Performance assessments of semi-automated noninvasive seizure detection in Scn8a mice

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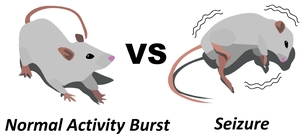
I. INTRODUCTION

Motivation: Preclinical epilepsy research often requires assessments for the number and severity of seizures in mouse model studies. This is typically accomplished through time-consuming tedious human effort to review EEG/EMG signals or video recordings. As a result, this also limits the number of mice studied in an experiment.

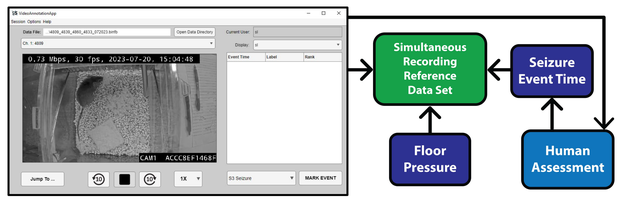
Approach to Address Problem: Develop automatic noninvasive prescreen algorithms for mouse seizure events based on sudden changes in activity/motion patterns captured by cage-floor pressure sensors. Detection algorithms are designed to miss very few seizure events, and combined with efficient visualization interfaces, human observers can jump to detected events and remove the false positives. Thereby greatly reducing the time and expense for assessing experimental results.



This poster summarizes results from machine learning studies to assess the feasibility of a time-saving method for the assessment of epileptic seizures in mice.

II. METHODS

Experiment: Feasibility was tested using 10 Scn8a mice (5m/5f, 1-3 months old) that exhibited seizures. These were continuously monitored for several days with piezoelectric sensors (located beneath the cage floor) and simultaneous video recordings.



- Video recordings were synchronized with of the cage-floor piezoelectric pressure signals and human observers labeled all observed seizure events by marking the event times that were stored in a database for the training and testing of machine learning algorithms.
- Six piezoelectric signal features related to signal energy and coherence were extracted over 2-second intervals with 1-second increments (50% overlap). These were examined to determine the feature with the best response to seizure onsets without regard to other non-seizure arousal responses (Phase 1).
- Feature sequence regions were then defined based on sustained high values from smoothed versions of feature sequences (Phase 2).
- Patterns of features within and around the region were characterized with region-based features and machine learning algorithms were trained and tested to regress to likelihood values that maximized the seizure detection rate while minimizing false positives.
- The dataset provided many more non-seizure arousals. To use data efficiently, a 5-fold cross-validation train and test method was used in conjunction with a bootstrapped sampling strategy for performance estimation.

III. TEAGER ENERGY (TE) AND SEIZURE LIKELIHOOD ESTIMATES

A locally scaled Teager Energy (TE) feature was found to have the most consistent response to seizure events (more than regular energy, line length, and signal coherence). The 3 main phases of the full algorithm are described below.

Phase 1: Arousal Detection:

- Compute TE over 2-second intervals, with 1 second overlap.
- Divide TE by lower quartile values from 1-minute neighborhoods (Blue Lines in plots below)
- All locally scaled TE peaks were considered arousals and potential seizure events

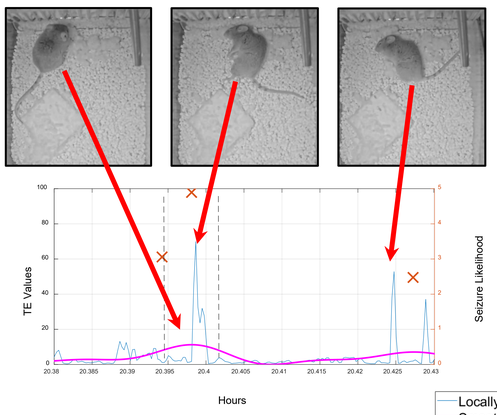
Phase 2: TE Sequence and Seizure-Related Features

- Low-Pass locally normalized TE time series (magenta line)
- Define event region to be where the low-pass signal drops to 75% of its peak value (black dashed vertical lines denote region boundary)
- Extract 6 features from and around region: Mean and Peak TE; Peak TE Relative position in region; TE region skewness; Ratio of TE standard deviation over TE mean; Ratio of TE standard deviation in bout area over TE standard deviation over 8-second interval starting 8 seconds beyond end of bout area

