Ocular Lens Microcirculation Model, A Web-Based Bioengineering Educational Tool

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Abstract— **Currently a comprehensive computational model of the human body is being developed at the Auckland Bioengineering Institute. As a part of this project, the development of a global model of the human eye - the virtual eye- is also in progress. This multi-scale virtual eye model is being developed to enable a powerful educational tool for students and researchers as well as a novel form of integrative diagnosis or treatment for individuals, based on the clinical data gathered. One of the most important aspects of the ocular tissue is its fluid dynamics which is known to affect the physiological and optical properties of the eye.**

During this project, a 3D finite element model of the fluid dynamics of the ocular lens was designed and executed on our high performance computer. This sophisticated computer model was then linked to a website, in order to elevate it from a local computer model to a global research and educational tool. The presentation of the 3D fluid microcirculation model of the ocular lens over the internet, combined with its user-friendly graphical user interface, has enabled it as a computer model to be used by students and researchers worldwide. Such exposure to the international lens community makes this model a unique debate point in order to obtain a better understanding of the ocular lens homeostasis and its role in the functionality.

Using the 3D microcirculation model to predict the effects of various perturbation conditions on the physiological and optical properties of the lens, could lead to better understanding of lens abnormalities such as cataracts and their causes. This model is particularly seen as a capability platform for the other ocular tissues' fluid dynamic models to be linked into a single virtual eye platform, which is going to be accessible via the internet.

Keywords— **bioengineering, computational modeling, education, ocular lens, microcirculation.**

I. INTRODUCTION

Bioengineering is often defined as the field of research that deals with the application of mathematical, computer and engineering models into physiological sciences. Bioengineering is also considered to be one of the youngest and most thriving fields of science in today's world. Every year new bioengineering curricula are being created around the world. It was estimated that there are about 50 new undergraduate programs in the US alone by 2003 and the numbers have grown exponentially ever-since [1].

One of the principal challenges of bioengineering education has been to create a perfect blend of physiological and engineering sciences, in order to equip its young graduates and researchers with essential tools to tackle the current health-sciences related issues. Such enriched mixture of independent yet related sciences is also needed to be delivered to the current students in a meaningful and conciseness manner, utilizing the modern media. For that reason, web-based education systems are being proposed by many authors from different backgrounds, to be most suitable form of teaching in today's academic environment [2],[3]. Realizing this necessity, here at the Auckland Bioengineering Institute (ABI), new bioengineering models of the human body are being developed hand-in-hand with innovative graphical and web-based methods of delivering the results to the global audiences.

The Physiome Project of ABI is an excellent example of the above approach [4]. This project is a worldwide public domain effort to provide a computational framework for understanding human physiology. It aims to develop integrative models at all levels of biological organization, from genes to the whole organism via gene regulatory networks, protein pathways, integrative cell function, and tissue and whole organ structure/function relations. Various modeling projects are being developed currently at the ABI (http://www.abi.auckland.ac.nz/uoa/home/about/our research/projects) to create the full computer model of the human body, and the virtual eye project is one of them (http://www.abi.auckland.ac.nz/uoa/home/about/our-research/projects/special-sense-organs).

The virtual eye project is an effort to develop an optically and mechanically correct 3D model of the eye, i.e., that can "see" what a person sees. It is intended to be used by scientists and students in the fields of bioengineering, optometry and ophthalmology, for investigating their issues of interest. To create a comprehensive model of the eye, each of its comprising tissues (e.g. lens, cornea, retina …) should be investigated independently and jointly with the rest, based on the existing literature models and experimentally obtained data.

One well-developed example of this kind of integrative modeling within the eye is the work that has been done on the ocular lens microcirculation system [5]. This model draws together a variety of empirical data from a range of experimental approaches and applies physical laws to these

data to infer a detailed integrative model of whole-lens fluid dynamics. The lens microcirculation computer model, as an essential part of the eye's fluid dynamics, has been developed at the ABI to be incorporated in the bigger virtual eye model. This model is now evolved to an educational web-tool for the use of students and researchers, interested in the fluid dynamics of the eye.

