Tools for convulsive seizures and interictal spikes detection

Daniel Diaz-Arce, Anis Ghouma, Pierre Guetschel, Théodore Papadopoulo, Massimo Mantegazza, Fabrice Duprat

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1 Introduction

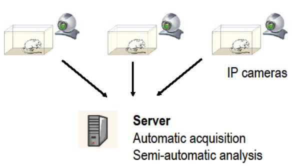
Epilepsy is a very invalidating and common disorder, and the use of rodent models of epilepsy to test new anti-epileptic treatments is of great interest. The ability to detect epileptic seizures in these models with automated or semi-automated methods is still a major challenge.

We have developed two new computer-based tools using Python language that,
1) enable the noninvasive semi-automated detection of convulsive seizures from videos,
2) enable the automatic detection of interictal spikes from Electrocorticogram recordings (ECoG).

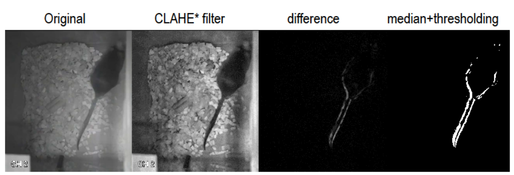
2 Detecting convulsive seizures from videos

Convulsive seizures are very serious phenotypic manifestations occurring in severe forms of epilepsy, they appear as clonic or tonic-clonic seizures with wild jumping. Our method is based on motion and its power spectral analysis calculated from video recording of freely moving mice. It helps the user to easily spot convulsive seizures within hundreds of hours of video recordings.

3 Non-invasive video-recording

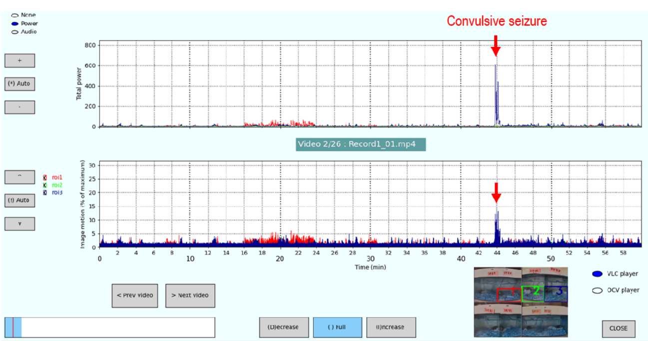


4 Semi-automated analysis: image motion calculation



*Contrast Limited Adaptive Histogram Equalization

5 Display of image motion and its spectral power



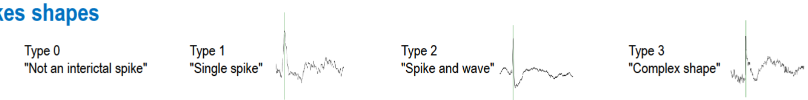
The main advantages of our method are 1) its noninvasiveness, the animals can be recorded in normal cages with minor modifications, 2) the high speed of the analysis with a good accuracy (88,8% accuracy in comparison to full video visual inspection, 93,2% accuracy in comparison to ECoG analysis), 3) the ability to acquire and analyze a very large number of files, thus long video lasting recordings, 4) the easy to use graphical interfaces, and 5) its cost-effectiveness

6 Detecting interictal spikes from ECoG signal using AI

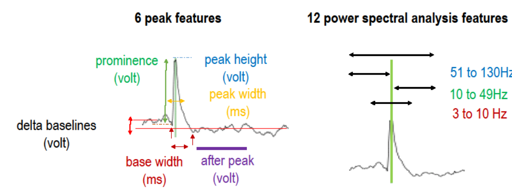
Interictal spikes is a typical feature of ECoG recordings and they are overrepresented in epileptic animals. The spikes are very short peaks (few tens of ms) and hence hard to spot within days of recordings. We have used a random forest classifier trained with 7000 manually classified peaks and using 18 peaks features to automatically classify thousands of peaks over long periods of acquisition.

7 Defining spikes shapes and features to train a classifier

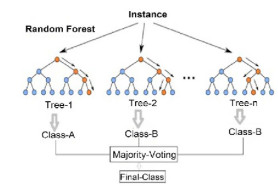
Spikes shapes



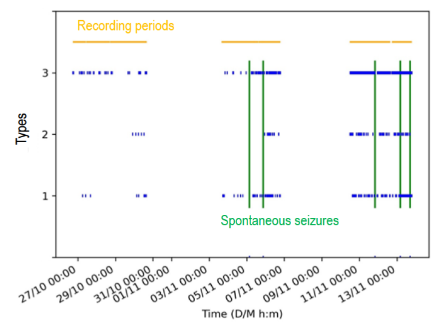
Spikes features



Training of a random forest classifier

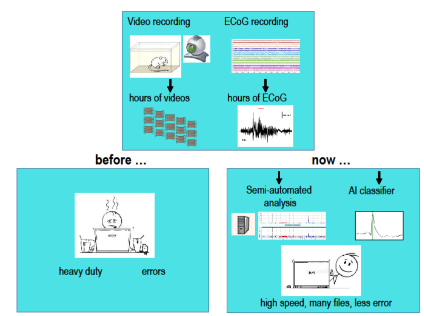


8 Using the classifier



When comparing the classifier results with manually classified spikes we obtained more than 80% accuracy

