Time series analysis for the study of rodent behavior

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Presentation of the lab. This postdoc will take place at the **Centre Borelli (ENS Paris Saclay)**. The Centre Borelli is a multidisciplinary research unit focusing on all applications of mathematics, neuroscience and biomedical research. It brings together multidisciplinary teams of mathematicians and experts in medicine, physics, mechanics, biology and engineering to conduct research driven by real data and use cases from science and industry.

Environment. The postdoctoral researcher will have the opportunity to fully integrate into an interdisciplinary team of mathematicians, computer scientists, biologists and clinicians. If successful, the postdoc may lead not only to scientific publications, but also to a valorization project. The postdoctoral researcher will also attend weekly laboratory seminars.

Context. Neurodegenerative diseases (NDs) such as Alzheimer's and Parkinson's are major public health issues. In order to better understand the etiology and evolutionary mechanisms of these pathologies, numerous teams of biologists and neuroscientists are working on animal models. One of the particularities of NDs is their impact on behavior. **Video monitoring** now makes it possible to study the behavior of rodents continuously over **long periods of time**. Although computer vision and artificial intelligence algorithms do exist for data analysis, they suffer from various problems (highly noisy data providing sometimes nonsensical results, impossibility of injecting expert knowledge linked to the disease studied, difficulty of using the algorithm's outputs for longitudinal follow-up or inter-individual comparison), which in practice severely limit their applicability and acceptability by the scientific community.

Related work. A range of analytical tools has been developed to facilitate the analysis of the vast amounts of video data (Wiltschko et al., 2020). Video tracking software not only allows for the extraction of movement trajectories but also enables the **breakdown of behaviors into smaller components or "syllables."** (Weinreb et al., 2024) These behavioral syllables represent the in the observation space, allowing researchers to dissect complex behaviors into more manageable and interpretable segments. A sequence of syllables, often called an **ethogram**, provides an overview of the **chronology of all behavioral events** occurring during the protocol (Luxem et al., 2022). We classify **action syllable estimation** methods into two main categories:

- Frame-wise classification: In this approach, each video frame is independently classified into an activity class. Examples include MotionMapper and B-SOID, which are unsupervised, and DeepEthogram, which is supervised and requires manual frame labeling. These methods apply a non-linear transformation to the video before classification.

- State-space models: Each activity is modeled using a simple dynamical system. An early version of Keypoint-Moseq (Weinreb et al., 2024), VAME (Luxem et al., 2022), and VDBE (Shi et al., 2021) use auto-regressive models, while the latest version of Keypoint-Moseq uses a switching linear dynamical system. A Markov process models transitions between activities. VAME, VDBE, and Keypoint-Moseq differ in several preprocessing steps involving complex deep transformations.

The latter category has been introduced partly because framewise classification methods **suffer from low temporal persistence** (Weinreb et al., 2024). For instance, frames containing outliers are often classified differently from the surrounding frames, necessitating post-processing. Consequently, metrics such as average activity duration are significantly affected. However, several works have shown that **the Markov property still produces spurious changes**, especially in the presence of noise (Nystrup et al., 2020). In addition, **action segmentation tools remain complex to use**, particularly when they do not work out of the box. For unsupervised methods, the calibration process is difficult because of the non-intuitive nature of the parameters. In addition, the evaluation of action segmentation methods is problematic due to the absence of feedback metrics. **This prevents their application in novel settings**. Also, existing algorithms for syllable discovery **do not allow for the incorporation of biological expertise or prior knowledge**, which could enhance the relevance of the results. For instance, incorporating constraints like the minimum duration of a behavioral atom or the possible types of transitions could improve the accuracy of the findings.

Once ethograms are computed, most studies extract **only basic features** such as the duration spent in particular syllables are derived from ethograms. More advanced methodologies extract a couple of frequent cycles or a hierarchical grouping of syllables based on their co-occurrence patterns, and then **qualitatively** analyze them.

Objectives. The overarching aim of this project is to propose new mathematical tools based on **time series analysis** in order to analyze these behavioral data in an automated, interpretable way that is in line with biological knowledge. To that end, the project first proposes to develop **new switching state-space models** (Balsells-Rodas et al., 2024; Lee et al., 2023; Liu et al., 2023; Berger et al., 2022; Chen & Poor, 2022; Costacurta et al., 2022) that inject constraints and expert knowledge. We will use our strong expertise in **change point detection** (Truong et al, 2020; Runge et al., 2023), which is a more general framework, to create robust methods and understand their theoretical properties. In a second time, we will **develop systematic approaches to extract discriminative features from these ethograms**. Specifically, our focus is on identifying frequent sequences of syllables that can characterize high-level activities. **Frequent (temporal) pattern mining** has produced various well-suited methods to address the challenges encountered in behavior analysis (Likhitha et al., 2020). Building on our expertise in creating symbolic distances that are robust to time warping and noise, we will also develop procedures that **effectively handle irrelevant patterns caused by noise** and account for **variations in activity lengths due to inter- and intra-subject variability**. Other approaches include NLP procedures and bioinformatic methods from genetic and genomic analysis. Finally, we aim to make all developed tools and methodologies accessible to neuroscientists to promote broader adoption within the scientific community. To that end, we will create **user-friendly open-source software** and online interactive demos (Combettes et al., 2024; Germain et al., 2024) to facilitate the integration of advanced techniques into existing research workflows.

This project is part of an ongoing collaboration with neuroscientists at NeuroPSI (Lucile Benhaim). To validate future methodological and mathematical contributions, open data sets as well as private ones are already available, in addition to a strong expertise in biology.

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