User’s Manual for HFO-Engine and EZ-Detect version 1.0.1

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Listserv for users: send email to hfoengine-request@freelists.org with 'subscribe' in the Subject field (no quotes)

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Release Notes

Thank you for your interest in HFO-Engine/EZ-Detect. This software was developed as part of Dr. Shennan Weiss's research efforts at University of California Los Angeles, Thomas Jefferson University, and the State University of New York Downstate and Dr. Diego Slezak's research efforts at the University of Buenos Aires. The code is written in Matlab (Digital Signal Processing DSP), Python (Webserver and MNE backbone), and C# (HFO-Engine client Micromed plug-in).

The purpose of this release is to promote and foster the research of high-frequency oscillations and their eventual clinical utilization. The software package serves as 1) an integrated plug-in for Micromed™ Brain Quick™ to select data and annotate HFO and spike events in the intracranial stereo-EEG (SEEG); and 2) A signal analysis pipeline for categorizing, and quantifying HFOs for further analysis in Matlab or Python. We ask that if you use this software in your research that you cite the papers included in the appendix of this document. This work was fully supported by NIH/NINDS K23 NS094633 (SAW), and a Junior Investigator Award from the American Epilepsy Society (SAW).

HFO-Engine/EZ-Detect is a research tool and is not intended for clinical use. It is designed for detailed HFO analysis and, in its current form, is poorly suited for intra-operative applications due to lengthy processing time to carry out the analysis. Also, the digital signal processing pipeline was designed and tested using human SEEG contact recordings from a variety of electrode manufacturers. It was also tested on, but not optimized for, human subdural electrode recordings. If you intend to use this software to analyze subdural recordings, or microelectrode recordings of the local field potential, modifications of the DSP code maybe necessary. Examples of DSP code for these applications are available from Shennan Weiss upon request.

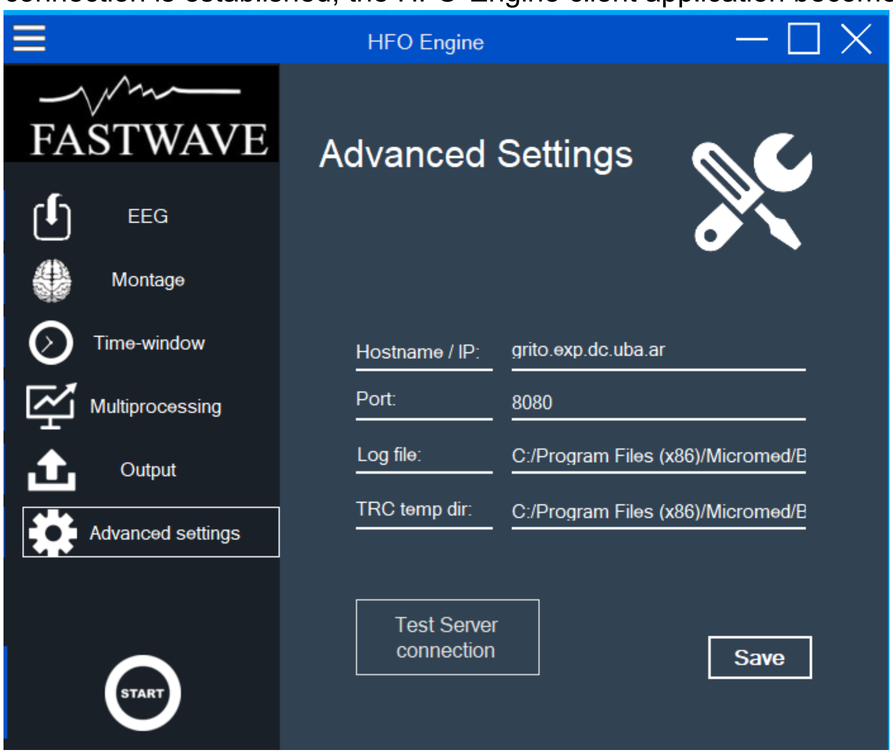
If you are a current or future Micromed software user, we hope that the HFO-Engine/EZ-Detect plug-in expands your ability to use Brain Quick to visualize HFOs in your iEEG data. We selected Brain Quick as the viewer for this software since it is well suited for visualizing HFOs using its built-in filters, sweep speeds, and annotation tools. If you are not a Micromed user, please enjoy the open-source DSP tools in this release on the GitHub site for your own projects and applications. The feature of HFO-Engine/EZ-Detect include:

1. A HFO analysis plug-in for Micromed Brain Quick that automatically displays HFO (ripple, fast ripple) and spike detections with built in file conversion tools to analyze EEG files from other hardware vendors.
2. A webserver for analyzing iEEG
3. Automatic detection of bad electrode contacts
4. Detection of HFO events in either referential montage (using CUDA-independent component analysis (ICA) for a “reference-less” EEG) or traditional bipolar montage
5. Excellent sensitivity and specificity of event detections using a Hilbert detector optimized based on the skewness of the amplitudes of the HFO filtered time series (improved upon by ICA methods)
6. EZ-top functions which perform a topographic analysis of the wavelet convolution of each detected event to categorize events as ripple on background (i.e. ripple on oscillation), ripple on spike, fast ripple on background, fast ripple on spike, or false HFO (due to filter ringing). Following categorization, the onset time, offset time, duration, frequency, and power of each event is derived in time-frequency space.
7. EZ-Pac functions which derive phase-amplitude coupling of HFO events with slower frequencies, including spikes, using phasor methods.
8. EZ-Mongo functions for uploading your HFO detections, after redacting false positive detections in Brainquick, to a MongoDB using Matlab functions.