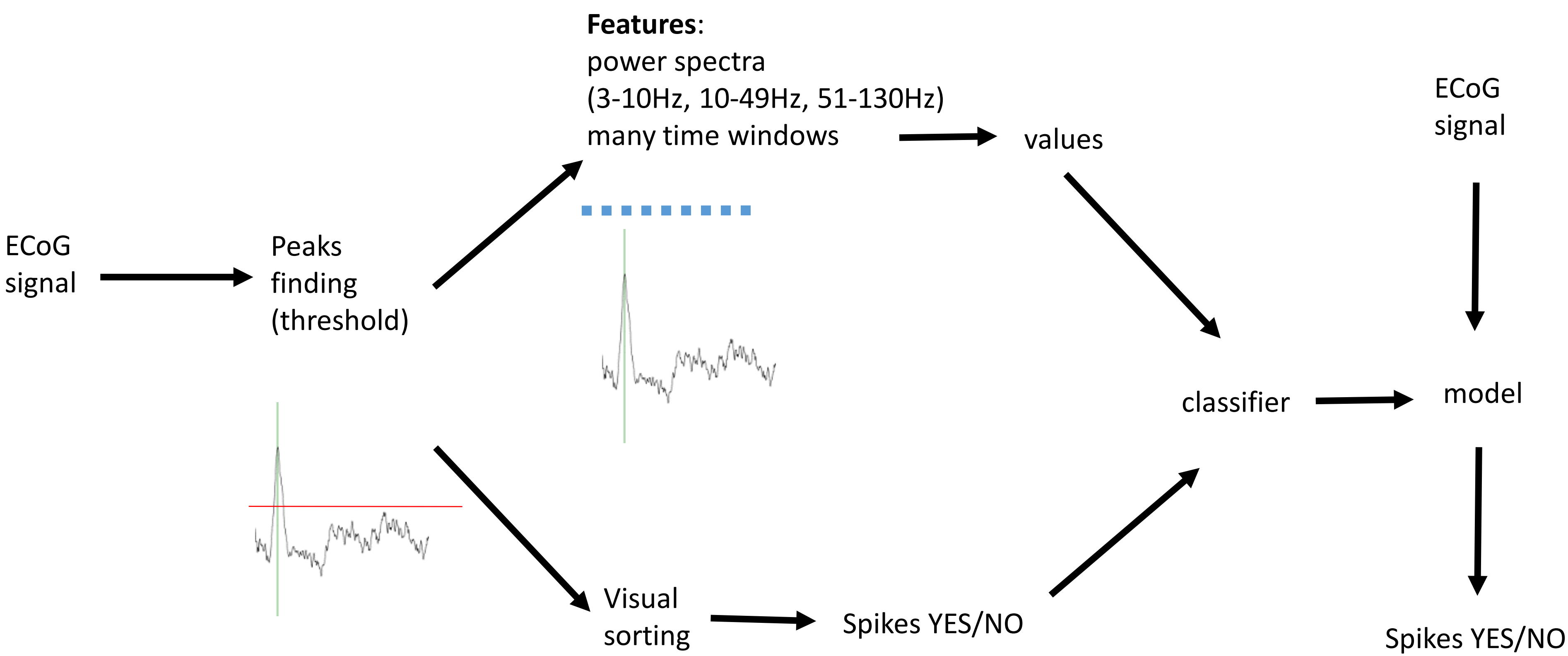
9 Conclusion

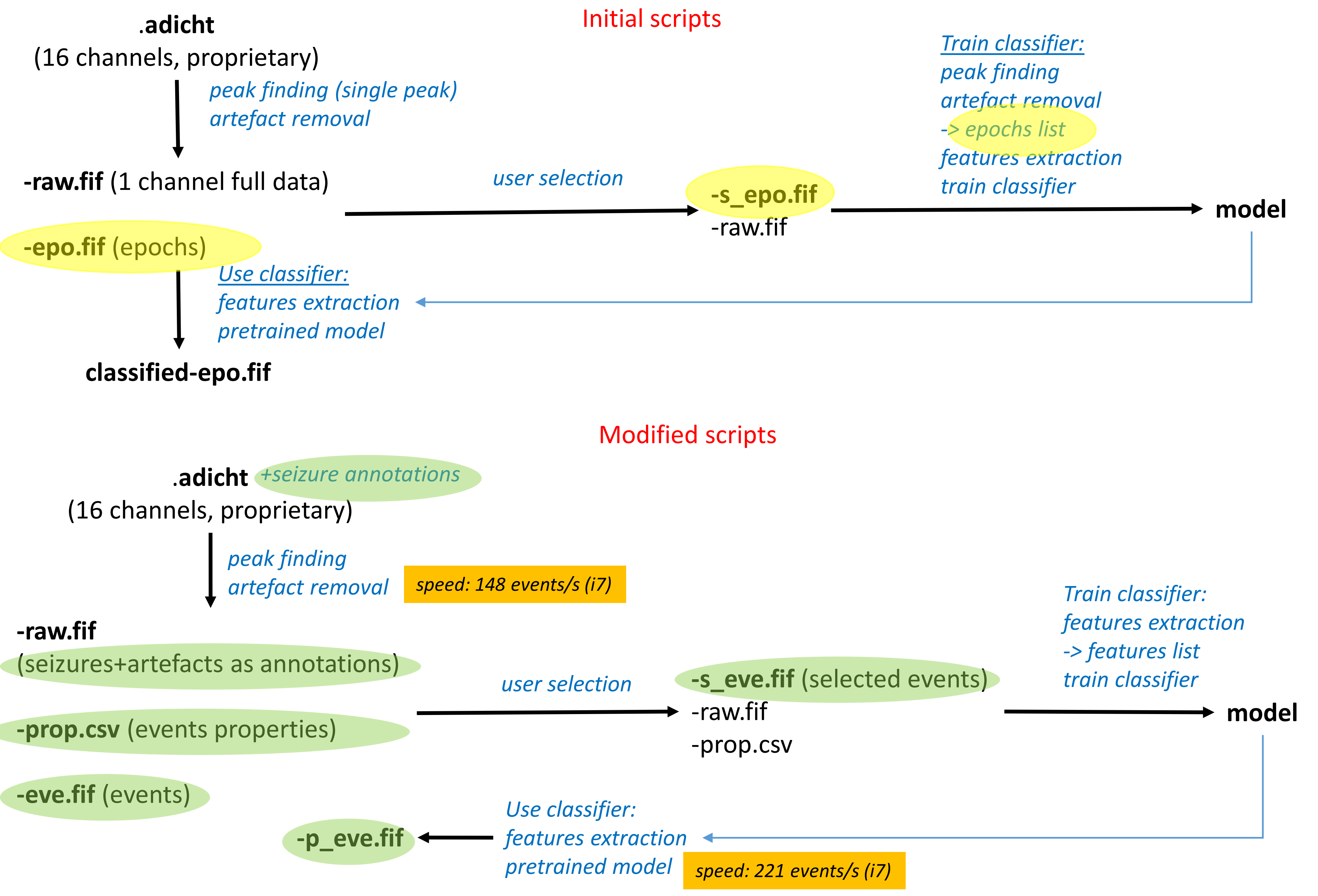


These new tools enable the analysis of hundreds of hours of video and ECoG recordings and give way to higher throughput analysis of our mice epileptic models.

Classifier for Interictal spikes search

Initial scripts Pierre Guetschel, Théo Papadopoulo INRIA

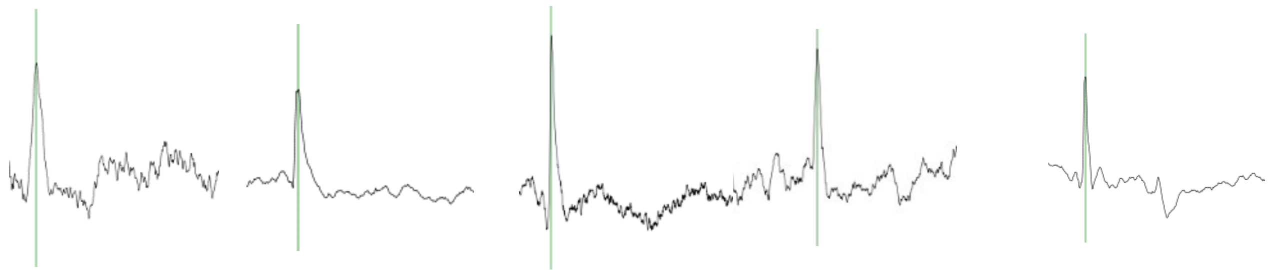



Initial scripts
.adicht
(16 channels, proprietary)
peak finding (single peak)
artefact removal
-raw.fif (1 channel full data)
-epo.fif (epochs)
user selection
-s_epo.fif
-raw.fif
Train classifier:
peak finding
artefact removal
-> epochs list
features extraction
train classifier
model
Use classifier:
features extraction
pretrained model
classified-epo.fif
Modified scripts
.adicht
+seizure annotations
(16 channels, proprietary)
peak finding
artefact removal
speed: 148 events/s (i7)
-raw.fif
(seizures+artefacts as annotations)
-prop.csv (events properties)
-eve.fif (events)
user selection
-s_eve.fif (selected events)
-raw.fif
-prop.csv
Train classifier:
features extraction
-> features list
train classifier
model
Use classifier:
features extraction
pretrained model
speed: 221 events/s (i7)
-p_eve.fif

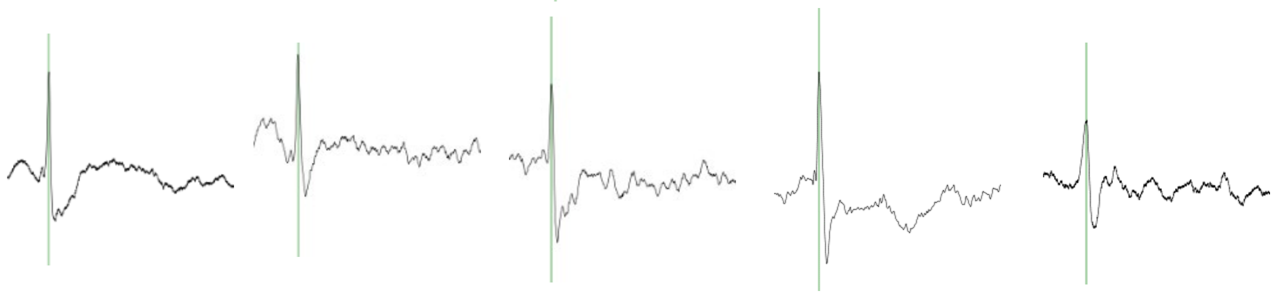
Redefining spikes types

Type 0 = not an interictal spike

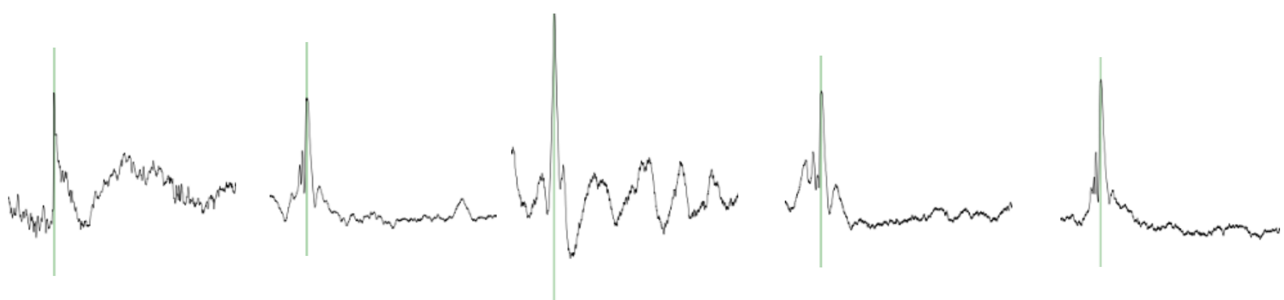
Type 1
"single spike"



