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Mice social behavior modeling and recognition for autism characterization

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Abstract (10 lines)*

Machine learning and computer vision tools enable the automatic detection and quantification of mouse behaviors, including those in mouse models of autism spectrum disorder (ASD). Over the past three years, our teams developed the Enhanced Mouse Tracker (EMT), which addresses key limitations of the existing Live Mouse Tracker system (LMT- https://livemousetracker.org). The EMT is an integrated solution that optimizes three key aspects: 1) error correction for reliable individual identification; 2) robust event detection using advanced algorithms, and 3) expanded functionality with new behavioral actions and analysis capabilities. Building on these advancements, we are now developing additional behavioral metrics in order to process, analyze, and extract new information from images, to propose sequences of actions representing complex behavior. We seek a candidate with expertise in programming and computer vision to develop and implement new modules for measuring repetitive behaviors and complex social interactions in wild type and ASD mouse models.

Keywords: mice behavior modeling and recognition, computer vision, machine learning, autism spectrum disorder, neuroscience.

Scientific question and Objectives (10 lines)*

Our aim is to automate the extraction of sequences of actions (rather than single action, such as grooming) that determine core ASD behavior (i.e. stereotypies) and social interaction behavior in the context of animal group interaction. Our approach enables continuous observation with high tracking accuracy, using more than two mice in an open space. Although challenges still remain, we believe that developing these new modules will significantly advance our understanding of behavioral differences between wild-type and ASD-like mouse models. This will be achieved through non-invasive, longitudinal, blind behavioral studies. The candidate will develop new tools, based on our novel EMT algorithms to analyze the behavior of freely moving mice during adulthood, infancy and adolescence.

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

The goal of our work is to analyze top-view videos of mice interacting with each other, acquired using a Kinect 2 (providing both depth and color images). To this end, we will use the Enhanced Mouse Tracker (EMT), which already integrates a framework for analyzing the behavior of small groups of mice (1-3), and we will extend its functionalities to analyze larger groups of mice. This study will include a statistical analysis of the quality of interactions between mice (touching frequency, proximity evolution, etc.) by exploiting trajectories. We will also provide a model for repetitive motion to be used for the detection of stereotypic behavior characteristic of ASD. Finally, by learning the spatio-temporal information of the extracted trajectories, we will derive social interaction models (wild type and ASD), to characterize behavior more accurately. This will allow us to determine whether the behavior of the mice differs from the observations and hypotheses of biologists.

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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 collaborative project brings together computer scientists specializing in image processing and shape recognition from the LIS research laboratory, and neurobiologists who are experts in brain and circuitry development and function from the IBDM and INMED laboratories. The three labs are interested in ASD and have collaborated for three years as part of the ANR ASDMOD project. Scientists at LIS use machine/deep learning and computer vision technology to improve ASD diagnosis, while scientists at the IBDM and INMED study mouse models of ASD. The three labs are already equipped with computers for storing and processing large amounts of data during long-term experiments. The LIS's expertise is necessary to develop algorithms that can to provide additional extracted features to document behaviors in an environment that allows social interactions to be maintained over a long period of time. This project will also enable the PhD candidate to develop interdisciplinary expertise in the application of computer science to neurobehavioral imaging.

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

Collaboration with Severine Dubuisson will concern the development of new tools for mice behavior analysis, relying on artificial intelligence (machine/deep learning) and computer vision. She will supervise the choice and the validation of the algorithms dedicated, in particular, to the social interactions between mice and their repetitive motion characterization.

Collaboration with F. Muscatelli and L. Fasano that bring the mouse models of ASD (*Tshz3, Magel2*), which have been well already characterized using classical tools to investigate their behaviors. They will bring all the knowledge of the different mouse models. They will supervise the experimental part on mice to allow the videos of the different male and female mouse cohorts established for two different ASD genetic (*Tshz3, Magel2*) mouse models and their controls. They will supervise the biological interpretation and validation of the data.

