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# UNBIASED ANALYSIS OF MOUSE SOCIAL BEHAVIOUR USING UNSUPERVISED MACHINE LEARNING

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## ABSTRACT

Mouse models are broadly used to study the mechanisms of neuropsychiatric disorders and to test potential treatments. In these models, automation to monitor behavioural differences during social interactions is currently limited. We propose in the present study a new method to conduct automatic behavioural classification, using an original unsupervised machine learning. We applied the proposed method to mice mutated in *Shank2*, a gene associated with autism spectrum disorders. We validated our results by comparing automatically extracted results to rule-based classifier labelling. We discovered seven behavioural states matching from 80 to 95% previous rule-based classification, and two unsuspected behaviours. Interestingly, we also highlighted genotype-related differences in two behavioural categories, namely locomotion and facing the conspecific.

**Index Terms**— unsupervised automated behavioural analysis, unsupervised classification, animal behaviour, autism spectrum disorder, mouse model, social behaviour

## 1. INTRODUCTION

Neuropsychiatric disorders such as autism spectrum disorders, schizophrenia, addiction or depression affect heavily the social life of patients. Monitoring their behaviour constitutes the main part of the diagnosis since physiological markers are still scarce. Mouse models are used to study the mechanisms behind these disorders as well as to test potential treatments. Investigations therefore concentrate on the behaviour –and more specifically social interaction- of these models.

Currently, the characterization of the social behaviour of mouse models relies on a small subset of social events selected by previous studies. Examining the behaviour in a more exhaustive way will allow to unravel hidden effects of pharmacological treatments in order to refine these ones.

To be able to process new quantitative measurements with less experimenter bias, behavioural studies are currently shifting toward computational analysis [1]. The emerging computer-vision techniques allow to track the animals, transforming video data into trajectories. In order to interpret behaviour, a description of its relevant parts -in an objective and quantitative manner- is needed. We therefore aim at developing an automatic behavioural classification.

## 2. CONSTRAINTS

To automatically extract behaviours, several unsupervised techniques have been developed since 2001 [2-6]. Among them, Braun *et al* [3] analysed blowfly behaviour. For this purpose, they used one global clustering, considering all features. This enables a less anthropomorphic labelling of the events in comparison with a manual human classification. But, as a drawback, this analysis is limited to describe the behaviour as a succession of events. It assumes that only one event exists at a given time, which is not adapted to the complexity of social behaviours. In our experiments, animals can perform several independent actions simultaneously. For instance, they can be moving or stopped and at the same time they can sniff or not their conspecific.

The only methods able to describe those simultaneous events are called rule-based classifiers [7-9] as they are filtering the data with geometric clues extracted from trajectories, such as the relative position of the animals, their distances and their speed. Those rules, also called repertoire of events [8], enable to deal with simultaneous events, but extract only behaviours that have been previously defined by experts. Therefore, those classifiers depend also on the thresholds provided by those experts. This labelling is anthropomorphic and prevents the observer from finding unexpected behaviours that could be key in the differentiation of the social phenotype within groups of animals.

In this paper, we propose to combine the advantages of both approaches: an unsupervised classification able to deal with simultaneous events, based on simple features extracted from the trajectory of the animals.

### 3. UNSUPERVISED BEHAVIOURAL CLASSIFICATION

We use a tracking method that provides the location of the head and of the tail base of the animals. We use those data as a legacy of our previous tracker [8] as it was designed to track specifically those parts of the animal which are known as key elements in the interaction of animals (the base of the tail is the ano-genital area). We nevertheless design the method so that it can include more detailed features.

We first detail how we create the features. These ones are then processed by an independent component analysis (ICA) that extracts independent descriptors. Each independent component (IC) displays a linear combination of the features. We then use a one-dimensional Gaussian mixture model (GMM) to generate on each IC a different clustering of exclusive behaviours (such as animal in contact, or not in contact).

#### 3.1. Features computation

The tracking [8] outputs are the two-dimensional location of the head and of the tail base, for both mice, at each time point. The ICs, extracted by the ICA, are orthogonal. We thus maximize the information extracted from those outputs by selecting any features, without considering the correlations between them.

These variables consist of distances and angles, measured at each frame or between consecutive ones for dynamic features. Table 1 displays the features extracted from head and tail location of both animals. Features are individual (1 to 4, i.e. length of the animal, speed), or social (5 to 13, i.e. distances, angles between animals). We then feed an ICA with the complete set of measured features.