Type 2
"spike and wave"



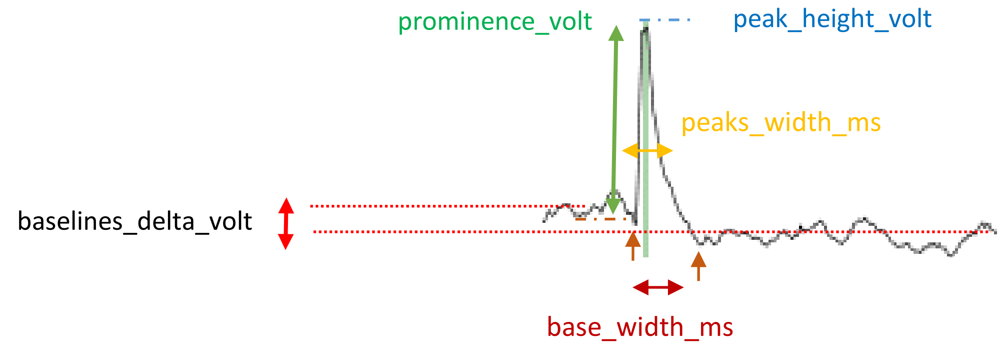
Type 3
"others"



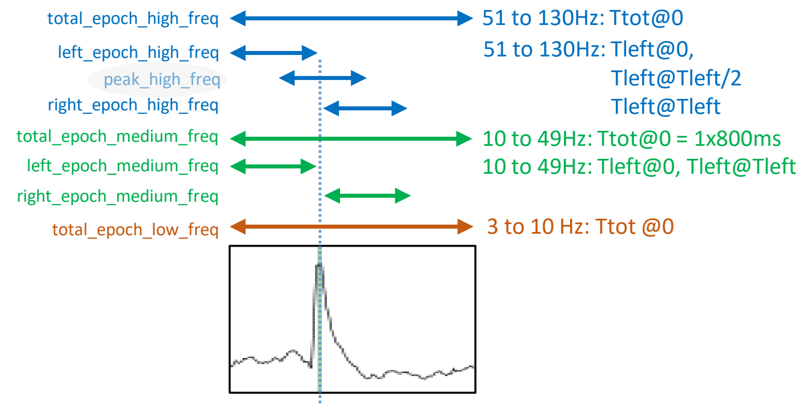
Modified scripts

Refining features

13 features model = 5 peak features +



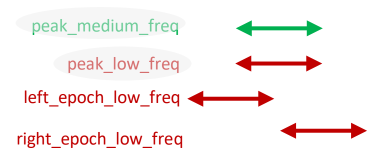
8 power spectral analysis optimised features



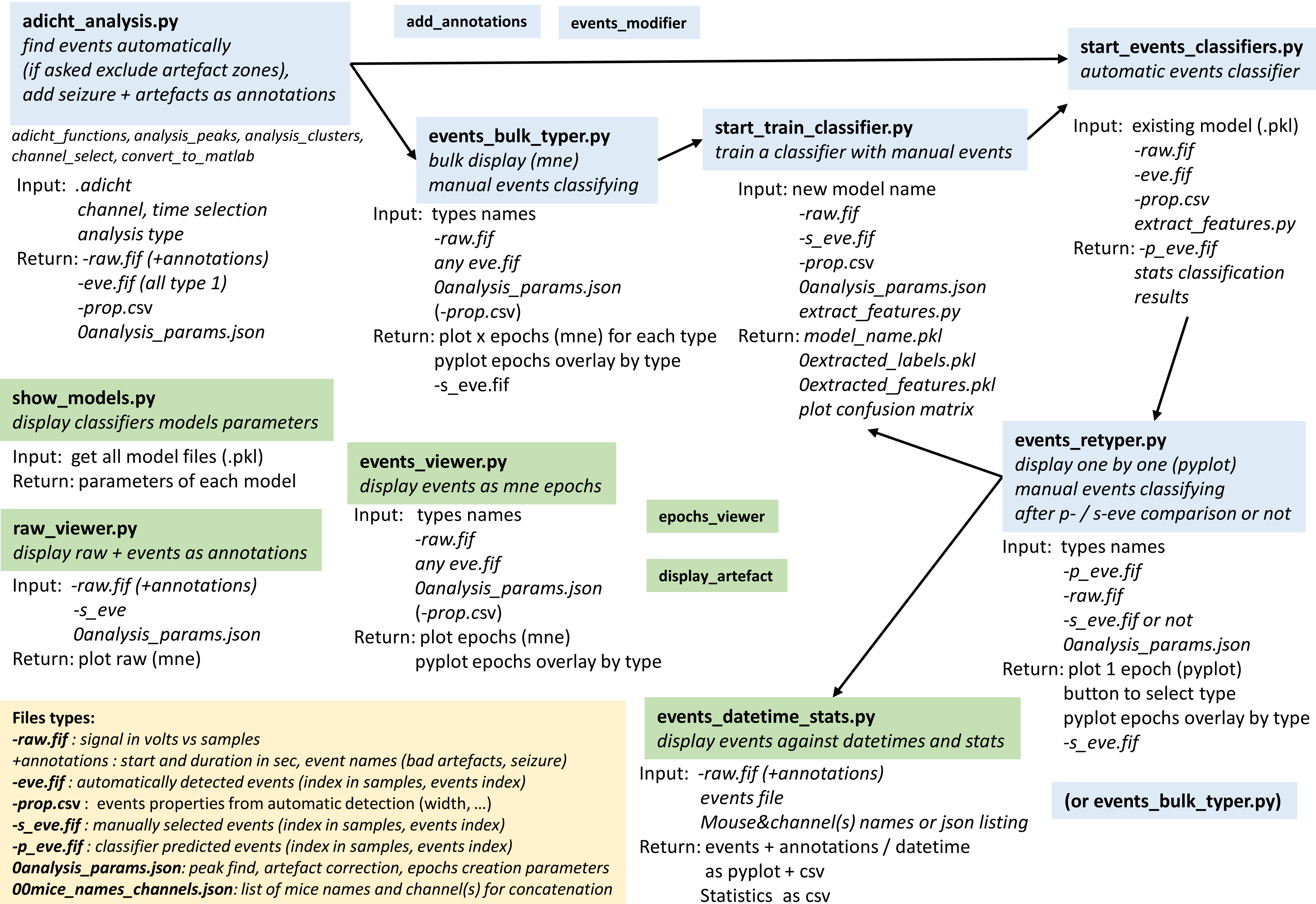
18 features model =

+ 1 peak feature

+ last 5 spectral features



8 features model (peak centered)


