3rd Biosignal Challenge 2019

Identification of seizure onset zone in invasive EEG

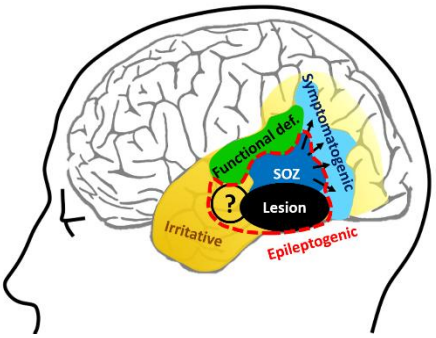
1st price 800 USD

2nd price 400 USD

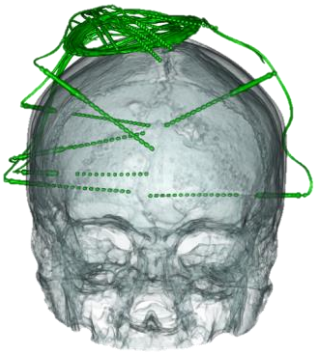
3rd price 200 USD

Introduction

Epilepsy is a group of neurological disorders that affects 0.5-1% of the population in developed countries. Focal epilepsy has been clinically defined as an ability of localized area of one hemisphere to produce seizures. The traditional notion of epileptic focus was replaced by the epileptic network concept, which describes interactions between sub-networks [1], [2] known as epileptic zones: the seizure onset zone (SOZ), the irritative zone, the epileptogenic lesion, the functional deficit zone, symptomatogenic zone and the epileptogenic zone. One-third of patients do not respond to antiepileptic drugs. The alternative approach of treatment is neurosurgical removal or disconnection of the epileptogenic zone (EZ).



The most reliable technique to determine EZ is invasive EEG (iEEG) exploration, although the spatial covering by the electrodes is sub-sampled and the EZ is therefore typically estimated based on a combination of many neurological examinations. The iEEG provides a high temporal resolution (<1 ms) of the brain activity in the close vicinity to the implanted electrode. Visual evaluation of iEEG is if focused on the identification of abnormal epileptiform waveforms in signals (shape, amplitude, frequency). The estimation of complex interactions between electrodes (brain areas) is possible only by using computational techniques. The main goal of the Biosignal Challenge 2019 is to develop an algorithm capable of detecting seizure onset time and localizing the area of the brain in which seizure originates - seizure onset zone (SOZ). The epilepsy surgery can result in seizure freedom in the majority of patients [3], [4]. Unfortunately, epilepsy surgery fails in more than 20% of cases.



Goals:

1) The development of the effective technique to detect epileptic seizures
2) Mark the exact seizure onset time
3) Identify the seizure onset zone (SOZ), i.e. iEEG channels that initiate seizures

Data and methods

Thirty-two patients (17 males, 15 females) with pharmacoresistant epilepsy based on malformation of coetical development (FCD: 11 type I, 18 type II, 3 type IIIa) underwent long-term iEEG monitoring as part of their presurgical evaluation. The age of the patients was 27±13 years (from 7 to 55). The average duration of epilepsy was 16±10 (median 13,5) years. The mean duration of postsurgical follow-up was 4±3 (median 3) years. Seizure outcome was assessed according to Engel's classification at the last follow-up (21 Engel I – seizure free, 11 Engel II-IV – seizure persistent) [5]. Data collection was approved by the institutional ethics committee and informed parental consent was obtained.

Invasive EEG signals (up to 128 channels) from subdural (ECoG) and/or depth (sEEG) macroelectrodes (Integra, Plainsboro, NJ, USA and Dixi Medical, BESANCON Cedex, France) were recorded by systems Stellate Harmony (sampling frequency *fs*=1 kHz, *n*=17) or Natus NicOne (fs=512 Hz, *n*=15). The recording setups were powered by 230V/50Hz. Contacts containing a large number of artefacts were manually removed after visual inspection. On average, 5.5±4.6 (median 5) contacts per patient were removed from 95.6±35 (median 107.5) recorded contacts. The dataset contained 300 seizures in total (9.3±8.2, median 7 per patient).