#### 3.2. Extracting independent components

Some of the computed features are highly correlated. We thus extract independent descriptors by processing a global ICA on all features, across all data points, of all experiments. We use the fastICA algorithm [10]. It performs an orthogonal rotation of prewhitened data that maximizes a measure of non-Gaussianity.

In this analysis, the number of ICs extracted needs to be tuned. ICs should respect the two criteria of orthogonality and non-Gaussianity to be considered as reliable source descriptors of the behaviour. Also, to get best ICs, we need to constrain the number of axis produced by the ICA by extracting less ICs than the original number of variables. Therefore, we need to find the correct range of ICs number that correspond to real sources. In such range, the extraction of a supplementary IC adds a new source, affecting only minimally the previously extracted ones. Above a certain ICs number, all or a part of these are thus rearranged to extract supplementary components.

**Table 1. Set of trajectory-based features, individual and social.**

1	length of the A animal vector	$\ \vec{T}_t^A \vec{H}_t^A\ $
2	speed of the head of the A animal	$\ \vec{H}_t^A \vec{H}_{t+1}^A\ $
3	speed of the tail base of the A animal	$\ \vec{T}_t^A \vec{T}_{t+1}^A\ $
4	directional change of the A animal vector	$\vec{T}_t^A \vec{H}_t^A \widehat{\vec{T}_{t+1}^A \vec{H}_{t+1}^A}$
5	distance between A and B heads	$\ \vec{H}_t^A \vec{H}_t^B\ $
6	distance between A head and B tail	$\ \vec{H}_t^A \vec{T}_t^B\ $
7	distance between A tail and B head	$\ \vec{T}_t^A \vec{H}_t^B\ $
8	distance between A and B tail	$\ \vec{T}_t^A \vec{T}_t^B\ $
9	speed of the A toward the current position of the B	$\left\  \frac{\vec{T}_t^A + \vec{H}_t^A}{2} \frac{\vec{T}_t^B + \vec{H}_t^B}{2} \right\  - \left\  \frac{\vec{T}_{t+1}^A + \vec{H}_{t+1}^A}{2} \frac{\vec{T}_{t+1}^B + \vec{H}_{t+1}^B}{2} \right\ $
10	speed of the A toward the next position of the B	$\left\  \frac{\vec{T}_t^A + \vec{H}_t^A}{2} \frac{\vec{T}_{t+1}^B + \vec{H}_{t+1}^B}{2} \right\  - \left\  \frac{\vec{T}_{t+1}^A + \vec{H}_{t+1}^A}{2} \frac{\vec{T}_{t+1}^B + \vec{H}_{t+1}^B}{2} \right\ $
11	angle between the A vector and the vector from A middle to B head	$\vec{T}_t^A \vec{H}_t^A \widehat{\frac{\vec{T}_{t+1}^A + \vec{H}_{t+1}^A}{2} \vec{H}_{t+1}^B}$
12	angle between the A vector and the vector from A middle to B tail	$\vec{T}_t^A \vec{H}_t^A \widehat{\frac{\vec{T}_{t+1}^A + \vec{H}_{t+1}^A}{2} \vec{T}_{t+1}^B}$
13	angle between A and B vectors	$\vec{T}_t^A \vec{H}_t^A \widehat{\vec{T}_t^B \vec{H}_t^B}$

In the formulae, H and T refer to the head and base of the tail point, respectively. Indexes A and B indicate if the point belongs to the studied animal A or to its conspecific B, and t refers to the studied frame number.  $\|\cdot\|$  is the Euclidian norm.

We therefore aim at extracting the maximum number of ICs which preserves the components found when fewer ICs are extracted.