II. Materials and methods

For the microcirculation model to be compatible and hence incorporable with the bigger virtual eye model, it had to be developed in similar programing environment. ABI has been developing its in-house sophisticated programming language for computational modeling called CMISS, which stands for Continuum Mechanics, Image analysis, Signal processing and System identification (www.cmiss.org). CMISS is a mathematical modeling environment that allows the application of finite element analysis, boundary element and collocation techniques to a variety of complex bioengineering problems [6]. It consists of a number of modules including a graphical front-end with advanced 3D display and modeling capabilities, and a computational back-end that may be run remotely on powerful workstations or supercomputers. A C/C++ coded graphical user interface (CMGUI) and a Fortran-77 coded computational engine (CM) are being implemented in CMISS; and ASCII and binary files are being utilized to connect the engine and the interface.

The CMISS visualization user interface (CMGU, www.cmiss.org/cmgui) is linked to the FIREFOX web browser and CMISS generated results are displayed in web page format via an ABI-authored FIREFOX extension called ZINC (www.cmiss.org/cmgui/zinc, Stevens et al. 2006). These webpages, not only could then be viewed online by researchers worldwide but also interactions with the models are made possible allowing the users to investigate the models' capabilities even further.

ZINC is being developed for Mozilla platform (www.mozilla.org) based applications such as the web browsers Mozilla and Firefox. The ZINC extension embeds the CMISS environment and exposes a javascript application programming interface (API). Web site developers can use the javascript API to add interactive 3D models and computational abilities to web pages. The Mozilla platform was chosen as the initial target for CMISS because it is supported on all the major operating systems; Linux and most other UNIX platforms, Mac and Microsoft Windows. Mozilla is free and its license, the Mozilla Public License (MPL) ensures public access to the source code.
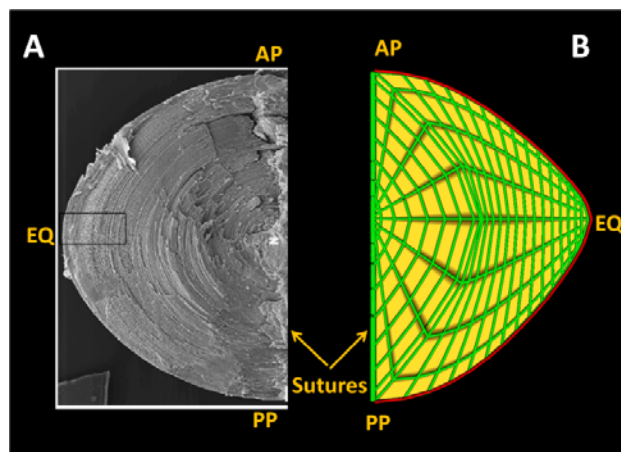

Fig. 1 Comparison of lens fiber cell geometry and its finite element mesh representation. A: Mouse ocular lens structure imaged with electron microscopy, reproduced from [7]. B: 2D projection of the half of finite element mesh generates using CMISS and visualized using CMGUI with the curved internal cuboid elements are outlines in green. The outer surface of the lens, colored in red, is where the computational boundary conditions are applied to the mesh. The points of reference are labeled (AP) anterior pole, (PP) posterior pole and (EQ) equator

Utilizing the above listed programming platforms, the 3D microcirculation model was implemented using common steps of computational models implementation. It started by creating a finite element mesh of the ocular lens, using suitable cuboid elements, on which future computations would be performed [Fig. 1].

During the subsequent phase, equations governing the fluid dynamics of the ocular lens, mostly derived by [8],[9], were implemented in the programming platforms. The next stage involved the setting of the initial boundary conditions on the generated mesh and then solving the created system using computational solvers. The convergence criterion was constantly controlled and when met, the calculated parameters were exported for the post processing and visualization of the results to be performed. The basic steps towards creation of a finite element model are profoundly covered by [10].

