**PhD PROPOSAL FOR THE**

**PASTEUR - PARIS UNIVERSITY INTERNATIONAL DOCTORAL PROGRAM**

Time for applicants to contact host laboratories: September 13 – November 2, 2017

Deadline for full application: November 13, 2017

Interviews: January 30, February 2, 2018

Start of the Ph.D.: October 1, 2018

**Title of the PhD project:** Two-photon Imaging of large-scale functional connectivity during multimodal sensory integration

**Keywords:** Two-photon imaging, multi-sensory integration, behaviour, neocortex

**Department:** Neuroscience

**Name of the lab:** Neural circuit dynamics and decision making

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**Doctoral school affiliation and University:**

ED3C, Université Pierre et Marie Curie

Presentation of the laboratory and its research topics:

How sensory information is processed and how it is modulated by other brain areas is a key question in systems neuroscience and focus of the research in my laboratory. The long-term goal of our research is to understand how neuronal networks in different parts of the brain interact during perception and which neuronal codes are used for these interactions. Using two-photon imaging, holography, multi electrode recordings, optogenetics, intracellular patch-clamp recordings and psychophysics, we are investigating how cortical and subcortical microcircuits interact in order to produce a behavioral output. To address these questions, we have been working on the sensorimotor system of the rodent neocortex, exploring how the population of primary somatosensory cortex neurons (barrel cortex) processes information while rodents receive tactile input to their whiskers. Furthermore, we have been working on the refinement of behavioural head-fixed paradigms (Mayrhofer et al., 2013) and the development of electrophysiological and optical methods to visualize and manipulate cortical neural activity. Tackled by the question how neuronal responses in somatosensory cortex can serve the animal to perform sensory discriminations within a short sampling interval, we are using a complex two-alternative forced choice discrimination paradigm which enables simultaneous two-photon calcium imaging of large neuronal populations and optogenetic interventions while the psychophysical performance of the animal is assessed (Musall et al., 2014; Mayrhofer et al., 2013). The use of two-photon calcium imaging aims at significantly increasing the number of neurons that can be sampled simultaneously, thereby unravelling the population code that these neurons may use to make a decision and how these neuronal network patterns change during learning. We are investigating neuronal activity at different time scales taking advantage of the very high temporal resolution of electrophysiological recordings and optogenetic stimulation and the possibility to track neuronal activity over several months using functional two-photon imaging (Margolis et al., 2012; Margolis et al. 2014). So far little is known about the contribution of different subsets of neurons to the network dynamics (e.g. cell types, cortical layers, cortical areas and inter-area connectivity) and how they contribute to the perception of the animal that can be measured using psychophysics. Specific labelling of different neuronal cell types and cortical as well as thalamocortical projection patterns using molecular tools and the possibility to specifically stimulate or inhibit neuronal activity using optogenetics allow us to identify behaviourally relevant neocortical computations.

Description of the project:

*(1 page, Arial font size 11: 600 words in total with at least 50% dedicated specifically to the proposed PhD project(s))*

To perceive and process the surrounding environment, our brain must integrate signals from multiple senses, as well as those arising from self-generated actions. However, research on sensory processing has mainly focused on individual modalities creating visual, auditory, olfactory or somatosensory research fields. Yet, it is known that multisensory information is combined in order to improve sensory discrimination both in humans and in rodents. The difficulty in studying multisensory perception and integration in the brain lies in the wide-spread computation of the complex information by different cortical and sub-cortical areas. Each sensory modality is processed in its unique sensory cortex and then fused at higher cortical stages. Simultaneous measurements of neuronal responses to different sensory stimuli, therefore, require large-scale recordings simultaneously in multiple cortical areas whereby still providing cellular resolution. The PhD project will involve novel two-photon imaging and optogenetic methods to overcome these technical obstacles to study multimodal sensory integration in the behaving animal. The host lab is routinely using several technical advances to record neuronal activity in large volumes at cellular resolution. This further allows cortex-wide and inter-hemispheric imaging of the information flow from sensory to higher cortical areas during multisensory discrimination tasks. The major aim is to unveil how multisensory information is integrated across different functionally connected cortical areas and how this information leads to a decision. This project will be divided into two parallel aims:

First, sensory discrimination in a multimodal virtual reality. Rodents have to run on a treadmill where a rotation encoder directly controls a virtual environment. This environment consists of visual and tactile stimuli that are provided depending on the running speed of the animal. Tactile stimuli are given to two selected whiskers, each on one side of the snout of the mouse to allow bilateral whisker discrimination. Visual stimuli are presented on a virtual reality projection system around the animal and consist of different visual objects drifting at speeds correlated to the movement of the animal.

The two objects also consist of virtual tactile textures with different spatial frequencies. In order to receive a reward at the end of a virtual corridor the animal has to discriminate the multimodal virtual objects and correctly report the location of a target object.

Second, simultaneous imaging of visual and tactile cortical responses during a discrimination task. Simultaneous imaging of visual and tactile cortical responses during a discrimination task. Neuronal activity will be recorded using two-photon imaging in visual and somatosensory cortex of mice performing the above described multisensory discrimination task. Following parameters will be assessed:

1. How is multisensory information integrated in neuronal activity of visual and somatosensory cortex?
2. Is the animal’s multimodal discrimination performance reflected in the sensory neuronal tuning properties?
3. What is the information that is projected between the different sensory areas?

The latter question will be answered by additional applying fluorescence tracers to visualize long-range projections neurons. The outcome of this aim will explain how multimodal sensory information is processed in the early stage of sensory cortex. Importantly, these bi-hemispheric visual and somatosensory cortical areas will be imaged simultaneously using a newly developed dual two-photon microscope. Together this will provide unprecedented insights into multisensory perception and processing in the brain.

References:

Musall S, von der Behrens W, Mayrhofer J, Weber B, Helmchen F, **Haiss F** (2014). Tactile frequency discrimination is enhanced by circumventing neocortical adaptation. ***Nature Neuroscience***, 17(11):1567-73.

Margolis D, Helmchen F, Weber B, **Haiss F** (2014). Chronic two-photon imaging of neural activity in the anesthetized and awake behaving rodent. In:Optical Imaging of Neocortical Dynamics. **Humana Press**.

MayrhoferJ, SkrebV, von der Behrens W, Musall S, Weber B, **Haiss F** (2013). A Novel Two-alternative Forced Choice Paradigm for Bilateral Vibrotactile Whisker Frequency Discrimination in Head-Fixed Mice and Rats. ***Journal of Neurophysiology***, 109(1):273-84.

Margolis D, Lutcke H, Schulz K, **Haiss F**, Weber B, Kugler S, Hasan MT, Helmchen F (2012). Reorganization of cortical population activity imaged throughout long-term sensory deprivation. ***Nature Neuroscience***, 15(11):1539-46.

Expected profile of the candidate (optional):

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