Neuronal Representations of Social Grammar in Murine Model of Neurodevelopmental Psychiatric Diseases.

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Abstract (10 lines)*

Social behavior, encompassing communication and interactions between conspecifics, plays a crucial role in survival and adaptation to new environments. These behaviors are often disrupted in neurodevelopmental and psychiatric disorders, yet the mechanisms underlying such abnormalities remain largely unclear. This project aims to decode the neural representations underlying social behavioral grammar in mice and to determine how these processes are altered in disease-relevant contexts. We will leverage state of the art statistical modeling and machine learning techniques to analyze natural social behavior, prefrontal neuronal ensemble activity in freely-moving mice, and different models of psychiatric disorders. By integrating experimental and computational approaches, this project will elucidate how prefrontal circuits encode social behavior and how these representations are disrupted in neurodevelopmental psychiatric disorders.

Keywords*

Social Brain - Naturalistic behavior - Neuronal activity - Mouse models of psychiatric diseases - Multimodal data integration - Grammar learning - Functional data analysis.

Scientific question and Objectives (10 lines)*

This project aims to decode and understand the associated neural representations of social behavioral grammar while identifying the fundamental elements of social behaviors, with a focus on neuropsychiatric disorders and sex differences. It is structured around the following objectives:

1. Identify and characterize the neural representations within prefrontal hubs that encode distinct modules of social behavior in naturalistic social interactions.

2. Develop and apply a quantitative framework to analyze social behavioral grammar and its neural representations in models of neurodevelopmental psychiatric disease.

*: Mandatory

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

Experimental: Natural social interactions in group-housed mice will be continuously tracked and monitored in real time using the Live Mouse Tracker, a system integrating computer vision and machine learning to extract detailed individual and collective behaviors.
In parallel, structured neuronal ensemble activity will be recorded prefrontal hubs of awake, freely moving, and socially interacting mice in the Live mouse Tracker using fiber photometry. By integrating behavioral and neural data, we will identify the neural representations that encode social behavioral modules under naturalistic conditions.
To address disease-relevant contexts, both genetic and environmental models of neurodevelopmental psychiatric disorders will be used to link disruptions in social behavioral grammar with altered in prefrontal ensemble activity.

Mathematical and computational: Organization of social interactions into meaningful sequences will be inferred using Markovian and Probabilistic Context-Free Grammar (PCFG) models. Particular emphasis will be placed on tailoring nonparametric Bayesian inference of PCFG, a cutting-edge technique in Natural Language Processing. The extracted latent rules, represented as parse trees, will be compared across the different experimental groups.
The building blocks and structure of grammar-specific neuronal representations will be uncovered using a multimodal data-integration pipeline linking latent parse trees with neuronal activity. This challenge will be addressed by leveraging Bayesian inference on PCFGs to develop a probabilistic data association framework. The pipeline will include advanced preprocessing, feature engineering, and both functional and topological data analysis stages.

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)

This project operates at the very frontiers of (i) basic research aiming to gather fundamental new knowledge in the field of behavioral neurosciences and neurodevelopmental brain disorders and (ii) modern statistical, machine learning methods and information theory. The project is grounded in a strong interdisciplinary collaboration between the neuroscience laboratory and the partner laboratory specialized in mathematics and computational modeling. The integration of these complementary approaches is essential to achieve the project's objectives. While our laboratory generates high-dimensional datasets from social behavioral tracking and neuronal recordings, the mathematical team will develop and implement computational models capable of identifying the structure and dynamics of social behavioral grammar and its neural correlates. This synergistic collaboration will allow the creation of innovative analytical tools that go beyond classical behavioral categorization, providing new insights into how prefrontal circuits encode social interactions. The project could not be achieved by either team alone.

*: Mandatory

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

This doctoral project will be jointly supervised by the neuroscience laboratory Sex Differences in Developmental Vulnerability to Neuropsychiatric Diseases (INMED, under the supervision of P. Chavis) and the mathematics and computational modeling group (under the supervision of J.-M. Freyermuth). The PhD student will collaborate closely with both teams and play a central role at the interface between experimental and computational neuroscience.

Within Team 1 (P. Chavis), the student will participate in data acquisition and preprocessing of behavioral and neuronal ensemble recordings using fiber photometry, in collaboration with a postdoctoral researcher and an engineer. Within Team 2 (J.-M. Freyermuth), the student will contribute to advanced data analysis, machine learning, and modeling of neural dynamics, working in close collaboration with an engineer from Team 2, an expert in machine learning deployment, and an engineer from Team 1, trained in the Century Master of Computational and Mathematical Biology and highly experienced in functional data analysis.

