PhD PROJECT PROPOSAL

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Neuromodulatory control of predictive processing in visual cortical circuits

Supervisor 1 (with name, email, affiliated laboratory and doctoral school affiliation)
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Abstract (10 lines)*

The brain constantly generates internal models to predict sensory input, and perception arises from comparing these predictions with external reality—a process best understood as predictive processing. How this computation is implemented and regulated in cortical circuits remains unknown. This PhD project will explore how serotonin and norepinephrine—key modulators of mood, arousal, and attention—shape predictive processing in the mouse visual cortex.

The candidate will combine computational modelling (Perrinet lab, INT) and experimental neuroscience (Rancz lab, INMED) to link theory and physiology. Biologically realistic spiking and normative models will generate testable predictions, validated through in vivo electrophysiology, imaging, and optogenetic manipulation during sensory-motor mismatch tasks.

This iterative model–experiment approach will reveal how neuromodulators balance internal predictions with sensory evidence, providing insight into the healthy brain and a foundation for understanding its dysfunction in mental disorders.

Keywords*

predictive processing
neuromodulation
cortical circuits
Mus musculus

computational neuroscience
spiking network models
in vivo electrophysiology
optogenetics
behaviou

Scientific question and Objectives (10 lines)*

Predictive processing posits that perception arises from comparing sensory input with internally generated predictions, but how this computation is implemented in cortical circuits remains unclear (Spratling 2017; Keller & Mrsic-Flogel 2018). This comparison between internal and external information must be flexibly weighted, and neuromodulators such as serotonin and norepinephrine are strong candidates for controlling this balance.

This project will investigate how these systems shape predictive processing in the mouse visual cortex through two complementary aims: (1) developing biologically realistic network models at the spiking (Davison 2020; Grimaldi 2023) and probabilistic (Ladret 2023) levels in the Perrinet lab, and (2) experimentally testing model predictions in the Rancz lab using in vivo recordings, optogenetics, and behaviour. We hypothesise that serotonin and norepinephrine dynamically modulate synaptic- and cell-intrinsic properties to dynamically set the precision of prediction error signalling across cortical layers.

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Proposed approach (experimental / theoretical / computational) and research plan (20 lines)*

This project combines state-of-the-art computational and experimental approaches.
The PhD candidate will develop spiking network models of the mouse visual cortex using realistic connectivity from anatomical and physiological data (Rancz lab) and the Perrinet lab's expertise in cortical modelling. These models will distinguish feedforward, lateral, and feedback pathways to build hierarchical cortical columns incorporating recurrent local circuits, long-range excitatory projections with feedforward inhibition, and pre- and postsynaptic neuromodulatory mechanisms. Normative frameworks will guide the design of optimal stimulation protocols using a recently developed optimisation method (Edgar 2019).
Model predictions will be tested with in vivo electrophysiology (Neuropixels) and calcium imaging during visuo-vestibular and visuo-motor mismatch tasks in a virtual reality setup developed by the Rancz team. Concurrent imaging of serotonergic and noradrenergic activity, together with optogenetic and pharmacological manipulations, will provide causal tests of model-derived hypotheses.
A central innovation is the use of model-based stimulus optimisation: generative models will produce maximally informative, reproducible ("frozen noise") and ecologically relevant stimuli, an approach established in the Perrinet lab (Ladret 2023). The candidate will extend this strategy to generate not only sensory inputs but also perturbations within the sensorimotor loop. This iterative model–experiment cycle will elucidate how neuromodulators shape cortical computations underlying predictive processing.

Interdisciplinarity and Implication of the two labs (15 lines)*

(In this section the collaboration of the two laboratories will be explained in details to explain why the project cannot be conducted by one team alone)

The project's success critically depends on the seamless integration of computational and experimental expertise. The candidate will develop spiking network and normative models of predictive processing and neuromodulation to generate quantitative predictions for cortical dynamics in the Perrinet lab (INT, Marseille). In the Rancz lab (INMED, Marseille), they will test these predictions experimentally through in vivo recordings, optogenetic manipulations, and behavioural paradigms probing sensory prediction errors.
The two approaches are mutually reinforcing: computational modelling provides theoretical precision and testable hypotheses, while experimental data deliver biological validation and critical feedback for model refinement. Together, the teams will build a genuine bridge between theory, physiology, and behaviour. This iterative loop—where model-driven experiments inform model design—will not only advance our understanding of predictive computation and neuromodulatory control but also yield principles relevant to neuromorphic AI. Ultimately, the project aims to reveal how predictive processing operates in the healthy brain, providing a foundation for understanding the circuit-level disruptions underlying mental disorders critically depending on the balance of internally generated mental states and external information.

Specify with whom the person recruited will collaborate and on what aspects *

Rancz lab – experimental part of the project. Will collaborate with a postdoc to be recruited.

Perrinet lab – theoretical part of the project. Will collaborate with a PhD student (already recruited) and a postdoc (to be recruited).

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PhD student's expected profile*

We seek a highly motivated and versatile candidate with a strong background in neuroscience or computational biology, eager to bridge experimental and computational approaches. Experience in either in vivo experimental neuroscience (e.g. in vivo recordings, behaviour, or optogenetics) or computational modelling (Python, neuronal network simulations) is essential. Familiarity with cortical circuit function and neuromodulation will be an advantage.
We encourage applications from candidates of all backgrounds and are committed to fostering an inclusive and supportive research environment.

Is this project the continuation of an existing project or an entirely new one?

Continuation.