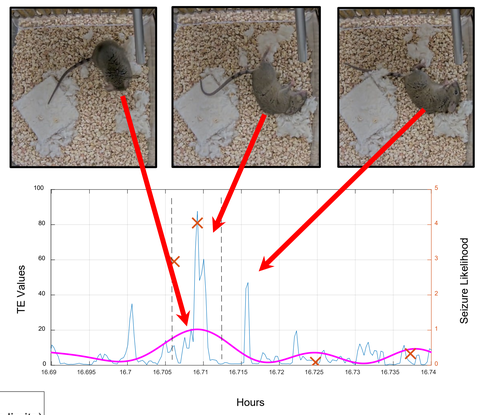
Phase 3: Likelihood regression:

- Regression algorithm derived with an Optimizable Ensemble Bagged Decision Tree.
- Ensemble decision tree regressor on 6 sequence-based estimated seizure likelihood, where 0 implies low likelihood and 5 implies high likelihood
- Implemented in MATLAB R2023b (MathWorks, Natick, MA)

Seizure Example:

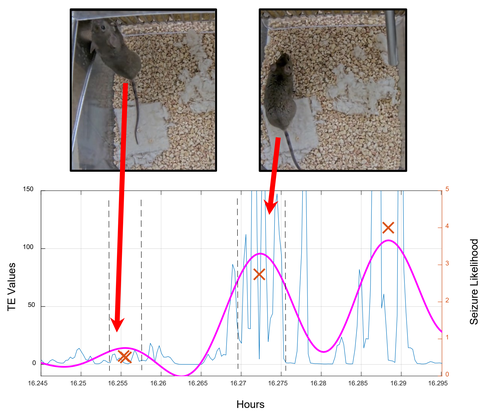


Seizure Example:

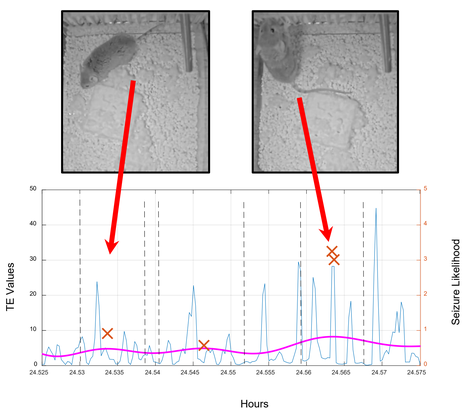


Locally Scaled TE Values
Smoothed TE (for arousal region limits)
Seizure Likelihood Values

Rearing and Locomotion Example:



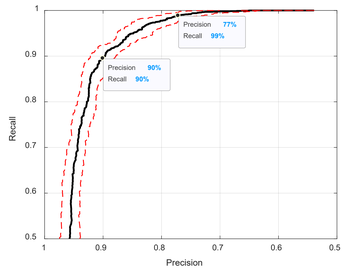
Rearing and Locomotion Example:



IV. PERFORMANCE RESULTS

Train and test samples were selected from **387 video verified seizures** and **7907 non-seizure arousal events** as determined by peak TE points (about 800 per day).

Ten bootstrapped 5-fold cross-validation train-and-test sequences were performed with 200 randomly selected seizure and 200 randomly selected non-seizure events. A bagged decision tree with 127 learners was used in each resampling. A recall and precision curve was created from the test outputs from each cross-validation by sweeping a threshold over the validation likelihood values and computing the recall and precision pair for each threshold. The average curve was computed over the 10 bootstrapped results and the 95% confidence values were also computed and shown with the dashed red lines.



Likelihood Threshold Values (0-5)

Expected Recall	Threshold	Precision
85%	3.32	92%
90%	2.67	90%
95%	1.56	85%
99%	0.78	77%

A linear regressor was also developed and tested with the same sampling procedure as above and for 90% recall it only achieved a 68% precision and at 95% recall, it dropped to 60% precision.

V. CONCLUSIONS

- Results demonstrate the feasibility of using cage-floor pressure sensors to detect sudden changes in activity as a screening tool for assessing the number of seizures in mice to greatly reduce the number of video sequences needing to be viewed and labeled.
  - **Example:** For a desired 90% seizure detection rate, a resulting 90% precision implies that 10% of the detected arousals that are not seizures will need to be viewed along with the true detected seizures. If the first pass detection resulted in 1000 arousal detections, only 100 of those will need to be viewed for false positive rejection after the second pass detection.
- A similar video interface used to observe and label events can present likelihood values with timestamp to quickly advance video to the detected positions and skip over the low likelihood portions of the video.
- The locally scaled TE and its regions were superior to regular energy and line length features to obtain higher recall and precision values. This likely due to the tremoring during the seizure events that TE is more sensitive to given the high frequency emphasis in its computation.
- Most seizures in this study were tonic-clonic, and algorithms learned these patterns. For other types of mice/seizures, a new algorithm may need to be trained.

VI. ACKNOWLEDGEMENTS

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