PhD student's expected profile*

Robust theoretical background in Neurosciences – Knowledgeable in animal experimentation- Strong attraction for computation and statistics - Collaborative and positive team spirit.

Is this project the continuation of an existing project or an entirely new one?
In the case of an existing project, please explain the links between the two projects (5 lines)*

This project is a continuation of an existing study in which we successfully characterized the fundamental elements of social behavioral grammar in groups of mice using advanced behavioral tracking. In that work, the underlying neuronal ensembles of social behavioral dynamics were hypothesized but not recorded due to time constraints. The present project builds on these findings by integrating fiber photometry recordings to characterize the corresponding neural representations in prefrontal circuits.

Two to five references related to the project*

1- De Chaumont F. et al. Real-time analysis of the behaviour of groups of mice via a depth-sensing camera and machine learning. Nat Biomed Eng. 2019 Nov;3(11):930-942.
2- Klibaite U. et al. Mapping the landscape of social behavior. Cell, 188 (8), 2249 - 2266.e23
3- Chen Y., Chien J., Dai B., Lin D., & Chen Z. S. (2024). Identifying behavioral links to neural dynamics of multifiber photometry recordings in a mouse social behavior network. Journal of Neural Engineering, 21(3), 036051. https://doi.org/10.1088/1741-2552/ad5702
4- Liang, P., Jordan, M. I., & Klein, D. (2009). Probabilistic grammars and hierarchical Dirichlet processes. In A. O'Hagan & M. West (Eds.), The Oxford Handbook of Applied Bayesian Analysis. Oxford University Press.

5- Loewinger, G., & al. (2024). *A Statistical Framework for Analysis of Trial-Level Temporal Dynamics in Fiber Photometry Experiments*. eLife (Reviewed Preprint). DOI: 10.7554/eLife.95802.2.

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

1- Silva-Hurtado T.J., Giua G., Lassalle O., Makrini-Maleville L., Strauss B., Wager-Miller J., **Freyermuth J-M.** Mackie K., Valjent E., Manzoni O.J. and **Chavis P***. Reelin Deficiency and Synaptic Impairment in Adolescent PFC following Initial Synthetic Cannabinoid Exposure. (2024) Biological Psychiatry: Global Open Science. Nov 28;5(2):100426.

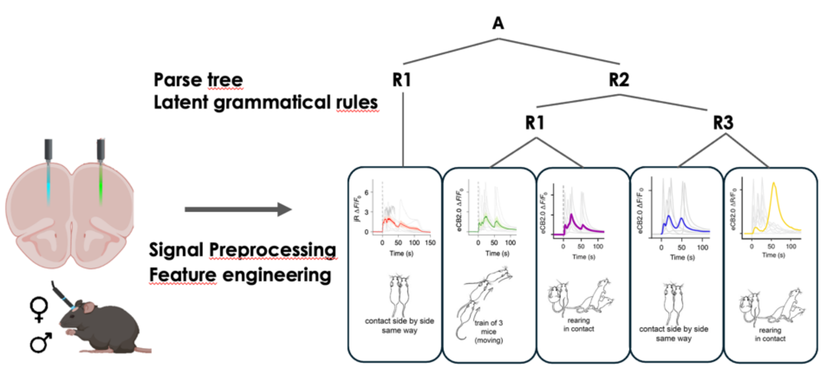
This publication was featured as a Commentary in BP:GOS: doi.org/10.1016/j.bpsgos.2025.100456

2- Iezzi D, Caceres-Rodriguez A, **Chavis P#*** and Manzoni OJJ#*. In utero exposure to cannabidiol disrupts select early-life behaviors in a sex-specific manner. (2022) Translational Psychiatry, 12(1):501. doi: 10.1038/s41398-022-02271-8.

3- El-Yaagoubi, A. B., **Freyermuth**, J.-M., & Ombao, H. A robust topological framework for detecting regime changes in multi-trial experiments with application to predictive maintenance. (2025) To appear in The Journal of Time Series Analysis.

4- Aston, J., Dehay, D., Dudek, A., **Freyermuth**, J.-M., Szucs, D., & Colling, L. Spectrum inference for replicated spatial locally time-harmonizable time series. (2023) Electronic journal of statistics, 17(1), 1371–1410.

Project's illustrating image



*: Mandatory