adicht_analysis.py
find events automatically
(if asked exclude artefact zones),
add seizure + artefacts as annotations
adicht_functions, analysis_peaks, analysis_clusters,
channel_select, convert_to_matlab
Input: .adicht
channel, time selection
analysis type
Return: -raw.fif (+annotations)
-eve.fif (all type 1)
-prop.csv
0analysis_params.json
add_annotations
events_modifier
events_bulk_typer.py
bulk display (mne)
manual events classifying
Input: types names
-raw.fif
any eve.fif
0analysis_params.json
(-prop.csv)
Return: plot x epochs (mne) for each type
pyplot epochs overlay by type
-s_eve.fif
start_train_classifier.py
train a classifier with manual events
Input: new model name
-raw.fif
-s_eve.fif
-prop.csv
0analysis_params.json
extract_features.py
Return: model_name.pkl
0extracted_labels.pkl
0extracted_features.pkl
plot confusion matrix
start_events_classifiers.py
automatic events classifier
Input: existing model (.pkl)
-raw.fif
-eve.fif
-prop.csv
extract_features.py
Return: -p_eve.fif
stats classification
results
show_models.py
display classifiers models parameters
Input: get all model files (.pkl)
Return: parameters of each model
events_viewer.py
display events as mne epochs
Input: types names
-raw.fif
any eve.fif
0analysis_params.json
(-prop.csv)
Return: plot epochs (mne)
pyplot epochs overlay by type
epochs_viewer
display_artefact
raw_viewer.py
display raw + events as annotations
Input: -raw.fif (+annotations)
-s_eve
0analysis_params.json
Return: plot raw (mne)
events_retyper.py
display one by one (pyplot)
manual events classifying
after p- / s-eve comparison or not
Input: types names
-p_eve.fif
-raw.fif
-s_eve.fif or not
0analysis_params.json
Return: plot 1 epoch (pyplot)
button to select type
pyplot epochs overlay by type
-s_eve.fif
(or events_bulk_typer.py)
events_datetime_stats.py
display events against datetimes and stats
Input: -raw.fif (+annotations)
events file
Mouse&channel(s) names or json listing
Return: events + annotations / datetime
as pyplot + csv
Statistics as csv
Files types:
-raw.fif : signal in volts vs samples
+annotations : start and duration in sec, event names (bad artefacts, seizure)
-eve.fif : automatically detected events (index in samples, events index)
-prop.csv : events properties from automatic detection (width, …)
-s_eve.fif : manually selected events (index in samples, events index)
-p_eve.fif : classifier predicted events (index in samples, events index)
0analysis_params.json: peak find, artefact correction, epochs creation parameters
00mice_names_channels.json: list of mice names and channel(s) for concatenation

Testing of various features

All trained with 5635 events and tested with 627

Model name	Nb of features	True type 0 events	True type 1 events	True type 2 events	True type 3 events	Total accuracy (%)
ef8 : Peak centered	8	43/63 68,3%	83/165 50,3%	73/105 69,5%	186/294 63,3%	61,4
ef13 : Peak and surrounding optimised	13	37/58 63,8%	84/164 51,2%	73/106 68,9%	210/299 70,2	64,4
ef18 : Peak and surrounding, all frequencies, afterpeak	18	45/63 71,4%	95/165 57,6%	84/105 80%	246/294 83,7%	75

ef8

Features	**Importances**
peaks_widths_ms	0.17
peak_low_freq	0.14
peak_medium_freq	0.13
bases_widths_ms	0.13
peak_high_freq	0.12
prominences_volt	0.11
peaks_heights_volt	0.1
baselines_delta_volt	0.09

ef13

Features	**Importances**
left_epoch_high_freq	0.12
peaks_widths_ms	0.11
peak_high_freq	0.09
total_epoch_medium_freq	0.08
left_epoch_medium_freq	0.08
prominences_volt	0.08
right_epoch_high_freq	0.07
total_epoch_low_freq	0.07
total_epoch_high_freq	0.07
bases_widths_ms	0.06
peaks_heights_volt	0.06
baselines_delta_volt	0.06
right_epoch_medium_freq	0.05

ef18

Features	**Importances**
afterpeak_volt	0.18
peaks_widths_ms	0.08
left_epoch_high_freq	0.08
peak_low_freq	0.07
peak_medium_freq	0.07
total_epoch_medium_freq	0.05
left_epoch_medium_freq	0.05
prominences_volt	0.05
right_epoch_high_freq	0.05
peak_high_freq	0.05
total_epoch_high_freq	0.04
right_epoch_low_freq	0.04
peaks_heights_volt	0.03
left_epoch_low_freq	0.03
total_epoch_low_freq	0.03
baselines_delta_volt	0.03
bases_widths_ms	0.03
right_epoch_medium_freq	0.03

Hyperparameters optimization

split random state=range(1, 100, 5), RF classifier random state=range(1, 200, 5):

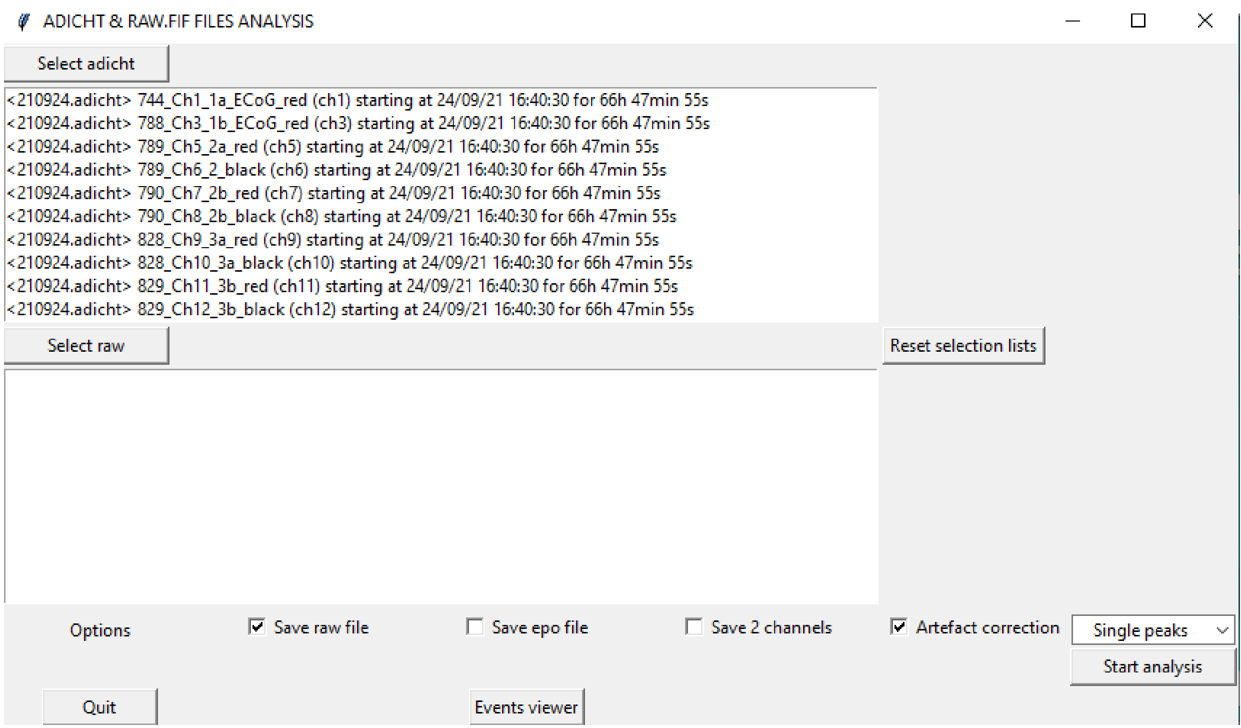
Bests: accuracy 83,1% : split random_state=21, RF classifier random_state =101
Worse: accuracy 73,2% : split random_state =26, RF classifier random_state =116

NEUROMOD STUDENT : random search, grid search, Bayesian optimization, … ?

n_estimators ***int, default=100*** The number of trees in the forest.
max_features ***{"auto", "sqrt", "log2"}, int or float, default="auto"*** The number of features to consider when looking for the best split
max_depth ***int, default=None***The maximum depth of the tree
min_samples_split ***int or float, default=2*** The minimum number of samples required to split an internal node
min_samples_leaf ***int or float, default=1*** The minimum number of samples required to be at a leaf node.
criterion***{"gini", "entropy"}, default="gini"***The function to measure the quality of a split