Definition of Epileptic Zones

The SOZ was defined as the area of the brain with the earliest occurrence of ictal discharges/activity, that differs from pre-ictal baseline activity [6]–[8]. Seizure onset times and delineated margins of individual zones were defined and represent an agreement between at least two clinicians who were involved in the presurgical diagnostic work-up. The precision of the seizure onset marking varies through the definition in 3 seconds tolerance. The seizure activity can propagate with a time delay (ms) to other regions by a neural pathway or affect another part of the brain (seconds), see Figure 1.

The irritative zone is defined as brain area which generates sharp (<100 ms) interictal epileptiform discharges (IED) in inter seizure period. Irritative zone often overlaps with SOZ [9].

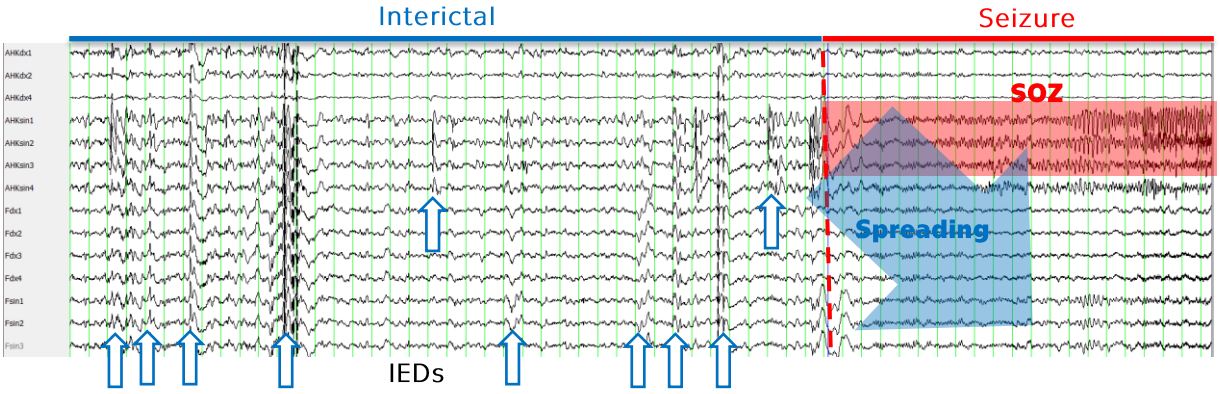


Figure 1: Example of a seizure in a reference montage. Interictal periods can contain IEDs - sharp non-seizure activity (arrows). The seizure activity is characterised by a change of iEEG in respect to the background interictal period. Seizure activity is often accompanied by an increase of signal energy in high frequency bands. Green lines mark a one-second window.

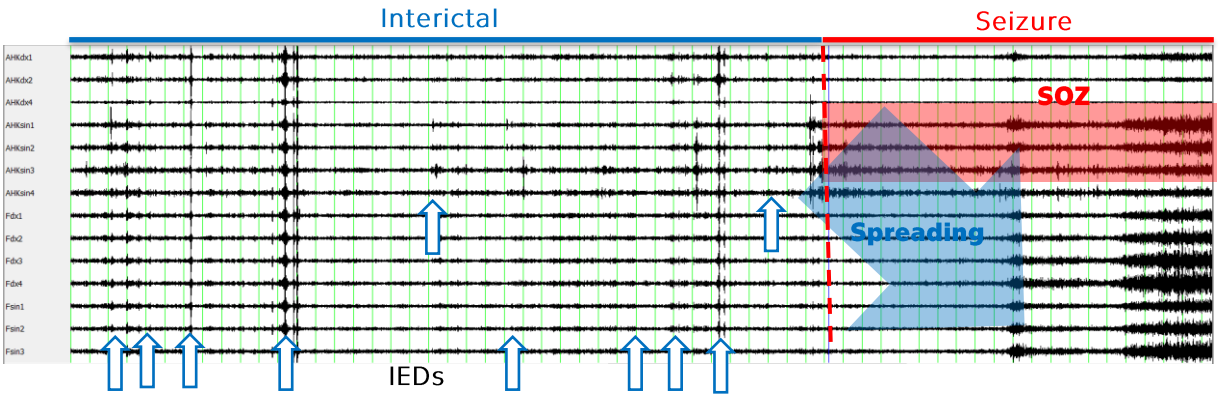


Figure 2: Example of a seizure in reference montage filtered by high-pass filter >50 Hz. Interictal periods can contain IEDs - sharp non-seizure activity (arrows). The seizure activity is characterised by a change of iEEG in respect to the background interictal period. Seizure activity is often accompanied by an increase of signal energy in high frequency bands. Green lines mark a one-second window.

