Principal Supervisor: Professor Rodrigo Quian Quiroga, Centre for Systems Neuroscience

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PhD project title: **Representation of concepts in the mouse hippocampus**

University of Registration: University of Leicester

**Project outline**

1. Project outline describing the scientific rationale of the project

Aristotle argued that human thoughts are based upon internal representations of the external world. Today this view constitutes one of the most basic principles of brain function. In fact, the brain extracts meaning from relatively limited sensory information, as we perceive the face of a particular person, rather than a combination of pixels and the particular features that compose it. But how does the brain create representations? More specifically, how do neurons encode specific concepts despite variable and disparate sensory inputs?

The PI has published strong evidence of conceptual representation in the human brain: neurons in the hippocampus are highly selective and invariant for specific concepts e.g. a neuron fired to different pictures of Jennifer Aniston but not to other people, places or objects. These so-called Concept Cells were found in experiments performed in patients with epilepsy implanted with intracranial electrodes for clinical reasons. While this clinical setup uniquely offers direct single neuron activity recording in awake and behaving humans, it has limitations: invasive single neuron recordings in humans are rare, the number and location of electrodes is determined by clinical and ethical criteria, and the time for performing experiments is limited.

**Our aim is to develop an animal model to study concept representations in the mouse hippocampus.** The advantages of such a model are: i) studying concept representations at different stages to understand the mechanisms involved in their formation, stability and plasticity; ii) using 2-photon imaging recordings, thus assessing the activity of large neural populations. Furthermore, within the context of our studies of concept representation in humans, this animal model will contribute to comparisons across species and, eventually, assess neural underpinnings of different cognitive abilities.

This project departs from the ‘dogma’ of spatial navigation in the rodent hippocampus since the ground-breaking discovery of "Place Cells" in the 1970’s. Our working hypothesis is that the function of the rodent hippocampus goes beyond spatial navigation – and is indeed an ideal system to study concept representations. The rationale for targeting the rodent hippocampus is based on: i) the finding of Concept Cells in this area in humans and the possibility to compare across species; ii) the fact that information from different sensory areas converges on the hippocampus in both humans and rodents, making it an ideal candidate for an abstract, concept representation; and iii) the increasing view that, as in humans, the rodent hippocampus is more generally involved in memory functions and that spatial locations are behaviourally relevant concepts in rodents, given the importance of navigation for survival.

We will study concept representations in the mouse hippocampus while the animals learn to discriminate between different versions of stereotyped objects (e.g. cubes, spheres), which are our proxy of concepts. For this we will perform 2-photon imaging recordings in head-fixed animals as they navigate a virtual reality environment (fully
functional in the PI’s lab) and learn to discriminate between the objects presented at random locations – animals will learn to approach some objects (rewarded) and avoid others. Neuronal recordings will be done with injected Ca\(^{2+}\) indicators for 2-photon optical imaging. Similar to the characterisation of Concept Cells in humans, we will evaluate the degree of selectivity and invariance for responsive neurons – i.e. to how many concepts and variants of the same object they respond to.

This study will provide training in in vivo electrophysiology and calcium imaging, using multiphoton methods in living animals. It will also provide the student with insights into the broader philosophy of how to study cognitive neuroscience and the successful student will join a team in which these techniques are already established at Leicester.

**Relevant BBSRC Strategic Research Priority:**
World Class Underpinning Bioscience

**Techniques that will be undertaken during the project.**

- Virtual-Reality setup for mice
- Behavioural studies in mice
- 2-photon imaging recordings

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