In the case of an existing project, please explain the links between the two projects (5 lines)*

The project forms an integral part and logical continuation of ongoing projects in both labs. The Rancz lab is currently building the biological knowledge to feed into the models and is imaging mismatch evoked neuronal activity. The Perrinet lab develops neuromorphic, low-power hardware implementing predictive processing algorithms for robotic perception, ophthalmic imaging, and large-scale Neuropixels data analysis. Integrating neurophysiological validation is key to embedding neuromodulatory, context-dependent mechanisms that enable adaptive behavior across sensory modalities.

Two to five references related to the project*

Spratling, M. W. (2017) A review of predictive coding algorithms10.1016/j.bandc.2015.11.003

Keller & Mrsic-Flogel (2018) Predictive Processing: A Canonical Cortical Computation. 10.1016/j.neuron.2018.10.003

Grimaldi A, Perrinet LU (2023) Learning heterogeneous delays in a layer of spiking neurons for fast motion detection. doi: 10.1007/s00422-023-00975-8

Ladret HJ, Cortes N, Ikan L, Chavane F, Casanova C, Perrinet LU (2023) Cortical recurrence supports resilience to sensory variance in the primary visual cortex. doi: 10.1038/s42003-023-05042-3

Walker EY, Sinz FH, Cobos E, Muhammad T, Froudarakis E, Fahey PG, Ecker AS, Reimer J, Pitkow X, Tolias AS (2019) Inception loops discover what excites neurons most using deep predictive models. doi: 10.1038/s41593-019-0517-x

Two main publications from each PI over the last 5 years*

Galloni AR, Ye Z, Rancz E (2022). Dendritic Domain-Specific Sampling of Long-Range Axons Shapes Feedforward and Feedback Connectivity of L5 Neurons. The Journal of Neuroscience; doi: 10.1523/jneurosci.1620-21.2022

Ambrad Giovannetti E, Rancz E (2024). Behind mouse eyes: The function and control of eye movements in mice. Neuroscience & Biobehavioral Reviews; doi: 10.1016/j.neubiorev.2024.105671

Grimaldi A.,Gruel A., Besnainou C., Jérémie JN., Martinet J., Perrinet L. (2022). Precise spiking motifs in neurobiological and neuromorphic data. Brain sciences; doi:10.3390/brainsci13010068

Boutin V., Franciosini A., Chavane F., Ruffier F., Perrinet L. (2021). Sparse deep predictive coding captures contour integration capabilities of the early visual system. PLoS computational biology; doi:10.1371/journal.pcbi.1008629

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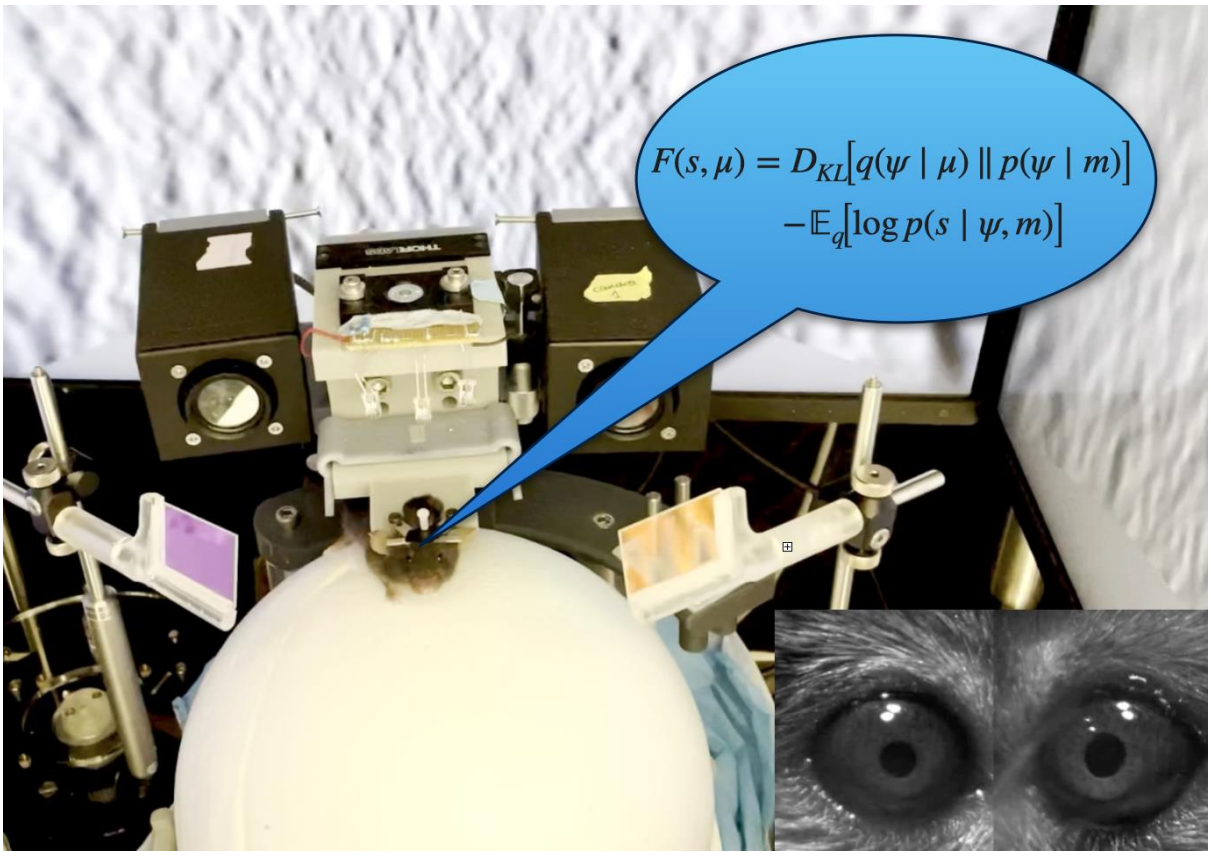
Project's illustrating image



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