Computed fields from the text format files created in CMISS were imported into CMGUI. However, since CMISS and CMGUI are local to ABI, installing and learning them by external researchers to view the computational models' results was considered to be unfeasible. Hence, CMGUI has been recently embedded directly into web-based applications, through the ZINC extension developed for the Mozilla Platform web-browsers.
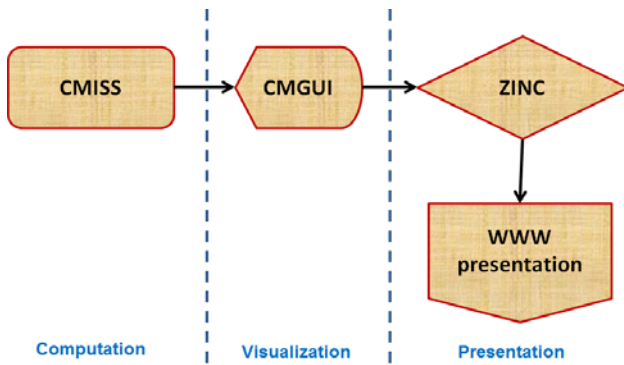
Fig. 2 Relationships among the programming platforms used in this project, and the steps towards making the model available online

The developed 3D microcirculation model is based on three programming bases to solve (CMISS), display (CMGUI) and convert the graphical end to web-format (ZINC). [Fig. 2] illustrates the incorporation of the developed microcirculation model in webpage format.

III. RESULTS

The microcirculation model is solved on a range of 'natural' and 'unnatural' boundary conditions extracted from the literature [9], listed in the table below [Table 1]. 'Unnatural' boundary conditions (e.g. lower temperatures) have been used in this model in order to mimic the perturbation experiments. It should be noted that due to the large size of the graphical presentation files, it was not practical to solve the model for all the perturbation points. For example to mimic the low temperature conditions, the model has been solved at 37, 27,17 and 7 degrees and then ZINC has interpolated the calculated fields for all the in-between temperature value points (e.g. 8, 9, etc.). These interpolations are implemented in a linear fashion such as if 10% drop in a certain field's values is caused by a 10% fall in temperature, then 5% decline of the temperature is modeled to lead to 5% decrease of the calculated field values.

In this model, the concentration of important ions for the lens microcirculation (i.e. sodium, potassium and chloride) alongside with electric potentials, hydraulic pressures, fluid velocity and fluxes, current densities and trans-membrane osomolarities are estimated under the normal and perturbed conditions. All these fields are passed on to the model's webpage and are illustrated on the graphical meshes upon request. The following figure [Fig. 3] is a snapshot of the webpage of the model.

The 3D microcirculation model is available online at (http://sitesdev.bioeng.auckland.ac.nz/evag002) and the readers are encouraged to view and use it.

Its predicting results are very well matched by those experimentally obtained and published in the literature. The

model can predict the fluid dynamics of the lens under wide range of the perturbation conditions, some still uninvestigated empirically. This data extrapolating capability of the model is valuable to all the researchers interested in this field and is deemed reliable since the model mimics the already obtained experimental data.

Table 1 Initial conditions at outer lens boundary for the present model, at normal and perturbed settings

Parameter	Value	Units
Extracellular sodium concentration	10-110	mM
Extracellular potassium concentration	8-108	mM
Extracellular chloride concentration	115	mM
Intracellular sodium concentration	7	mM
Intracellular potassium concentration	100	mM
Intracellular chloride concentration	10	mM
Temperature	280-310	K

IV. CONCLUSIONS

During this project, a 3D model of fluid dynamics of the ocular lens was designed and executed on ABI's high performance computer (HPC). The results of this research were found to be in agreement with the predictions of the previous models of the microcirculation [8],[9],[11].

The presentation of the 3D microcirculation model over the internet, combined with its comprehensible graphical user interface (GUI), gives it a unique capability as a computer model to be used by researchers globally. This exposure to the international lens community makes this model a unique tool in acquiring a better understanding of the ocular lens and its fluid dynamics. Using the 3D model to predict results of different changes in the lens could lead to better understanding of lens abnormalities such as cataracts and their causes. For example lack of antioxidant delivery to the center of the lens, caused by weakened microcirculation system and reduced fluxes inside the lens, which is hypothesized to be the major cause of age-related cataracts, can be modeled and studied with the current model and in the human lens in the future.