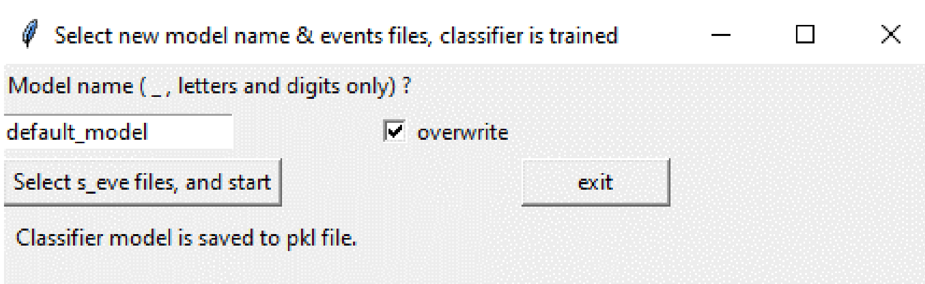
bootstrap, ***bool, default=True*** Whether bootstrap samples are used when building trees. If False, the whole dataset is used to build each tree.

min_weight_fraction_leaf, ***float, default=0.0*** The minimum weighted fraction of the sum total of weights (of all the input samples) required to be at a leaf node.
max_leaf_nodes, ***int, default=None*** Grow trees with max_leaf_nodes in best-first fashion. Best nodes are defined as relative reduction in impurity
min_impurity_decrease, ***float, default=0.0***A node will be split if this split induces a decrease of the impurity greater than or equal to this value.
oob_score ***bool, default=False*** Whether to use out-of-bag samples to estimate the generalization score. Only available if bootstrap=True.
random_state, ***int, RandomState instance or None, default=None*** Controls both the randomness of the bootstrapping of the samples used when building trees and the sampling of the features to consider when looking for the best split at each node (if max_features < n_features)
warm_start ***bool, default=False*** When set to True, reuse the solution of the previous call to fit and add more estimators to the ensemble, otherwise, just fit a whole new forest.
ccp_alpha, ***non-negative float, default=0.0*** Complexity parameter used for Minimal Cost-Complexity Pruning.
max_samples, ***int or float, default=None*** If bootstrap is True, the number of samples to draw from X to train each base estimator.

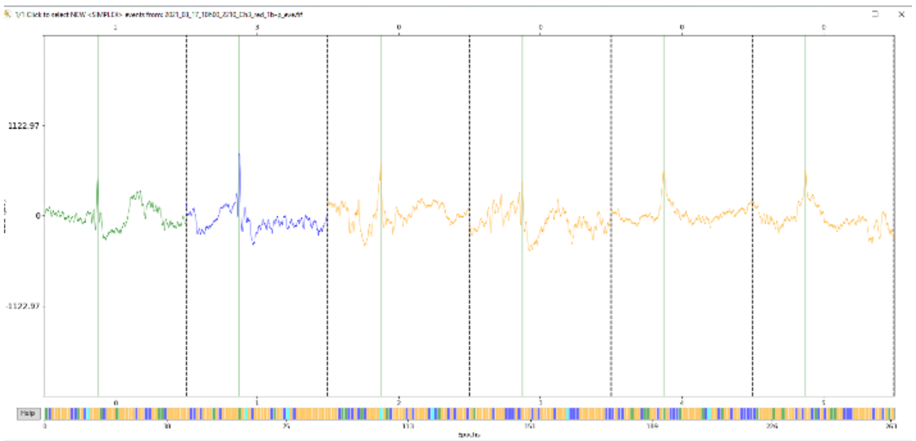


Adicht analysis

Train classifier



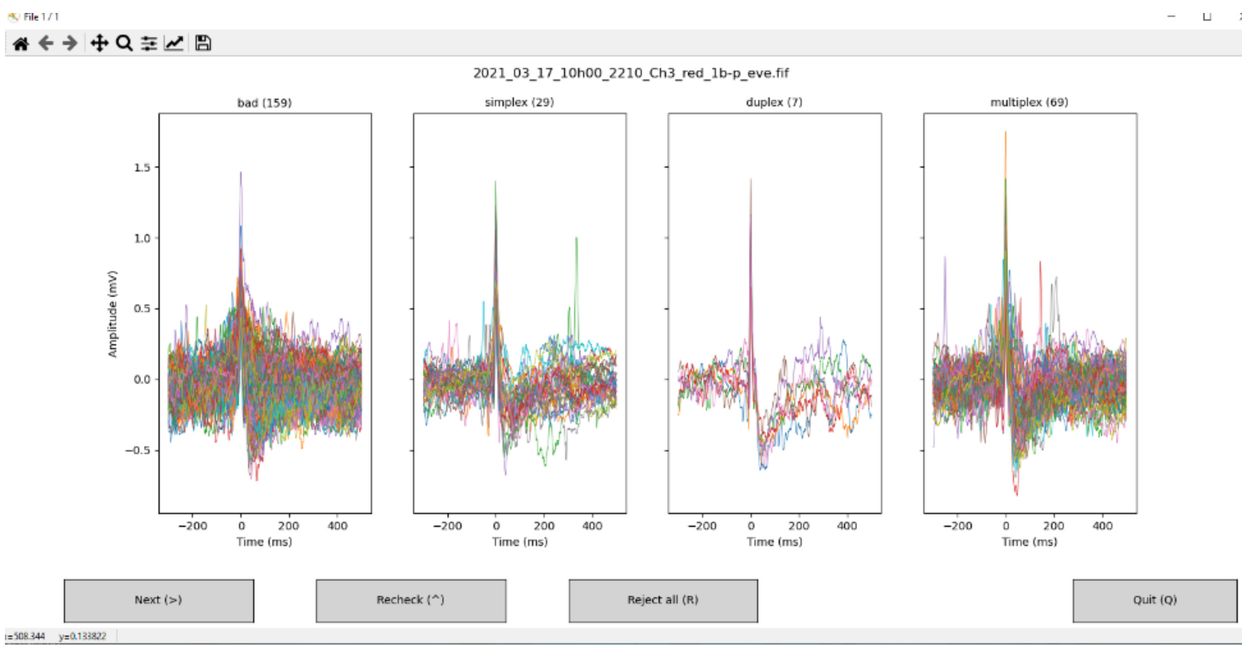
Events bulk typer



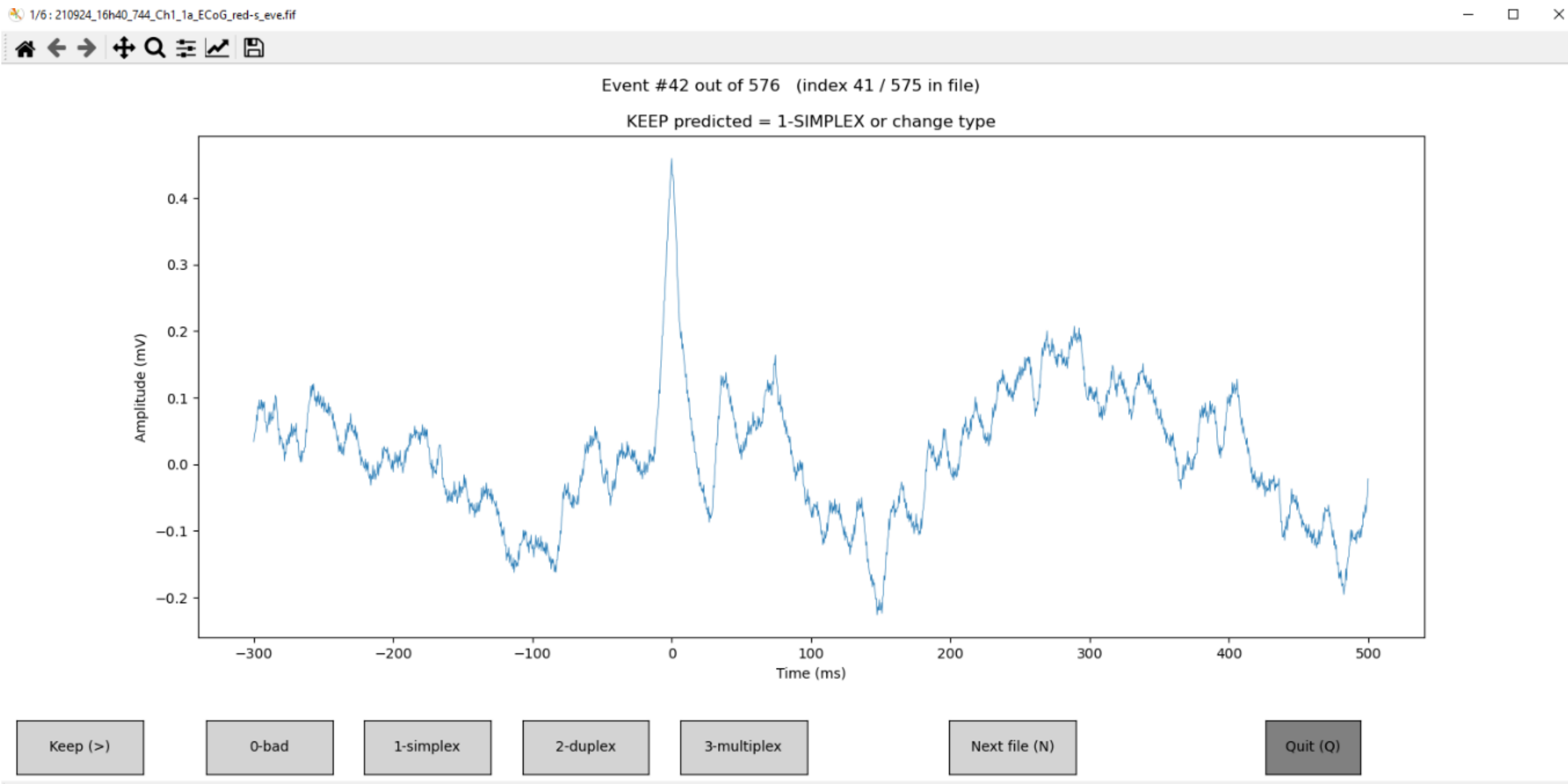
1/1 Click to select NEW <DUPLEX> events from: 2021_03_17_10h00_2210_Ch3_red_1b-p_eve.fif