ICA extracts a set  $IC(n)$  of  $n$  ICs.  $IC_n^i$  denotes the element number  $i$  of  $IC(n)$ . We need to estimate in which proportion the elements of  $IC(n-1)$  are preserved in their original form in  $IC(n)$ . To consider that an IC of  $IC(n-1)$  is well preserved, it should be strongly correlated with one of  $IC(n)$  and the least possible with the other ones. For this purpose, we designed a criterion to evaluate the IC preservation. The preservation of an  $IC_{n-1}^i \in IC(n-1)$  in  $IC(n)$  is estimated by the function:

$$F(i, n) = \left[ 2 \max_{j \in \{1, n\}} \left( Cor(IC_{n-1}^i, IC_n^j) \right) \right] - \sum_{j=1}^n Cor(IC_{n-1}^i, IC_n^j)$$

We aim to select the number  $n$  of ICs preserving the most  $IC(n-1)$ . For this purpose, the ICA is used to generate an increasing number of ICs, beginning with 2. The chosen number will be the first local maximum of the mean:

$$C(n) = \frac{\sum_{i=1}^{n-1} F(i, n)}{n-1}$$

### 3.3. Gaussian mixture model based clustering

We now process previously generated ICs separately. In order to describe qualitative behavioural expressions, all time points need to be clustered based on this quantitative descriptor. As an IC distribution is non-Gaussian, we choose a one-dimensional GMM based clustering [11], which ensures to model the IC by more than one Gaussian distribution (GD) and to generate more than one behavioural category. The GMM is fitted by maximizing the likelihood  $\mathcal{L} = \prod_{i=1}^T \sum_{j=1}^N p_j \mathcal{N}(x_i, \mu_j, \sigma_j^2)$ , where  $T$  and  $N$  are respectively the number of data-points and GDs and  $p_j \mathcal{N}(x_i, \mu_j, \sigma_j^2)$  the weighted probability density of  $x_i$  in the  $j$ -th GD. To perform this computation we use the expectation maximization algorithm.

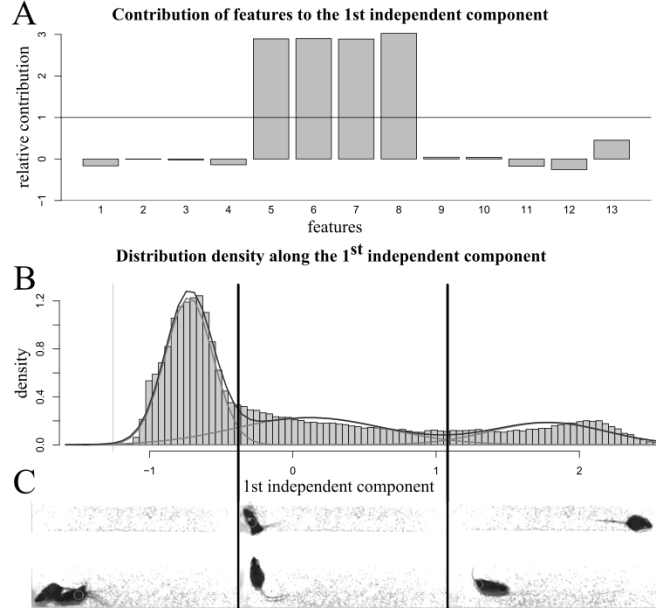
In order to prevent over-fitting of the data-set, we restrain the number of GDs mixed in the model. As the goal of the computed models is to allow a reliable clustering, we select the number of distributions that fits the best to the data while mixing the least possible the clusters. For this purpose, several GMM are fitted with an increasing number of GDs, beginning with 2. We select the processed model by maximizing the function  $\prod_{i=1}^t p_{k(i)} \mathcal{N}(x_i, \mu_{k(j)}, \sigma_{k(j)}^2)$ , where  $k(i)$  denotes the number of the GD which gives the highest density probability for  $x_i$ . This penalizes the models with respect to the overlapping of these GDs, and constrains the number of GDs. For each IC, the GMM producing the first local maximum of this criterion will be used.

The equality points of the probability of two GDs are defined as thresholds segmenting behaviours along the IC (Figure 1B). For each IC, all time points are clustered in a certain number of behavioural events. An animal will thus exhibit as many behavioural states at each time point as the automatically selected number of ICs.

### 3.4. Segmented video editing

Thanks to the results provided by the GMM, we retrieve the events that are exclusive, and therefore go back to the original footage to display the video corresponding to this axis of the classification. As those events can be very brief (less than a second to a few seconds), we created a program in Icy [12], that automatically edits the source video. This allows to display the final result of the classification. For each threshold of each IC, we perform two editing. The first one regroups all the sequences during which the value on the IC is inferior to the threshold. The second one regroups the rest, the ones with a value superior to the threshold. These videos are thus successions of numerous sequences where the animals are each time exhibiting the same behaviour.

