Modeling the eye as a window on the body

organized by
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Workshop Summary

Overview

Alterations in vascular and structural functions, due to aging or systemic diseases, often emerge in the eye as well as in different organs in the body. The eye is a unique organ where vascular and structural changes can be visualized and measured non-invasively in vivo.

This workshop brought together researchers from different fields, such as mathematics, statistics, medicine and biomedical engineering, to exchange ideas on the potential of using mathematical models of the eye to:

- get insights on the effects of aging and systemic pathologies, such as hypertension and diabetes, on the ocular tissue and functionality;
- achieve a better understanding of the processes that regulate the level of intraocular pressure (pressure inside the eye) and oxygenation in the retinal tissue.

The goals of the workshop were to assess the current state of ocular research and to pursue multiple directions for future research and collaboration.

We had participants from Universities in the United States, Great Britain, Italy and France. The mornings on each of the five days of the workshop had two lectures. On Monday afternoon an open session with all the participants was held in order to generate a list of open problems. In the afternoons of Tuesday to Friday participants broke up into groups of 2-6 people to discuss some of these open problems.

Summary of talks

The morning lectures aimed to discuss the current state of the art and open problems from various points of view: clinical, mathematical, statistical or engineering. On the first day, Giovanna Guidoboni and Simone Cassani discussed the state of the art of modeling in ophthalmology from theory to applications; Carlo Bruttini gave a review on the relationship between the eye and vascular systemic diseases from a clinical perspective. On Tuesday, Anita Layton presented mathematical models of kidney physiology and pathophysiology in relation to kidney-targeting dugs for diabetes; Giovanni Ometto presented recent work on image processing of retinal microaneurisms in diabetic retinopathy. On Wednesday, Umar Quareshi presented reduced-order models for vascular networks, with applications to the pulmonary circulatory systems; Yuan Wang gave a review on statistical analysis techniques to study tree-structured data. On Thursday, Andrea Arnold gave a review on the Bayesian approach in parameter estimation using filtering and data; Lorenzo Sala presented recent work on connecting the eye to the brain and on developing a virtual ocular simulator. On Friday, Lucia Carichino gave a talk on coupling vascular and structural dynamics in the

eye; Giovanni Montesano presented recent work on retinal imaging using optical coherence tomography angiography.

Afternoon problem sessions

A total of 8 problems were selected after the open discussion on the first day of the workshop, and participants later chose to take part in one of these groups. The groups were organized in such a way that each of them contained at least one expert in medicine. Two groups stayed the same for the entire duration of the workshop; additional groups were created on Wednesday afternoon and continued working together for the rest of the week.

- One group worked on studying how aging influences the eye. After a general discussion on all vascular and structural effects of aging, the group decided to focus on modeling neovascularization in wet age-related macular degeneration (AMD). AMD neovascularization is responsible for severe vision loss, and modeling this phenomenon involves sophisticate and interesting multiphase and multiscale modeling techniques. By the end of the workshop, the group developed a preliminary reduced-order model that includes the effect of anti-VEGF (anti vascular endothelial growth factor) treatments on the neovascularization growth. The participants agreed to follow up on this project and plan to use the model in synergy with clinical images/data provided by some of the group participants.
- Aqueous humor, the fluid filling the anterior and posterior chamber of the eye, has a lot of important functions, among which the regulation of intraocular pressure. Elevated intraocular pressure is a well-established risk factor for glaucoma and irreversible blindness. Aqueous humor production involves a filtration process from the fenestrated capillaries of the ciliary body into the anterior chamber. This process is very similar to the kidney nephron glomerulal filtration. One group decided to work on developing a compartmental model of aqueous humor production, inspired by previous models of kidney, that will accounts for the effect of the different ion channels and of different ocular medicine/drops on the intraocular pressure.
- Color Doppler imaging is a common imaging technique used to assess the blood flow velocities in several vessels in the body. Specifically in the eye, blood flow velocities are assessed in the retrobulbar vessels (ophthalmic artery, central retinal artery, posterior ciliary arteries) and the participants shared their knowledge about the hemodynamic changes in glaucoma. One of the participants then presented the results from his work evaluating the blood velocities in the pulmonary system of patients affected by pulmonary hypertension. Since both hypertension and glaucoma are two forms of disease related with age, the group then discussed the potential similarities between the ocular and pulmonary system. Finally, the group decided to create a collaboration in the future aiming to integrate the knowledge of the different participants in the pulmonary and retinal systems to investigate the effect of age on the blood flow velocities in the retrobulbar vessels. For this specific aim that will be developed in the next months, data previously collected from retrobulbar vessels of healthy individual of different ages will be used.
- It has been reported in the clinical literature that retinal oxygen consumption is greater in dark than light in healthy humans. One of the groups worked on using mathematical model in order to characterize possible mechanism responsible for the

differences in oxygenation. The group worked on modifying earlier developed numerical model of retinal oxygenation to account for oxygen consumption changes in light or dark environments. The model contains six levels of retinal tissue with capillaries arranged in two layers and includes oxygen transport due to concentration differences between blood and tissue. The group was working on quantifying blood flow required to achieve the oxygen concentration levels reported in the clinical literature. While the group was unable to provide rigorous explanations of the reasons to oxygenation differences, a couple of hypotheses were proposed which will be worked on in the oncoming months.

- One group worked on early imaging related warnings and diabetes progression. The group participants analyzed first of all the current imaging techniques used to evaluate the vascular lesions of diabetic retinopathy, such as fluorescein angiography and optical coherence tomography. Given the expertise of one the participants in color Doppler imaging, he proposed to discuss about its possible application for the diabetic retinopathy. The use of color Doppler imaging for the evaluation of the retrobulbar vessels has been exploited in glaucoma, but its potential application in the field of diabetes has not been extensively investigated. The group therefore further discussed the potential use of color Doppler imaging derived parameters, such as the waveform parameters in the ophthalmic artery, central retinal artery and posterior ciliary arteries, for the assessment of the diabetes progression. They therefore planned to follow up in the next months in order to plan a study using this specific technique to assess the blood flow velocities in diabetic patients, analyzing specifically the waveform parameters of retrobulbar vessels of patients with diabetes over a long period of time, in order to define its potential clinical application for the assessment of the disease progression.

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