Application of machine learning methods in non-invasive, automated seizure detection in rats

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I. INTRODUCTION

Motivation: Preclinical epilepsy research often requires methods to assess the number and severity of seizures in animal studies. This is typically accomplished through time-consuming and tedious review of electroencephalographic or video recordings with human observation and scoring.

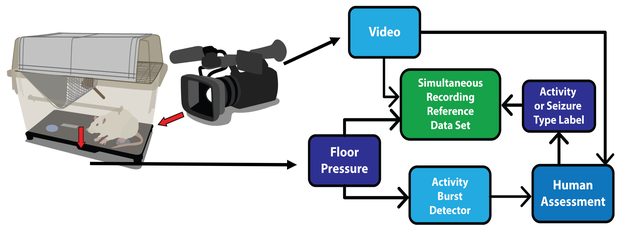
Approach to Address Problem:
Develop an automatic prescreen algorithm for seizure events based on sudden changes in activity captured by cage floor pressure sensors. Use signal features related to activity bursts from seizures and those of normal activity changes to detect a high percentage of actual seizures, while limiting the number of false positives.

Normal Activity Burst ***Seizure***

Apply machine learning to train an algorithm to regress activity burst features to likelihood values, such that a trade-off between false negatives and false positives can be adjusted via a threshold the user can set based on either a desired detection or false positive rate.

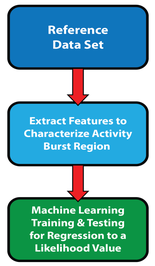
II. METHODS

Experiment: Feasibility was tested with 37 adult Wistar rats, previously treated with lithium chloride/pilocarpine to induce acute status epilepticus. These were continuously monitored for several weeks using piezoelectric sensors (located beneath the cage floor) and simultaneous video recording.



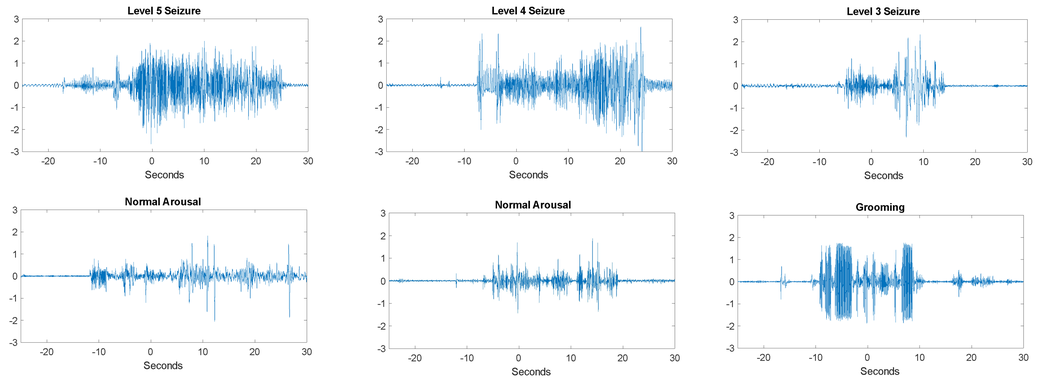
Recordings of the piezoelectric signals were processed to identify a set of candidate seizure events (identified by detecting sudden bursts of activity in the pressure signal). These candidates were then labeled based on a manual review of the video according to observed behavior (Racine seizure level, grooming, arousal, etc). Labeled events were then compiled into a reference data set (**1289 verified seizures**, Racine level 3-5; **1481 other behaviors** such as arousal or grooming) to train and test machine learning algorithms.

Signals were processed to derive a line length feature time series in 1-second intervals, and peaks in that series were used to identify activity bursts throughout the recording. Then 9 additional features were extracted in the regions surrounding these peaks, and machine learning algorithms were applied to regress a likelihood value for discriminating seizures from non-seizure events using a five-fold cross-validation training and testing cycle.