PhD student's expected profile*

We expect a candidate with a background in computer science (a high level in Python programming is required) and strong skills in deep/machine learning and image and video processing for tracking and behavior analysis. The candidate will be involved from LMT building to development of imaging software.

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 builds on the collaboration between three teams (ANR ASDMOD 2023-2026), on modeling complex autistic-like behavior in mice. Initially based on the Live Mouse Tracker (LMT) algorithm, this project uses the LMT to track, identify and characterize 33 actions in up to four animals of both sexes, with no time limit. However, despite the many advantages of this system, we identified several dysfunctions (e.g. tracking errors, overestimation of the number of actions, undetected actions and inconsistent actions) that prevented a rigorous behavioral analysis. To address these issues, we have developed the Enhanced Mouse Tracker (EMT), which includes a comprehensive toolkit aimed at improving three key areas: 1) identifying and correcting of errors; 2) ensuring greater robustness and more realistic results by using new event detection algorithms; and 3) adding of new actions and functionalities. One article is in preparation and a patent application has been filed. This work is the result of genuine interdisciplinary collaboration and provides a solid foundation

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for tackling more complex behaviors in the present project.

Two to five references related to the project*

S Fang, C Achard, **S Dubuisson**. Modeling the synchrony between interacting people: application to role recognition.
In Multimedia Tools and Applications 77 (1), 503-518, 2018

M. Morel, C. Achard, R. Kulpa and **S. Dubuisson**. Time-series averaging using constrained dynamic time warping with tolerance, inPattern Recognition, 2017.

Bertoni A, Schaller F, …**Muscatelli F**. (2021): Oxytocin administration in neonates shapes hippocampal circuitry and restores social behavior in a mouse model of autism. *Mol Psychiatry*. doi:10.1038/s41380-021-01227-6

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

Severine Dubuisson :

1) G Franchi, A Bursuc, E Aldea, S Dubuisson, I Bloch. Encoding the latent posterior of bayesian neural networks for uncertainty quantification, IEEE Transactions on Pattern Analysis and Machine, 46(4):2027-2040, 2023

2) Jules Collenne, Jilliana Monnier, Rabah Iguernaissi, Motasem Nawaf, Marie-Aleth Richard, Jean-Jacques Grob, Caroline Gaudy-Marqueste, Séverine Dubuisson, Djamal Merad. Fusion between an Algorithm Based on the Characterization of Melanocytic Lesions' Asymmetry with an Ensemble of Convolutional Neural Networks for Melanoma Detection. Journal of Investigative Dermatology, 144(7):1600-1607, 2024.

Laurent Fasano :

Molitor J, Graniou J, Salin P, Castets F, Fatmi A, Kerkerian-Le Goff L, **Fasano L**[ca], Caubit X[ca], Gubellini P[ca]. Altered striosome-matrix distribution and activity of striatal cholinergic interneurons in a model of autism-linked repetitive behaviors. Molecular Psychiatry 2025 PMID 40908363

Caubit X, Gubellini P, Roubertoux PL, Carlier M, Molitor J, Chabbert D, Metwaly M, Salin P, Fatmi A, Belaidouni Y, Brosse L, Kerkerian-Le Goff L[ca], **Fasano L**[ca]. Targeted *Tshz3* deletion in corticostriatal circuit components segregates core autistic behaviors. Translational Psychiatry. 2022. PMID 35292625.

Françoise Muscatelli :

Barelle, P.Y. …Bouret S, **Muscatelli F.** *Investigation of a Novel Mouse Model of Prader-Willi Syndrome with Invalidation of Necdin and Magel2* . J Clin Invest. Insight 2025 Mar 6:e185159.

Bertoni A, Schaller F, …**Muscatelli F**. Oxytocin administration in neonates shapes hippocampal circuitry and restores social behavior in a mouse model of autism. *Mol Psychiatry*. 2021 doi:10.1038/s41380-021-01227-6

Project's illustrating image

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