1/1 Click to select NEW <MULTIPLEX> events from: 2021_03_17_10h00_2210_Ch3_red_1b-p_eve.fif

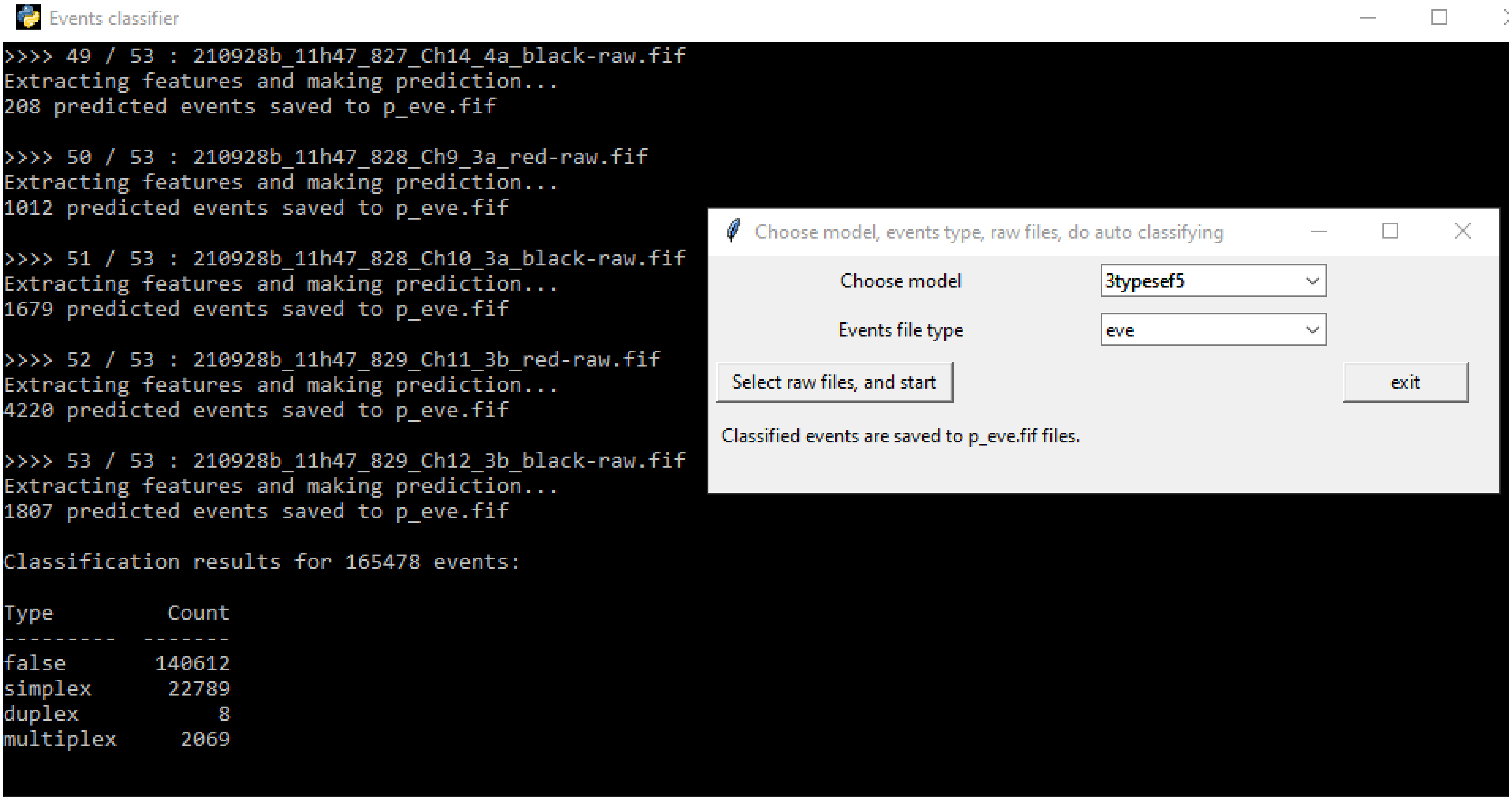
1/1 Click on NEW BAD EVENTS, to keep <simplex> <duplex> <multiplex> events from: 2



Events typer



Events classifier



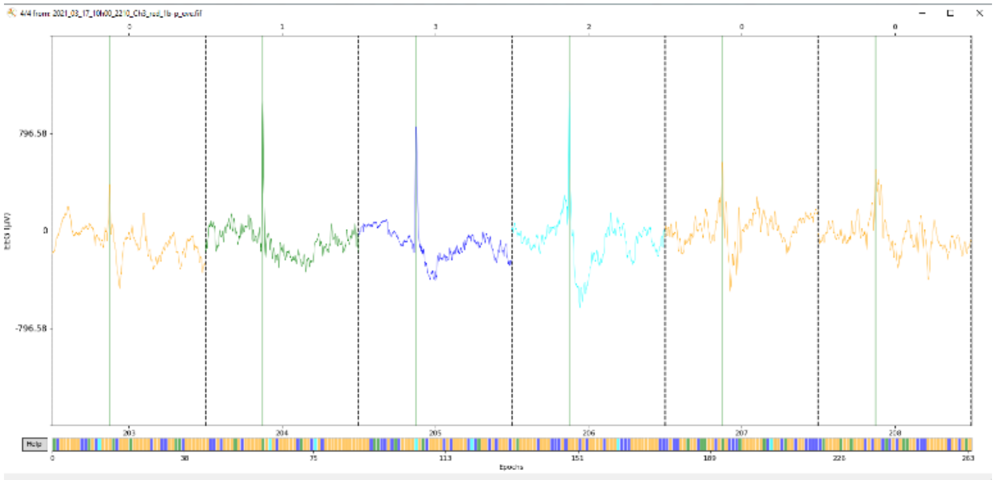
14 channels of 6811 minutes analysed in 19 min = 4915x