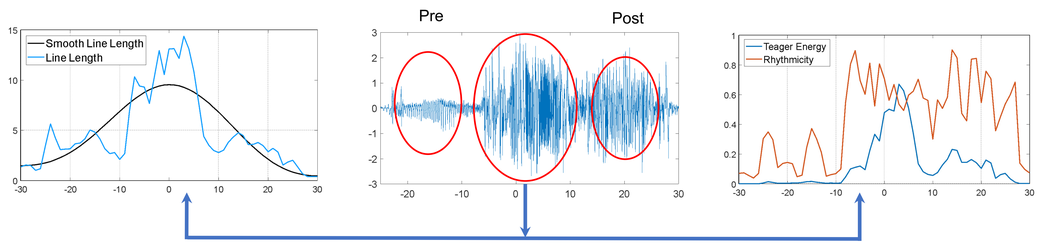


III. FEATURE EXTRACTION

Examples of pressure signal regions from activity bursts associated with seizure and non-seizure events:



Activity burst region



Activity Burst Detection:

- Compute signal line lengths over 1-second intervals
- Scale values by exponentially weighted previous values after median filtering to create larger amplitudes for sensitivity to sudden changes relative to preceding signal

Candidate Region Segmentation:

- Select largest 100 line-length values per day
- Smooth the line length sequence
- Find points where smoothed line lengths drop below 75% of the peak to determine activity burst region
- Find an 8-second segment before the burst region (pre)
- Find an 8-second segment after the burst region (post)

Regression algorithm derived with an Optimizable Bagged Decision Tree:

- Nine features used to predict seizure level score interpreted as likelihood, where 0 implies no seizure.
- Implemented in MATLAB R2023a (MathWorks, Natick, MA)

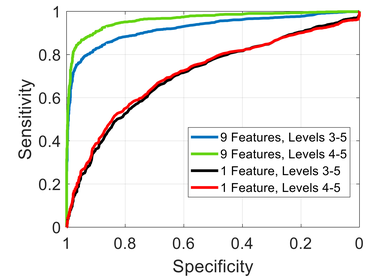
Nine Features Related to Burst Region:

- High-frequency energy (**Teager Energy**) based features consisting of statistics within the burst region and ratios relative to the pre- and post-regions.
- **Line Length** based features consisting of statistics on the peak values and shape distribution in activity region.
- **Regularity/Rhythmicity** properties of the pressure signal in activity region.

IV. RESULTS

For all test likelihood predications pooled over the 5-fold cross-validation train-and-test sequence, receiver operating characteristic curves were generated by sweeping a decision threshold over all values while computing the number of seizure detection agreements (sensitivity) and non-seizure detection agreements (specificity) for each threshold value.

1304 seizures with levels 3 through 5 were used with **1482 non-seizure events** in a 5-fold cross-validation train-and-test procedure with 9 activity region-based features in an ensemble decision tree regression algorithm. Results were compared with a simple linear regression using the maximum line length value used for the initial activity burst detection.



Seizures levels 3 to 5

Threshold for Sensitivity	Resulting Specificity 9-Feature	1-Feature
0.8	0.92	0.46
0.9	0.76	0.22
0.95	0.51	0.074

Seizures levels 4 to 5 only

Threshold for Sensitivity	Resulting Specificity 9-Feature	1-Feature
0.8	0.98	0.46
0.9	0.91	0.22
0.95	0.82	0.065

V. CONCLUSIONS

- Results demonstrate the feasibility of using pressure sensors to detect sudden changes in activity as a screening tool for assessing the number of seizures in rats.
- The regression of activity-based features to a likelihood approach enables the use of a simple threshold to adjust the trade-off between an acceptable loss of true seizures and the number of false detections that need to be examined by video during a final screen, thus saving a significant amount of time over having to examine the entire recording.
- While baseline normalized maximum line length values are useful for selecting an initial set of candidate seizures, this feature does not perform well in discriminating between activity burst from non-seizure and seizure events. Less than 1% of the non-seizures are rejected when using a threshold corresponding to a 95% seizure detection rate. There is not much difference in performance when the weaker, level 3 seizures are not considered.
- The use of additional features that describe patterns around and during the activity burst region dramatically reduces the number of false detections that need to be screened out by human observation. At a 95% seizure detection level, 51% of non-seizure events are properly rejected, effectively reducing the time needed to screen for seizures by half. When level 3 seizures are not considered, 82% of the normal activity bursts are rejected.

VI. ACKNOWLEDGEMENTS

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