

## Job description

**Internship subject: Modeling the contribution of thalamo-cortical circuits to individual differences in behavioral flexibility**

Supervisor: Mehdi Khamassi

Starting date: 01/10/2024

Duration: 1d/week during S1, full-time during S2 until 30/06/2025

Level of studies required: M1/engineering

Host laboratory: ISIR (*Institut des Systèmes Intelligents et de Robotique*), Campus Pierre et Marie Curie, 4 place Jussieu, 75005 Paris.

## Contact person

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Send your application by email, with [internship subject] in the subject line, a CV and a covering letter.

Application deadline: 30/09/2024

## Description of the internship

**Subject: Modeling the contribution of thalamo-cortical circuits to individual differences in behavioral flexibility**

The ability to generate flexible behavioural responses is crucial for survival in complex and dynamic environments. Within a population, behavioural output is typically quite variable, leading to individual choices with differential adaptive values<sup>1</sup>. Understanding the neural bases of these specific behavioural traits is currently a growing issue as it may be a key element to better understand the trajectories that may lead to pathological states<sup>2</sup>.

While past research has largely considered the role of highly evolved brain regions such as the prefrontal cortex, the importance of subcortical regions has been increasingly recognized over the past few years. This is especially true for the mediodorsal thalamus (MD) which has extensive and multiple reciprocal connections with prefrontal areas and especially the orbitofrontal cortex (OFC), a well-known key hub for flexible behaviours<sup>3</sup>, making it an important hub for executive functions<sup>4</sup>. Functional dysconnectivity within thalamocortical circuits is associated with many conditions and neuropsychiatric disorders such as Schizophrenia, obsessive-compulsive disorder, ADHD or addiction<sup>(e.g., 5,6)</sup>. But the mechanisms by which these circuits may contribute to behavioral flexibility are still largely unknown.

In this project, we hypothesize that MD-OFC circuits may constitute a key element for understanding the neural underpinnings of **variable behavioral output ranging from adaptive to maladaptive decision-making**. Our preliminary dataset and model suggest that the MD->OFC functional connection is critical to support efficient flexible behaviour. We thus **hypothesize that inter-individual variability in the learning strategy employed depends on the individual functional endophenotype of this pathway**.

Sous la co-tutelle de :

In this work, we will first model experimental data collected by our collaborators at the CNRS INCIA in Bordeaux where rats learn to choose between different levers that have different reward probabilities, different uncertainty levels, and subject to abrupt task changes. At a second stage, we will derive theoretical predictions from this modeling work in order to prepare for the new experiments that our collaborators will perform during a new ANR-funded project starting in October 2024. This ANR project also includes PhD funding at ISIR which could start in October 2025 in extension of the present internship.

The current task includes unsignalled abrupt changes to which the animal has to adapt, requiring a constant exploration-exploitation trade-off. The present version of the task is an extension of a task where we have previously shown that dopamine blockade impairs the exploration-exploitation trade-off in rats<sup>7</sup>. Here we will compare an OFC-lesioned group and an MD-lesioned group with a control group, all alternatively facing difficult versus easy task conditions, where the contrast between levers' reward probability is manipulated to make the best option more or less easy to find.

We predict that OFC lesions will impair rat performance only in the difficult condition, where subcortical structures involved in reward-based learning may be insufficient to learn the task. We will develop alternative computational models which may explain these behavior impairments through the manipulation of different model parameters. We will then simulate these models to verify that they can reproduce rat behavior, and fit them to the experimental data to find the best model. We will then evaluate whether significant model parameters change explain the data. We will finally perform model simulations in novel extensions of the task in order to derive theoretical predictions which could drive future experiments.

## References

1. Boogert NJ, Madden JR, Morand-Ferron J, Thornton A. Measuring and understanding individual differences in cognition. *Philos Trans R Soc Lond B Biol Sci.* 2018;373(1756).
2. Addicott MA, Pearson JM, Sweitzer MM, Barack DL, Platt ML. A Primer on Foraging and the Explore/Exploit Trade-Off for Psychiatry Research. *Neuropsychopharmacology.* 2017;42(10):1931-1939.
3. Schoenbaum G, Khamassi M, Pessiglione M, Gottfried JA, Murray EA. The magical orbitofrontal cortex. *Behav Neurosci.* 2021;135(2):108.
4. Wolff M, Halassa MM. The mediodorsal thalamus in executive control. *Neuron.* 2024;112(6):893-908.
5. Giraldo-Chica M, Rogers BP, Damon SM, Landman BA, Woodward ND. Prefrontal-Thalamic Anatomical Connectivity and Executive Cognitive Function in Schizophrenia. *Biol Psychiatry.* 2018;83(6):509-517.
6. Yacou MA, Chowdury A, Easter P, Hanna GL, Rosenberg DR, Diwadkar VA. Sustained attention induces altered effective connectivity of the ascending thalamo-cortical relay in obsessive-compulsive disorder. *Front Psychiatry.* 2022;13:869106.
7. Cinotti F, Fresno V, Aklil N, Coutureau E, Girard B, Marchand AR, Khamassi M. Dopamine blockade impairs the exploration-exploitation trade-off in rats. *Sci Rep.* 2019;9(1):6770.

PARTIE RESERVEE A L'USAGE INTERNE

Gratification

Le versement d'une gratification au stagiaire est obligatoire dès lors qu'il est accueilli par l'entreprise plus de 2 mois : soit l'équivalent de 45 jours.

Gratification :  OUI  NON

Equipe/service de rattachement

ACIDE

Publication de l'offre :

L'offre sera publiée sur le site web du laboratoire (<https://www.isir.upmc.fr/nous-rejoindre/opportunites/>), sur les réseaux sociaux Twitter et LinkedIn, et sur Euraxess.

Date souhaitée pour la publication de l'offre :

Date : asap

Commentaires

Veuillez déposer votre demande à l'adresse suivante, merci: [annonce\\_recrutement@listes.isir.upmc.fr](mailto:annonce_recrutement@listes.isir.upmc.fr)