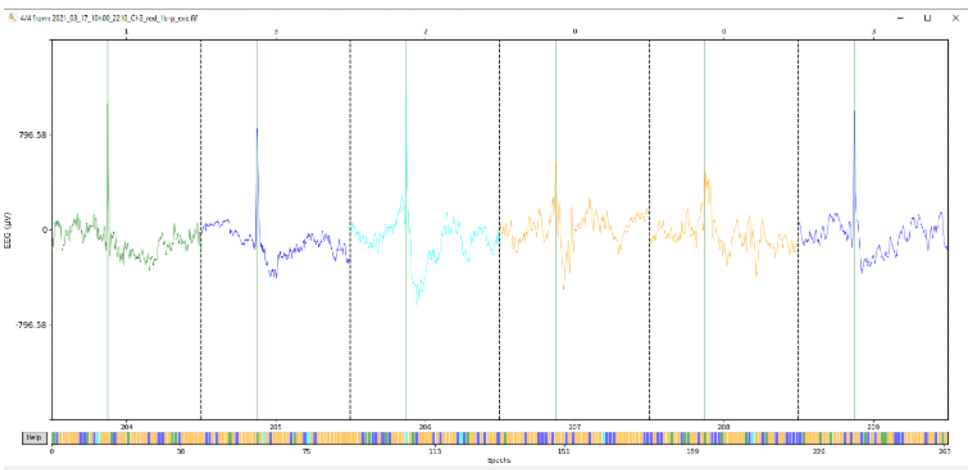
Show models

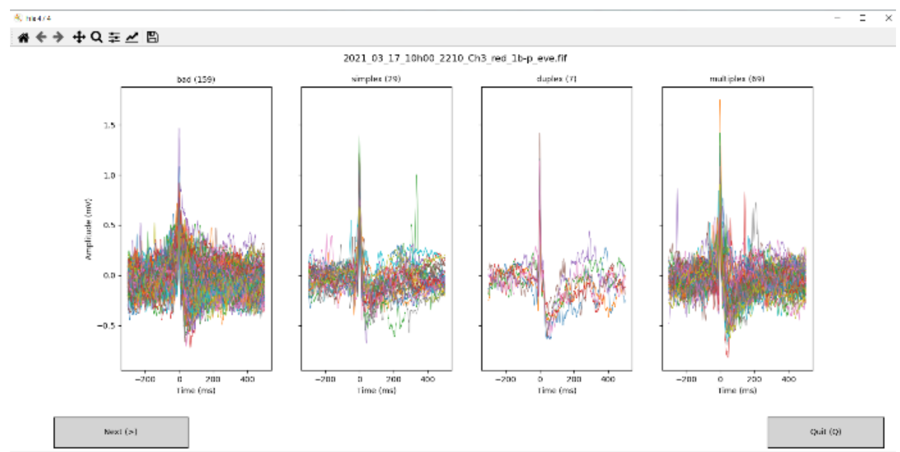
```
#### MODEL 3typesef5.pkl ####

>> find_peaks_args : {'height': [0.001, 0.003], 'threshold': [0, 4], 'prominence': 0.0005, 'wlen': 600, 'width': [10, 20
0], 'rel_height': 0.5, 'distance': 600}
>> find_artefacts_args : {'t_window': 3, 'max_ratio': 3, 'artefact_radius': 3.0, 'min_length': 20.0, 'online': True, 'pr
eheat': 20.0, 'stride': 0.2}
>> extract_features_args : {'use_total_spectrum': True, 'use_left_spectrum': True, 'use_peak_spectrum': True, 'use_right
_spectrum': True, 'use_peak_prop': True, 'freq_ranges': ((3.0, 10.0), (10.0, 49.0), (51.0, 130.0)), 'epoch_durations': (
0.3, 0.5)}
>> clf : RandomForestClassifier(criterion='entropy', n_jobs=4, random_state=42)
>> tmin : -0.3
>> tmax : 0.5
>> sfreq : 2000.0
>> raw_file 88:
>> spike_reference_file 88:
>> features_names 18:
['total_epoch_low_freq', 'total_epoch_medium_freq', 'total_epoch_high_freq', 'left_epoch_low_freq', 'left_epoch_medium_f
req', 'left_epoch_high_freq', 'peak_low_freq', 'peak_medium_freq', 'peak_high_freq', 'right_epoch_low_freq', 'right_epoc
h_medium_freq', 'right_epoch_high_freq', 'prominences_volt', 'peaks_heights_volt', 'peaks_widths_ms', 'bases_widths_ms',
 'baselines_delta_volt', 'afterpeak_volt']
-----------------------  -----------
Features                 Importances
afterpeak_volt           0.18
peaks_widths_ms          0.08
left_epoch_high_freq     0.08
peak_low_freq            0.07
peak_medium_freq         0.07
total_epoch_medium_freq  0.05
left_epoch_medium_freq   0.05
prominences_volt         0.05
right_epoch_high_freq    0.05
peak_high_freq           0.05
total_epoch_high_freq    0.04
right_epoch_low_freq     0.04
peaks_heights_volt       0.03
left_epoch_low_freq      0.03
total_epoch_low_freq     0.03
baselines_delta_volt     0.03
bases_widths_ms          0.03
right_epoch_medium_freq  0.03
```

