2) elicit vasoconstriction rather than vasodilation in retinal arterioles. Model predictions seem therefore to support the conjecture that NO increase may be responsible for suppressing flicker-evoked vasodilation in diabetic retinopathy.

Keywords: visual neuroscience; mathematical modelling; retinal regulation; retinal disfunction.

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Polarimetric interferometry to objectively evaluate the optical properties of corneal stroma

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Abstract — A new non-invasive method, has been developed to objectively evaluate the optical properties of stroma, based on the interferometric analysis of diffractive and polarizing effects related to the birefringent properties of corneal collagen fibrils. The new method shows a relevant impact on corneal surgeries specifically for lamellar transplantation where, due to the polarizing properties of stroma, the alignment between collagen fibrils of donor cornea with patient collagen fibrils orientation has shown an improvement of visual acuity post op. Further studies on regularity of cornea isogyre pattern are showing a strong impact of this new method on early stage diagnosis of corneal disease.

Keywords: corneal cross; isogyre; melatope; birefringence.

Computational corneal biomechanics in clinic

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Abstract — Corneal topographers and air-puff devices aim at completely characterizing the so-called 'corneal biomechanics', a collection of features that describes the corneal behaviour. The European FP7 project (PopCorn) was born with the goal of integrating both technologies together. Between the novelties, computational models were included as an integral part of the clinical assessment. Automatic patient-specific (P-S) reconstruction of the cornea, alongside material prediction based on finite element simulations, optimization, and fitting were used to strive forward in the a priori surgical planning. Both methodologies show a good performance in retrieving the P-S geometry of the cornea (error < 1%), and the maximum deformation amplitude of a non-contact tonometry (error ~ 5%). Nevertheless, physiological and no-physiological corneas cannot be classified solely in terms of material, at least with a single experiment. Eventually, and due to the interplay of different factors (geometry, material, and pressure), results coming from air-puff devices should be handled with care.

Keywords: non-contact tonometry; corneal biomechanics; patient-specific; material characterization.

Biomechanical evaluation of central and peripheral Descemet membrane endothelial graft

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Abstract — Corneal endothelial transplant is the gold standard treatment in cases of corneal endothelial cellular dysfunction. Preparation, delivery and unfolding of the graft are technically demanding. We assessed the biomechanical behaviour of Descemet membrane to better understand DMEK graft behaviour and to select the right diameter and donor age graft. The biomechanical behaviour was tested using atomic force microscopy on five corneas unsuitable for

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transplantation. Peripheral cornea was found to be stiffer than the centre (respectively, 3171.89 MPa, 2837.20 MPa). Elastic modulus of both centre and periphery of the cornea exhibited a trend to decrease with age. In addition, central cornea becomes stiffer than the periphery in older patients, while the peripheral cornea was stiffer in younger patients. Atomic force microscopy is a suitable technique for evaluating biomechanical behaviour of DMEK grafts. One interpretation of this varied behaviour is that the type and quantity of collagen change with age and with location.

Keywords: cornea transplant; endothelial keratoplasty; atomic force microscopy; biomechanical behaviour.

The effect of serum proteins on dynamic interfacial properties of silicone oils in vitrectomized eyes

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Abstract — The formation and stability of emulsions in vitrectomized eyes is linked to the properties of the silicone oilaqueous humor interface, in particular the surface tension. In the presence of natural surfactants, such as serum and plasma, the value of the surface tension is likely to change, but little quantitative information is presently available. To this end we perform accurate experiments measuring the interfacial properties of silicone oil (Siluron 1000) with an aqueous solution in the presence of endogenous-like proteins. It is found that the surface tension is significantly reduced when physiologically realistic concentrations are used. Moreover, the obtained values of the dilational viscoelastic modulus are compatible with the formation of stable emulsions.

Keywords: vitrectomy; silicone oil; surface tension; emulsion.

A stochastic model of stroma: Interweaving variability and compressed fibril exclusion

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Abstract — Hyperelastic constitutive models of the human stroma accounting for the stochastic architecture of the collagen fibrils and particularly suitable for computational applications are discussed. The material is conceived as a composite where a soft ground matrix is embedded with collagen fibrils characterized by inhomogeneous spatial distributions typical of reinforcing stromal lamellae. A multivariate probability density function of the spatial distribution of the fibril orientation is used in the formulation of the lamellar branching observed on the anterior third of the stroma, selectively excluding the contribution of compressed fibrils. The physical reliability and the computational robustness of the model are enhanced by the adoption of a second order statistics approximation of the average structure tensors typically employed in fiber-reinforced models.

Keywords: hyperelasticity; second order structure tensors; compressive fibril exclusion; lamellar branching.

Mathematical modelling of ocular and cerebral hemo-fluid dynamics: Application to VIIP

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Abstract — This work aims at investigating the interactions between the flow of fluids in the brain and eyes and their potential implications in the development of visual impairment and intracranial pressure (VIIP) syndrome in astronauts. We propose a reduced (0-dimensional) mathematical model of fluid circulation in eyes and brain, which is embedded into a simplified whole-body circulation model. This model allows us to predict fluid redistribution in the upper body vasculature and variation of the intracranial (ICP) and intraocular (IOP) pressures. The model results suggest that, by taking into account some effects of microgravity, it is possible to observe IOP increase, blood flow decrease in the choroid and ciliary body circulation. These findings provide clues on the role that vascular components may play in VIIP pathogenesis, for which astronauts could be screened on earth and in-flight.

Keywords: visual impairment and intracranial pressure syndrome; intracranial pressure; intraocular pressure; blood flow.