We put those two jumping-cut videos side by side (Figure 1C), to help an expert watching several times the same events in order to be able to affect a ‘‘humanly readable’’ label to each event found by the program. We also display the mix of features implied in the ICs (Figure 1A).



**Figure 1: A. Contributions of features relative to the first IC. B. Distribution density along the first IC. C. Auto-edited frame examples (2 mice – contrasted for printing purpose).**

## 4. EXPERIMENTAL RESULTS

### 4.1. Biological data

We studied the social behaviour of 13 *Shank2*<sup>-/-</sup> and 16 wild-type female mice. Behavioural experiments were approved by the ethical committee CETEA Institut Pasteur n°89. The subject mouse was placed in a test cage 30 minutes before an unknown female was introduced [13-14]. Their 4-min interaction was video-recorded from the top. Mice were then tracked using Mice Profiler [8]. We obtained the (x,y) location of the head and base of the tail of the two mice at 15 frames per second.

### 4.2. Implementation

The ICA and the GMM were conducted with R software, using respectively the icafast function from ica package and the Mclust function from mclust package.

Based on the previously described constraints, we used ICA to extract  $n=7$  ICs, each of which segmented by 1 to 2 thresholds. We focus on behavioural components frequently expressed, by neglecting thresholds that isolate less than 2,5% of the frames.

We also perform a cross-validation, on 10 sub-sampling of the original data-set. The algorithm provided sets of 7 ICs, similar to the one generated with the complete data-set, each clustered by the same number of thresholds in the same ranges of values.

**Table 2. Set of behavioural events defined by the new method.**

behaviour name according to editing	IC	cluster
contact	1	<T1
intermediate distance	1	$\in [T1, T2]$
long distance	1	>T2
A behind B	2	<T
A faces B	3	>T
A goes away from B	4	<T
A comes toward B	5	<T
parallel head to tail axis same way	6	<T1
parallel head to tail axis opposite ways	6	>T2
parallel trajectories same direction	7	<T1
parallel trajectories opposite directions	7	>T2

A refer to the subject animal and B to its conspecific, for each IC the threshold T or the two thresholds T1 and T2 allow to locate the clusters which are either below or above them.

### 4.3. Method validation: comparison to Mice Profiler

We found 7 behaviours homologous to the elementary events present in the repertoire of Mice Profiler [8]. (correlation rate in brackets) Contact (95%), A behind B (93.2%), A faces B (92.9%), A escapes B (87.2%), A follows B (80.7%), beside same way (85.9%) and beside opposite ways (83.3%).

Two additional behaviours were detected with the 7<sup>th</sup> IC (Table 2), see biological results. The algorithm thus allowed to discriminate between behaviours that were not previously expected.

### 4.4. Biological results

Significant genotype-related differences were observed in 4 behavioural events (table 2). *Shank2*<sup>-/-</sup> females spent significantly: more time at intermediate distance of the conspecific; less time facing it; more time going toward it; and more time going away from it in comparison with wild-type littermates (Wilcoxon tests, with Bonferroni correction for 13 tests, with respective P-values: 0.033; 0.016;  $1.7 \times 10^{-5}$ ;  $6.2 \times 10^{-3}$ ). The increase in movement behaviour is coherent with the diagnosed hyperactivity [13] and the reduced facing to the conspecific matches with the lack of social interest [14].

We also unveiled a new behaviour: animals walking in parallel trajectories, with or without contact. The behaviours related to parallel trajectories do not have any homologous events described in Mice Profiler. These behaviours were thus unsuspected before we used the unsupervised algorithm to discover them, and will be further investigated.

## 5. CONCLUSION

In this paper, we detailed a new algorithm able to classify social behaviours without human supervision. Compared to previous work, we added the capability for the classifier to label several different independent behaviours occurring simultaneously. More complex behavioural states can now be described by the co-occurrence of those behaviour.

We also showed that the classifier revealed new events that were not labelled before, such as the “parallel trajectories” event. Those new behaviours can now be used as new indicator of restoration of social behaviour in *Shank2*<sup>-/-</sup> female mice, and their study in other models of neuropsychiatric disorders is likely to be informative.

In our future work, we will increase the number of features to reveal more behaviours. We also hope that this method will benefit from being applied to other data set consisting of other kind of features, especially future tracking extracting more detailed outputs.

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