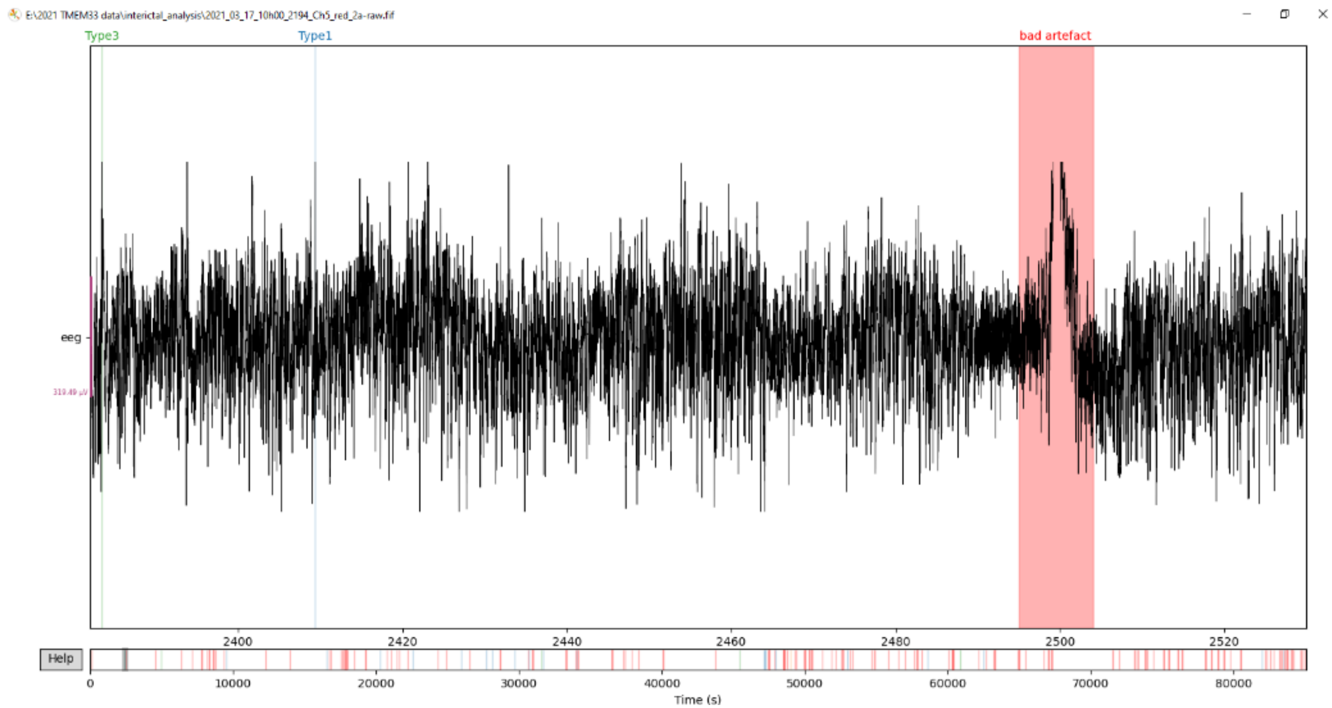
Events viewer

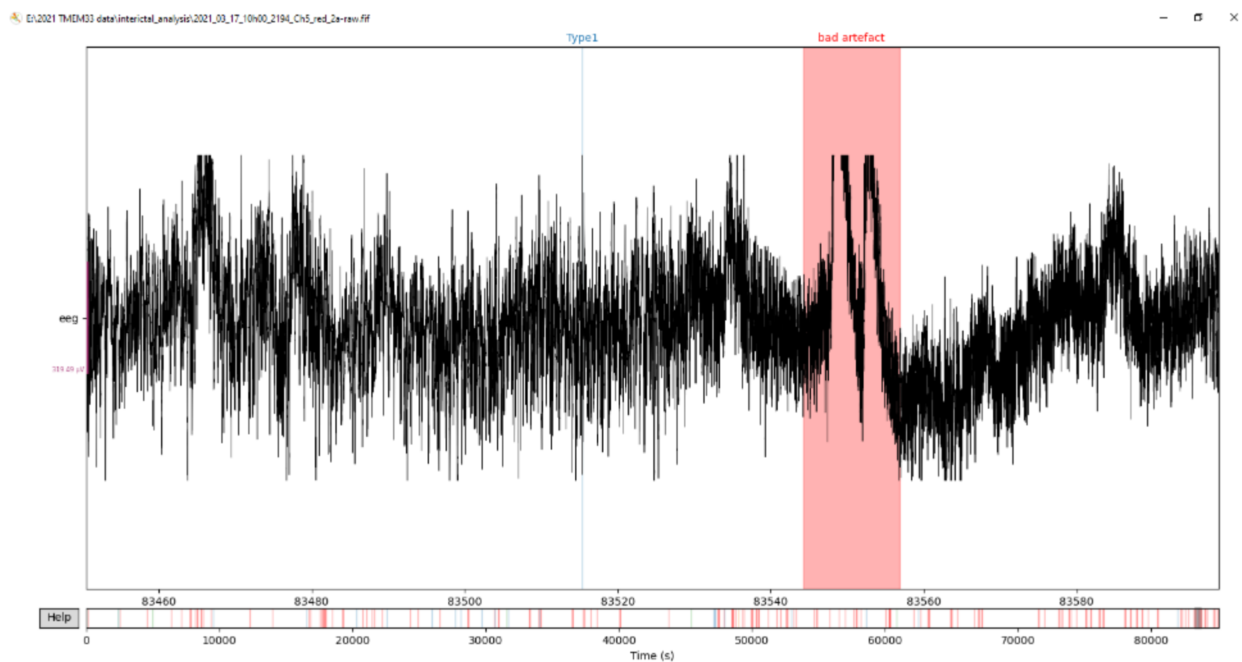




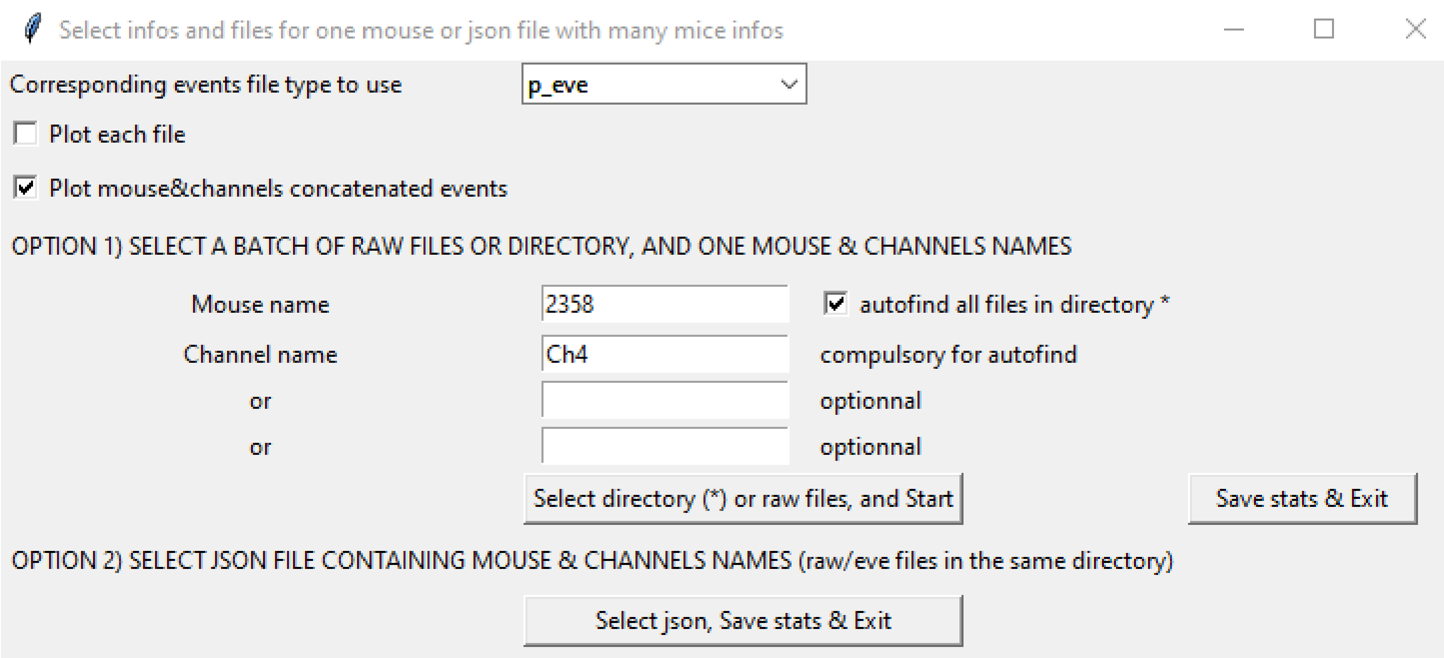


Raw viewer


E:\2021 TMEM33 data\interictal_analysis\2021_03_17_10h00_2194_Ch5_red_2a-raw.fif
Type3
Type1
bad artefact
eeg
2400
2420
2440
2460
2480
2500
2520
Help
0
10000
20000
30000
40000
50000
60000
70000
80000
Time (s)


E:\2021 TMEM33 data\interictal_analysis\2021_03_17_10h00_2194_Ch5_red_2a-raw.fif
Type1
bad artefact
eeg
83460
83480
83500
83520
83540
83560
83580
Help
0
10000
20000
30000
40000
50000
60000
70000
80000
Time (s)

Events datetime stats



.json file

```
{"serie": "TMEM33",
"infos":[
["2193", "Ch1", "Ch7", "Ch11"],
["2193", "Ch2", "Ch8", "Ch12"],
["2210", "Ch3", "", ""],
["2210", "Ch4", "", ""],
["2194", "Ch5", "", ""],
["2194", "Ch6", "", ""],
["2245", "Ch7", "", ""],
["2245", "Ch8", "", ""],
```

.csv file

B	C	D	E	F	G	H	I	J
mouse_name	channel_name1	nb_files	duration_sec	nb_seizures	nb_type0	nb_type1	nb_type2	nb_type3
2210	Ch3	5	428261	0	748	198	19	327
2210	Ch4	5	428261	0	725	180	13	293
2245	Ch7	5	428261	0	749	23	0	28
2245	Ch8	5	428261	0	1887	31	1	26
2354	Ch11	3	257525	0	43	25	1	27
2354	Ch12	3	257525	0	309	36	0	29
2356	Ch15	5	428261	0	1209	151	0	90
2356	Ch16							
2358	Ch3	6	581477	1	899	59	1	31
2358	Ch4	7	673552	1	1384	273	1	85
2363	Ch7	7	673552	0	1917	47	4	164
2363	Ch8	7	673552	0	1842	70	4	481
2364	Ch11	7	673552	2	2421	649	0	78
2364	Ch12	7	673552	2	2678	356	0	71
2357	Ch13	7	673552	0	6443	27	0	105
2357	Ch14	7	673552	0	7617	24	0	150
2193	Ch1	4	340848	0	44	4	0	7
2193	Ch2	4	343376	0	113	12	0	5
2194	Ch5	5	428261	0	2387	124	2	49
2194	Ch6	5	428261	0	2395	226	3	69
2195	Ch9	4	340848	0	447	15	0	14
2195	Ch10	4	344939	0	469	9	0	3
2196	Ch13	5	428261	0	6452	49	0	26
2196	Ch14	5	428261	0	4437	38	0	20
2319	Ch1	7	673552	0	4167	88	3	75
2319	Ch2	7	673552	0	2201	60	0	75

Values for 2358_Ch4, from 7 p_eve files

.jpg file