TIP 1: For the detection of the seizure onset, focus on the increase in higher frequency activity with a longer duration than IED. However, some seizures can start even with low-frequency activity.

Detection validation

Your detected seizure onset time will be compared with clinical markers and the average absolute difference for individual patient will be computed. The final inaccuracy Δt will be averaged from all patients (30% of final score). If the algorithm does not detect the seizure in a dataset, the difference will be penalised by 60 s. The computational demands will make 10% of the final score.

$$\Delta t = \frac{1}{P}\sum_{p=1}^{P}\left(\frac{1}{N(p)}\sum_{n=1}^{N(p)}\left|t_{seizure}(p,n) - t_{detection}(p,n)\right|\right)$$

P is total number of patients indexed by p; $N(p)$ represents total number of seizures of patient p, $t_{seizure}$ is seizure onset time marked by clinician, and $t_{detection}$ is time of your seizure onset detection.

The clinically marked SOZ is compared to SOZ identified by you. The overlap is tested by standard methodology using sensitivity (*SEN*) and precision by Positive Predictive Value (*PPV*) [11]–[13]: true positive (*TP*) – number of matched channels, false positive (*FP*) – number of channels marked outside the SOZ, false negative (*FN*) – number of unmarked SOZ channel. Sensitivity (*SEN*) represents the agreement of active-nodes with SOZ channels, and *PPV* is the percentage of active-nodes within SOZ. The final performance is assessed from the average of SEN and PPV (60% of final score).

$$SEN = 100 \times TP/(TP+FN)\ (\%)$$

$$PPV = 100 \times TP/(TP+FP)\ (\%)$$

$$PERFORMANCE = (SEN+PPV)/2\ (\%)$$

TIP 2: Optimize your algorithm to achieve the best performance as a trade-off between *SEN* and *PPV*.

iEEG data:

We randomly selected 1/3 of individual patient seizure recordings (but max. three) and collected them to training dataset, in total 73 seizures. Remaining part will be used for blind testing of your algorithm. The patient's ID prefix all files from P01* to P32*.

~~https://owncloud.cesnet.cz/index.php/s/9KWCNakiQOUuGDc~~ (Incorrectly stored SOZ markers, we apologize)

https://owncloud.cesnet.cz/index.php/s/Rn0M68HIaRijjpm

Data contain three minutes multichannel iEEG, that is composed of two-minutes pre-ictal and one-minute that follows the seizure onset. Seizure duration varies from five seconds up to few minutes. Therefore, some files cover whole seizure with a post-ictal period in the last minute. The iEEG was recorded and stored in referential mode (unipolar). Each channel is named (header.label), a neighbour shares text prefix+number (e.g. A1, A2, A3..., next B1, B2, B3...).

TIP 3: To remove common mode rejection of floating reference or reference contamination you can subtract the common average reference of all channels.

TIP 4: The best approach is to recalculate the original signals to bipolar ones (info in structure header.labels_bipolar). The identified SOZ channels must by inversely recalculated to referential montage and localization can be blurred, Table 1. It is a trade-off between the quality of signals and precision.

Seizure file container (e.g. P01_seizure001.mat):

d ... (time×channel) matrix of iEEG records. Each iEEG channel is in column
t ... (time×1) vector of time baseline in seconds
fs ... sampling frequency in Hz
sot ... seizure onset time in seconds
soz ... (n×1) vector of channels clinically marked as a seizure onset zone corresponds to columns in "d "
iz ... (m×1) vector of channels clinically marked as an irritative zone corresponds to columns in "d "
header.label ... (channel×1) cell array contains string name of channels (e.g. Ga2, Ga3, Ga4 ... FM1, FM2, FM3, FM4)
header.labels_bipolar ... (channel×2) cell array contains information for the recalculation from the referential to bipolar montage. The first column contains the bipolar name of electrode pair, the second column marks the column in „d". E.g.: The bipolar pair Ga2-3 is a difference between channels Ga2 and Ga3. d_bip(:,1)=d(:,header.labels_bipolar{1,2}(1)) - header.labels_bipolar{1,2}(2). **Warning:** If you apply the bipolar recalculation, the identified SOZ channels must be inversely recalculated to reference montage (e.g. the identified SOZ in bipolar channel 1 could be in both referential channels, i.e [1 2]). It leads to blurring of localization of SOZ.