A meshfree approach to cornea-aqueous humor interaction during tonometry tests

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Abstract — The dynamic tonometer test (air puff test) is an invivo investigative procedure routinely utilized in ophthalmology to estimate the intraocular pressure (IOP). A rapid localized air jet applied on the anterior surface induces the inward motion of the cornea, which interacts with the aqueous humour - filling the narrow space between cornea and iris - with a strong influence on the dynamics of the cornea. Potentially the test, quick and painless, could be combined with inverse analysis methods to characterize the patient-specific mechanical properties of the human cornea. As a step towards this aim, the present study describes a fluid-structure interaction (FSI) approach based on a simplified geometry to simulate the anterior chamber of the eye undergoing the air puff test. We regard the cornea as a nonlinear elastic and isotropic membrane described through an analytical model and discretize the weakly compressible Newtonian fluid with a meshfree particle approach. Numerical analyses reveal a marked influence of the fluid on the dynamics of the cornea. Additionally, we investigate the possibility to use the dynamics of the test to estimate the intraocular pressure.

Keywords: meshfree methods; particle methods; collocation methods; fluid-solid interaction; fluid-dynamics; air puff test.

Fluid-structure interaction of the non-contact tonometry test

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Abstract — The study of the corneal biomechanics has gain interest for its applications on predicting refractive surgery outcomes and the study of a number of pathologies affecting the cornea. In this regard, non-contact tonometry has become a popular diagnostic tool in ophthalmology, and as an alternative method to characterize corneal biomechanics. Since identification of material parameters using non-contact tonometry tests rely on the inverse finite element method, accurate and reliable simulations are required. In this work we present a full fluid structure simulation of a non-contact tonometry test accounting for the effect of considering the presence of the humours. Results indicate that when inertial effects are considered, not including the humours may lead to overestimating the corneal displacement and therefore to an overestimation of the actual corneal stiffness when using the inverse finite element method.

Keywords: corneal mechanics; fluid structure interaction; non-contact tonometry.

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A mathematical model of fluid transport across the retinal pigment epithelium

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Abstract —We propose a mathematical model of fluid transport across the retinal pigment epithelium (RPE), aimed at understanding the mechanisms that govern the flow. Quantitative description of this flow is relevant, as fluid accumulation in the sub-retinal space is related to several pathological conditions such as, in particular, age related macular degeneration (AMD). Possible mechanisms that drive water flow across the RPE are osmosis and electro-osmosis. We develop a model, which couples electrophysiology and fluid dynamics in the RPE. The model predicts the existence of ion concentration gradients in the cleft gap between adjacent cells and these gradients drive an osmotic flux, which is comparable with the measured water flux across the RPE. We also find that local osmosis is the dominant mechanism for water transport and electro-osmotic flow is subdominant, and this result is robust with change of parameters.

Keywords: retinal pigment epithelium; osmosis; electro-osmosis.

Thermodynamical derivation of a nonlinear poroelastic model describing hemodynamics-mechanics interplay in the Lamina Cribrosa

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Abstract — In this paper we formulate a poroelastic model starting from a model of species diffusion in an elastic material. The governing equations are derived from general thermomechanical principles. We carefully revise the role of the energy-stress Eshelby tensor, mutuated from the framework of tissue growth, in describing the hemo-mechanical behaviour of the tissue. The model accounts for nonlinear deformations of the solid matrix and deformation induced changes in porosity and permeability. The model is applied to study the mechanics of the lamina cribrosa in the eye. This is a porous tissue at the head of the optic nerve. Deformation of this tissue and impairment of blood flow induced by tissue deformation are considered to be related to the pathogenesis of glaucoma.

Keywords: poroelasticity; blood perfusion; species diffusion; large deformations.

Saccadic movement effects on intraocular drug delivery for a wet-AMD clinical case

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Abstract — Nowadays, intravitreal injections are the gold standard for the treatment of age-related macular degeneration (AMD). The prediction of the transport mechanism for the injected anti vascular endothelial growth factor (anti-VEGF) is needed in order to understand its distribution and consumption after each injection. Thus, this study aims at implementing a full model of the vitreous drug delivery. The main novelty of this work is the coupling between an experimental evaluation of the scleral permeability and a numerical analysis of the saccadic dependency of the transport phenomena.

Keywords: computational fluid-dynamics; vitreous drug delivery; saccade; age-related macular degeneration.

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Assessment of the fluid dynamic performance of a vitreous cutter

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Abstract — Vitreous cutters are surgical devices used during vitrectomy to remove the vitreous humour from the eye and replace it with tamponade fluids. Aim of the present work is to assess the performance of a vitreous cutter (the EVA Phacovitrectomy System by DORC) used with different needle sizes and blade shapes. The analysis is based on laboratory measurements of fluid flow performed using the particle image velocimetry technique.

Keywords: vitrectomy; PIV; vitreous cutter.

Effect of an iris-fixated intraocular lens on corneal metabolism: A numerical study

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Abstract — One of the possible risks associated with the implant of iris-fixated intraocular lenses (pIOL) is loss of corneal endothelial cells. We hypothesise that this might be due to alterations in corneal metabolism secondary to the lens implantation. To verify the feasibility of this assumption we propose a mathematical model of the transport and diffusion of metabolic species in the anterior chamber and the cornea, coupled to a model of aqueous flow. Results are obtained both with and without the pIOL in the case of closed eyelids. The results suggest that glucose availability may be significantly reduced at the corneal endothelium. However, it must still be verified whether this finding has a clinical relevance.

Keywords: intraocular lens; aqueous flow; corneal metabolism.

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