

# MATHEMATICAL MODELING OF RETINAL CIRCULATION: FUNDAMENTAL MECHANISMS AND IMPACT ON RETINAL DISEASES

Francesca Malgaroli<sup>1</sup>, Paola Causin<sup>2</sup>, Giovanna Guidoboni<sup>3,4</sup>, Riccardo Sacco<sup>1</sup>  
and Alon Harris<sup>4</sup>

<sup>1</sup> Politecnico of Milano, piazza Leonardo da Vinci 32, 20133 Milano, Italy,  
francesca.malgaroli@polimi.it

<sup>2</sup> University of Milano, via Saldini 50, 20133 Milano, Italy

<sup>3</sup> Indiana University–Purdue University at Indianapolis, IN, USA

<sup>4</sup> Indiana University School of Medicine, Indianapolis, IN, USA.

**Key words:** *Ocular Microcirculation, Oxygen Transport and Delivery, Vessel Autoregulation, Tissue Perfusion*

Ocular circulation is a delicate mechanism, charged to maintain the homeostasis of retinal function in response to physiological stimuli. It is crucial to understand the processes underlying the regulation of ocular circulation, their impairment being at the origin of severe retinal disorders[1], affecting millions of people worldwide. In particular, several retinopathies have been associated with alterations in oxygen ( $O_2$ ) tension in the retinal ganglion cells ( $O_2$ -RGC) and in the  $O_2$  tension difference across the walls of retinal arterioles ( $O_2$ -wall). Many factors influence  $O_2$ -RGC and  $O_2$ -wall, including blood pressure  $O_2$  tension upstream of the arterioles, haematocrit and plasma viscosity. Current imaging techniques lack the ability to measure  $O_2$ -RGC and  $O_2$ -wall in vivo in humans at multiple sites, simultaneously. Here, as envisioned in [2], we use a mathematical model to estimate, quantify and compare the influence of parametric changes in blood pressure, blood plasma viscosity and oxygen inlet tension on the levels of  $O_2$ -RGC and  $O_2$ -wall, which are nonlinearly related quantities. The retinal vasculature is modeled as a three-layered structure: arterioles and venules (described as fractal trees) lie in the superficial layer proximal to the vitreous; capillaries lie in the intermediate and deep layers. The retinal tissue is modeled as an eight-layered structure, with different metabolic demands in each layer. Blood flow is approximated using a generalization of Poiseuille's law in each vascular segment, where blood viscosity is assumed to change with haematocrit and blood viscosity. Oxygen transport, diffusion and consumption, as well as the interaction between them, are modeled along the vasculature, across the arteriolar walls and through the retinal tissue layers using different mathematical models of reduced hierarchical complexity. Autoregulation mechanisms occurring in the arterioles, which are known to play a relevant role in retinal microcirculation [3], are included as well in the model in order to get insights into these

complex phenomena. The model predicts that  $O_2$ -RGC is very sensitive to the individual patients conditions. In particular, elevated haematocrit and blood viscosity noticeably reduce  $O_2$ -RGC, and this might help explaining why these conditions are considered risk factors for ocular diseases. The model also predicts that  $O_2$ -wall is particularly sensitive to inlet oxygen tension but not to the other parameters. It would be interesting to test this concept experimentally, since  $O_2$ -wall has been suggested as an important factor in retinal blood flow autoregulation.

## REFERENCES

- [1] Bonomi L, Marchini G, Marraffa M, et al., Vascular risk factors for primary open angle glaucoma: the Egna-Neumarkt Study. *Ophthalmology*, **107**, 1287–1293, 2000.
- [2] Harris A, Guidoboni G, Arciero JC, et al. Ocular hemodynamics and glaucoma: the role of mathematical modeling. *Eur. J. Ophthalmol.*, **23**(2), 136–146, 2013.
- [3] Arciero J, Harris A, Siesky B, et al. Theoretical analysis of vascular regulatory mechanisms contributing to retinal blood flow autoregulation. *Invest. Ophthalmol. Vis. Sci.* **54**(8), 5584–93, 2013.