In summary, the current 3D model of the mouse lens is a first step towards implantation of human lens models and prediction and investigation of lens pathologies. The ultimate goal of modeling the fluid dynamics in the ocular lens is to create a comprehensive computational model of the fluid dynamics of the human eye. Such system linked with the models from the rest of the body (e.g. blood pressure and sugar level models) can lead to an extensive model of the human body, which can be used by students and scientist to investigate the links between these phenomena and eye pathologies such as cataracts.
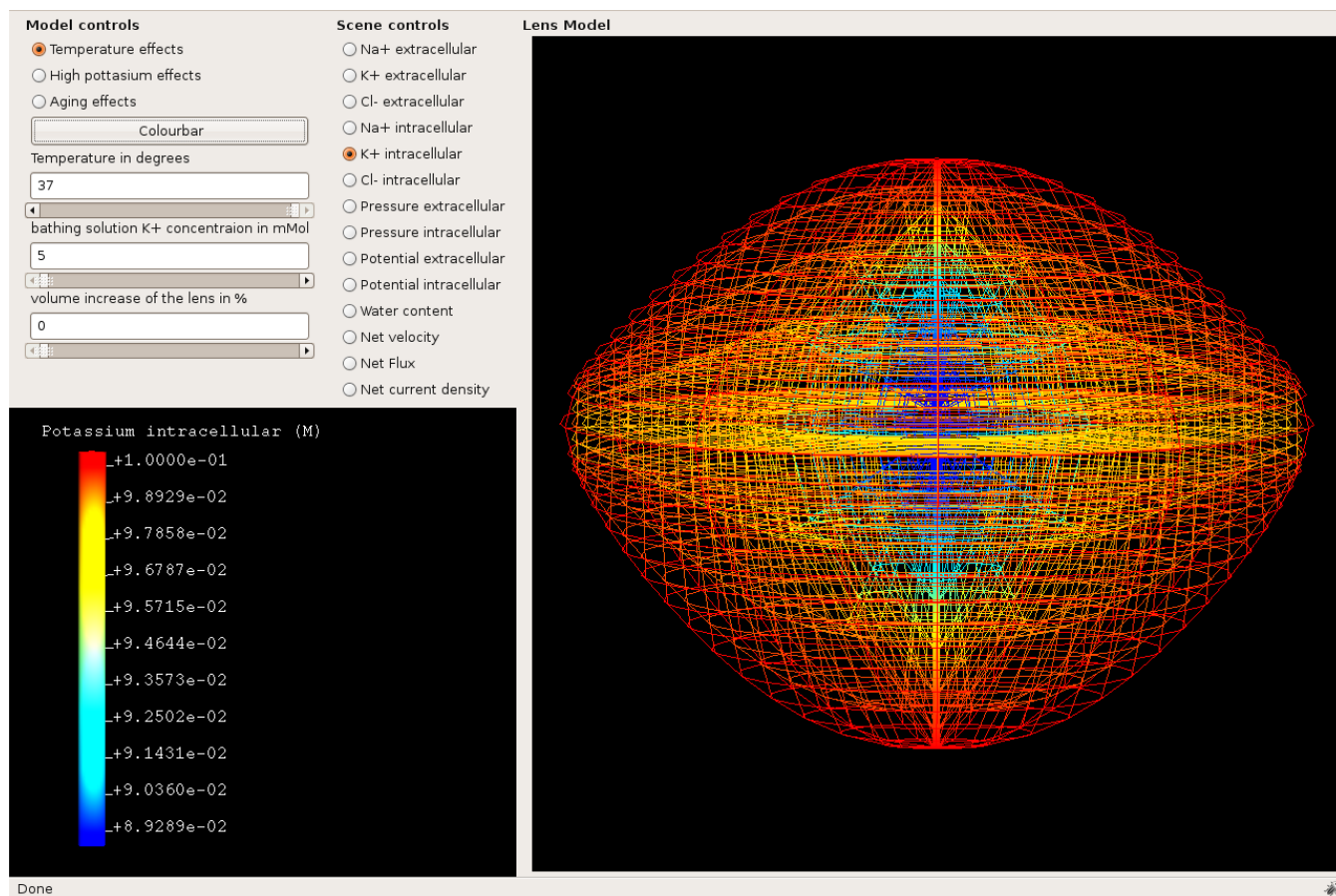
F<small>IG</small>. 3 Screenshot of the 3D lens microcirculation system presentation in webpage format using the FIREFOX web browser. The model controls are in upper left part, the main screen displaying the lens at right and the color-bar associated with the visualized data and its labels is located lower left of the image

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R<small>EFERENCES</small>

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