

**Project title:** Analysis of cell network rewiring in the aging human outer retina

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**Background:** Visual processing starts in the outer retina (OR), where photoreceptor (PR) cells sense photons that trigger electrical responses. Retinal pigment epithelial (RPE) cells are located external to the photoreceptor layer and have critical functions in supporting cell and tissue homeostasis and thus sustaining a healthy retina. The visual system is highly energy demanding. It is suggested that with progressive ageing or in the context of risk factors that promote age-related blinding diseases, RPE cells are increasingly unable to execute all tasks at an optimum level. Therefore, RPE cells may compromise their own vital functions and/or stop supporting the PR cells, which either way ultimately results in PR cell death and vision loss. It remains enigmatic how RPE cells integrate and prioritize different interlinked processes, and the associated energy demands of the whole (OR and choroid) system.

**The PhD project will address the following questions:**

- How is available energy distributed along energy-demanding (repair) processes?
- Are there specific networks, processes, and energy properties common to larger groups of individuals/patients?
- Can we identify targets for network- and energy-centric steering that are likely to shift energy priorities in the OR towards restoration (if applicable, in personalized approach)?

**The approach** is to construct computational network models in RPE and PR cells that focus on key cellular energy supply and consumption processes. The mechanistic models will be constrained by the incorporation of gene (and protein) expression levels based on bulk data and individuals from different age-groups. Additionally, we will model anatomical changes during aging and how this causes cell networks to rewire. The generated models will be exploited to predict how alterations of networks and associated energy-requiring processes steer the systems towards favouring homeostasis and restoration processes.

**Techniques:** Computational methods to ODE-based model building and analysis (e.g. Matlab, Python); translate cell and tissue processes from publications into computer-readable language and rules; protein-protein-interaction network analyses (network representation using Cytoscape and Cell Designer); bioinformatics databases; statistical analysis of gene and protein expression data in single cells and bulk/ tissue samples (R programming language).

