Master 2 Internship

Studying the impact on vision of silencing cells in the retina

Context. The process of vision begins in the retina. This thin neural tissue, located at the back of the eye, is able to convert light from different parts of the visual scene into a «code » sent to the brain. This code is composed of electrical impulses (« spikes ») emitted by specific cells in the retina, the retinal ganglion cells (RGCs). A human retina contains ~1 million RGCs (45,000 in mouse) and each of these cells sends information (shape, motion, color, ...) from its immediate surrounding about the visual scene. Therefore, the brain receives, via the optic nerve, a stream of spikes emitted by one million of parallel channels, each conveying a piece of information about our external world. Amazingly, the brain can recreate images from interpreting these highly compressed “barcodes” or trains of spikes. This ability is partly due to the astonishing functional diversity of RGCs, each interpreting a different feature of the visual scene. It is all these parallel streams of information that impart the complexity of visual scenes to our brain visual areas. How precisely this complexity is encoded in the spike trains produced by the population of RGCs is, however, largely unknown. Adding to the complexity even further, RGCs interact with each other during the encoding of complex visual scenes.

Project. At present, over 30 RGC subtypes have been identified, typically on the basis of common anatomical features or basic functions (e.g. sensitivity to motion, orientation, motion direction, …). A natural question is how is vision impaired if one of these cell types is inactivated ? Interestingly, a new technology (DREADD technology) allows to address this question as it affords to acutely and reversibly manipulate the excitability of specific RGC subtypes (e.g. switch them on and off) during visual tasks, in behaving animals. Therefore, presenting the same visual stimulus, when cells from a given population are either active or inactive will not only help identify and characterize these cells amongst the entire RGC population, but it will also shed light about their role in population encoding of complex visual scenes. Also, as RGCs talk to each other while encoding complex images, turning off one population should affect the activity of the remaining RGCs in a measurable way.

The project "*A novel approach to functional classification of retinal ganglion cells*" (2017-2020), funded by the Leverhulme Trust, involving the Institute of Neuroscience (Newcastle, England), and the Biovision team (INRIA Sophia Antipolis, France) intends to explore this research question working on the mouse retina. It is at the interface between experimental neurosciences and modelling. The Biovision team (https://team.inria.fr/biovision/) is in charge of mathematically analyzing the effects of silencing sub-populations of RGCs on the retina’s response to visual stimuli and to propose a simulation platform allowing to reproduce experimental findings and to anticipate new effects. This is the subject of a Master 2 + PhD thesis (PhD funded for 3 years by the Leverhulme Trust).

For the Master 2 phase of the project, the goal is to use and update the Inria software VirtualRetina [2] and Enas [3] so as to reproduce, in simulations, the effect of silencing populations of cells when simple stimuli are presented.

The progression is organized in steps:

1) From experiments performed in Newcastle, the student will identify new specific RGC subclasses involved in the retinal response to various light stimuli and will compute their response to light.
2) Fit the response of each of these cell types with a spatio-temporal function and use it to mimic them in the retina simulator VirtualRetina designed by the Biovision team (http://www-sop.inria.fr/neuromathcomp/public/software/virtualretina/).
3) Design an effective lateral connectivity between these cells (inter- and intra-class) in the Virtual Retina so as to emulate their interactions. Wiring will be inspired from physiology and synaptic weights will be learned using a method developed by our group in the Renvision european project https://www.renvision-fp7.eu/.
4) After these steps we will have a retina stimulator mimicking the experimental setup, where some cells types can be easily switched on and off. We will then try and reproduce the effects of switching of cells in experiments for simple stimuli (full field, white noise, gratings). We will then quantitatively compare the spike trains produced by the simulator to those observed in experiments using the Enas tools (https://enas.inria.fr/)

This Master will be followed by a PhD funded by the Leverhulme Trust, conditional upon satisfactory performance during the initial Master phase. The internship will be done at Inria Sophia Antipolis under the supervision of B. Cessac, in close collaboration with E. Sernagor (Newcastle), from March 1st to August 30th 2017, including several visits to Newcastle.

Profile. We seek a student with strong skills in computer science (C++, makefile, QT), good skills in mathematics and having a strong interest in biology and neuroscience.

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References

[1] Portelli G, Barrett JM, Hilgen G, Masquelier T, Maccione A, Di Marco S, Berdondini L, Kornprobst P, Sernagor E (2016) Rank Order Coding: a Retinal Information Decoding Strategy Revealed by Large-Scale Multielectrode Array Retinal Recordings. eNeuro 3(3). [2] A. Wohrer and P. Kornprobst , Virtual Retina: a biological retina model and simulator, with contrast gain control. Journal of Computational Neuroscience Volume 26:2, pp. 219-249, 2009
[3] ENAS: A new software for spike train analysis and simulation Bruno Cessac, Pierre Kornprobst, S Kraria, H Nasser, Daniela Pamplona, Geoffrey Portelli, T Viéville [Research Report] RR-8958, Inria Sophia Antipolis; Inria Bordeaux Sud-Ouest. 2016