Table 1: Blurring effect of analysis in referential vs. bipolar montage

Original data		Bipolar data		Result
Referential	Ref. channel	Bipolar	Ref. channel	Ref. channel
A1	1	A1-2	1-2	1
A2	2	A2-3	2-3	2
A3	3	A3-4	3-4	3
A4	4	A4-5	4-5	4
A5	5	B1-2	6-7	5
B1	6	B2-3	7-8	6
B2	7	B3-4	8-9	7
B3	8	B4-5	9-10	8
B4	9			9
B5	10			10

clinically marked SOZ
result of analysis from bipolar montage in required reference montage

TIP 5: Download standalone application Alenka 0.9.9 for the visual inspection of iEEG signals (GPU required). The software allows to read the mat-file, filter the signals and show signals in bipolar montage. The functionality in all platforms is not guaranteed.

https://github.com/machta/Alenka/releases

HF: frequency of high pass filter
LF: frequency of low pass filter
Referential to bipolar montage: Select the recording montage in red square. In Montage menu select "Add Bipolar Montage (neighbours only)".
Ctr+Scroll: Increase/decrease selected chanel amplitude.
Shift+Scroll: Increase/decrease all channels amplitude.
Alt+Scroll: Zoom time baseline.

Requirements:

The student teams (max. three persons) send the application to e-mail biosignalchallenge@fel.cvut.cz with full name(s), school/university affiliation, a degree of education. The registration will be closed on March 15, 2019 or over cross 50 participants. The Biosignal Challenge 2019 is an international competition for students from the European Union or the United States of America. We reserve all rights to cancel the competition without any financial refund.

Your algorithm must be programmed in MATLAB software (2015b-2018b) and uses only commercial toolbox in a list below or uses functions with free licences (GNU etc.). Your solution sends to email biosignalchallenge@fel.cvut.cz up to May 13, 2019 and must contain:

- MAIN_fun2019.m
- All extensions (functions, tools, supported data files etc.)
- Short report (PDF) of (1) algorithm functionality and used MATLAB version, (2) computational demands, and (3) results on selected/full training dataset (precision of seizure onset detection, SEN, PPV)

The main function have to be in form:

```
[sot,soz]=MAIN_fun2019(data)
```

sot ... is relative time of detected seizure onset in seconds from start of signal
soz ... indexes of column correspond to data.d identified as seizure onset zone
data ... structure of data container, e.g. data=load('P01_seizure.mat')

Supported toolbox:

- Bioinformatics Toolbox
- Control System Toolbox
- Curve Fitting Toolbox
- Deep Learning Toolbox
- DSP System Toolbox
- Fuzzy Logic Toolbox
- Image Processing Toolbox
- Model Predictive Control Toolbox
- Optimization Toolbox
- Parallel Computing Toolbox
- Signal Processing Toolbox
- Statistics and Machine Learning Toolbox
- System Identification Toolbox
- Wavelet Toolbox

TIP 6: All participant can request MATLAB licence in the official webpage:

https://www.mathworks.com/academia/student-competitions/biosignal.html

Expected results

The clinical assessment is accepted as the gold standard, but the evaluations are strongly subjective influenced by many factors (diagnose, results of imaging, anatomy etc.). Therefore, it may not fully agree with the objective results of automated detection.

In our laboratory, we have achieved the detection inaccuracy of the seizure onset 1.87±4.45 (median 0.44) seconds.

The ability to localize SOZ has been 70% performance (*SEN*=77% and *PPV*=57%). Although the performance looks low, the results better correlate with post-surgical outcome (p<0.01).

TIP 7: Keep Calm and Carry On!

Acknowledgement

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