Automated interactive tool for reliable seizure detection in rat and mouse models of genetic and acquired epilepsies

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Prolonged video-EEG monitoring in chronic epilepsy rodent models has become an important tool in pre-clinical drug development of new therapies, in particular for anti-epileptogenesis, disease modification and drug resistant epilepsy.

Despite the fact that most of the EEG acquisition software packages contain automatic seizure detection modules, many researches still prefer to identify the seizures by themselves, visually inspecting the EEG and the video, which is, especially in case of prolonged recordings, very time-consuming and tedious process.

THE ALGORITHM

We have developed an *easy to use, reliable, computational tool* for *detection of electro*graphic seizures from prolonged EEG time series in rodent models of epilepsy - our

ASSYST Tool

The tool utilizes an advanced time-frequency analysis which detects the EEG segments with excessive activity in certain frequency bands. This is achieved by calculating a special measure, **Spectral Band Index** (**SBI**), as a function of time, using running time window.

The processing algorithm has two main steps:

In the first step, performed by the computer, the program calculates the spectral band index and based on it selects the events of interest. It also automatically defines the starts and ends of the events.

In the second step user visually examines the selected events and classifies them as seizures, artefacts or other events. User can also refine the starts and ends of the events and make annotations/comments to each event.

In addition to these main steps there are several auxiliary processing steps, such as Artefact removal and Parameter control.

We found that ictal EEG in rodent models contains a strong component with frequency about 20-21 Hz, and that this component is not present in the inter-ictal EEG (i.e., it is specific for seizures only).

This peculiarity comes from the frequency composition of single discharges, or individual spike wave complexes, within the seizures in these animals.



Here we show arbitrarily taken examples of single spike-wave complexes from these rat models and their amplitude frequency characteristics.

It is evident that in all cases the frequency spectrum has a single expressed peak at frequency close to 20-21 Hz.

An example of SBI plot of artefact-free recording.

This animal had 4 seizures during the recording period, all of them are clearly seen in the spectral







band index plot.

]	The ratio of smallest ictal SBI to largest inter-ictal SBI is > 10
this gives	a very safe margin for distinguishing seizures from inter-ictal events

The spectral band index calculated for the narrow frequency band around 20-21 Hz clearly distinguishes the seizures. Post-SE model, 12 days long recording.



PERFORMANCE

The tool was tested on several spontaneously seizing, chronic epilepsy rat and mouse models.

The records contained in total almost **19 500** seizures. The program detected 100% of seizures in all records in all models. In several cases the program found seizures that had not been previously annotated by conventional EEG/VEEG assessment method. These events were verified afterwards by expert and were confirmed to be seizures.

> ASSYST allows the user to classify the identified epileptiform events into different user-defined categories (e.g., short or long seizures, spike-wave discharges (SWD), interictal spikes, etc.). The classified events can be saved into a text or Excel file.



MODEL RATS	No of Animals	No of So Annotated	eizures Detected
Post-SE (status epilepticus) model of temporal lobe epilepsy	119	989	993 (+4)
FPI Fluid percussion injury model of post-traumatic epilepsy	9	43	49 (+6)
GAERS Genetic Absence Epilepsy Rat from Strasbourg	41	8733	8733
WAG/Rij Wistar Albino Glaxo/Rijswijk model of absence epilepsy	14	825	825
Total for rats	183	10590	10600

MICE

FPI Fluid percussion injury model of post-traumatic epilepsy	7	305	305
Mutant mouse model on a variant of strain backgrounds in the gene Gabrg2	4	55	55
Mutant mouse model on a variant of strain backgrounds in the gene Gria4	8	601	601
Mutant mouse model on a variant of strain backgrounds in the gene Scn8a	4	453	453
Other mutant mouse models	10	7457	7457
Total for mice Total (rats and mice)	33 216	8871 19461	8871 19471

Major factors that ensured effective performance of the algorithm:

An advanced technique of short term spectral

- **1.** analysis based on original Similar Basis Function (SBF) algorithm, which, unlike conventional FFT
 - is applicable to short time windows
 - may calculate the Fourier transform within arbitrary frequency band of interest
 - with arbitrary frequency resolution

Discovery of specific frequency domain peculiari-2. ties of epileptiform activities in the brains of ro-

dents

Using our tool, researchers will reduce the time needed for the identification of sei**zures** in long term EEG recordings **by** >95%.

Max processing time per 1 day record	5 min
Min processing time per 1 day record	0.1 min

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ASSYST may be used not only for seizure or SWD detection, but also for detection of other epileptiform activity, such as interictal spikes or high-frequency oscillations (HFO).



CONCLUDING REMARKS

• The ASSYST program *significantly reduces the* processing time, while the final decisions are still made by the expert user user; the program helps to focus the user only on those fragments of the EEG that might contain seizure or other epileptiform activity.

• The tool is *easy to use*, as it requires minimal user intervention in setting the processing parameters.

• The program *is reliable* – in almost 20000 seizures processed there there were *no seizures missed*.

• We see the ASSYST program as a substantial aid that will help researchers to significantly facilitate the process of seizure identification in long-term EEG recordings in rats (e.g., pre-clinical research and therapy development).