As mentioned in the installation guide, it is recommended that someone with a strong background in computer science installs and tests the HFO-Engine/EZ-Detect webserver for your laboratory.

Connecting HFO-Engine Client to the HFO-Engine Server

The HFO-Engine server is intended to operate on a Linux system and was designed to function on the cloud (Amazon, Google, etc). The server is started by running the ./start_server.sh --production command (see installation guide). If you are encountering errors with the HFO-Engine server, or would like to improve upon it, I recommend the free version of Visual Studio Code which supports Python with Conda using a Flask webserver. To test that HFO-Engine client, on your Windows machine, can connect with the HFO-Engine server open the HFO-Engine executable in your Micromed plugins directory. You will be greeted with a dialogue box message that the “grito” server cannot be found. This is the development server from the University of Buenos Aires, and it cannot be accessed. To connect to your server in the HFO-Engine application click on “Advanced Settings”, then enter the hostname or IP address of the HFO-Engine/EZ-Detect webserver, you may also need to change the port depending on your configuration, **click on SAVE**, then click on test connection. If the connection is established a dialogue box will open saying that the connection is established. If not, the dialogue box will say the connection is down. If the connection is down, please read the installation guide for further instructions for debugging the problem. Note that if HFO Engine/EZ-detect server cannot compile then the webserver will be down. Once the dialogue box says the servers is up, and the connection is established, the HFO-Engine client application becomes fully functional.

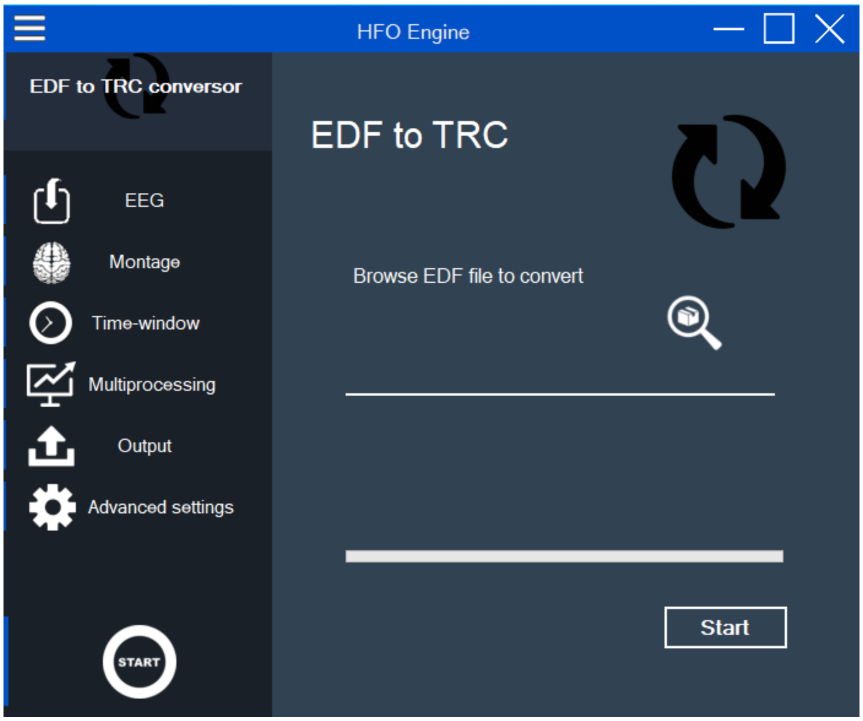


Converting EDF files to TRC files

HFO-Engine/EZ-Detect has a built in TRC file writer that is built upon the backbone of MNE. Please feel free to use this TRC writer for your own applications. This architecture allows you to convert other EEG file formats storing iEEG data to TRC. We recommend that you use our TRC writer rather than Brain Quick’s EDF2TRC converter because our converter was built for use with the HFO detector. EDF files can be converted to TRC files in two ways. In method 1) click on the three horizontal lines in the upper right corner of the HFO-Engine client and follow the instructions to convert the EDF file and download the TRC file from the webserver. In method 2) use MNE commands in Python on the webserver machine to directly convert the EDF to TRC. A sample script of the commands used to convert EDF to TRC in Python edf2trcutils repository on the GitHub. Once you have created the TRC file you will need to manually add the file to the Brain Quick database and enter the coded information for the patient.

Method 1 for converting EDF to TRC files is certainly the most convenient, but two obstacles must be considered. The first is that http can not transmit files >3-4 GB reliably, and the second is that HFO-Engine/EZ-Detect can only analyze 128 channels maximum at a time. The reason for the latter limitation will be explained later. Thus, if you have a EDF or TRC file that is hours long or has over 128 channels we suggest using method 2 to split the EDF files into multiple TRC files for analysis by the detector. To be a versatile user of the HFO-Engine/EZ-detect software you need to become familiar with the MNE tools highlighted in the edf2trcutils repository to build your TRC files.

Splitting the duration or channels of the files is not necessarily problematic, because HFO-Engine/EZ-Detect analyzes the files in 10-minute blocks, and these blocks are reconstituted in the MongoDB. Also, viewing over 128 channels of annotated iEEG data can be difficult and having two separate files can be advantageous.



Creating montages

After opening the TRC file you plan to analyze in Brain Quick you must first create and save the montages that HFO-Engine/EZ-Detect will use for the analysis to the TRC file.

HFO-Engine/EZ-Detect relies on the montages that are constructed in Brain Quick and saved to the TRC file before being uploaded to the HFO-Engine server for proper analysis. This feature allows the user to exclude certain channels, select channels best suited for referential or bipolar analysis, and specify the bipolar channel pairs. HFO-Engine/EZ-Detect expects two saved montages, a suggested/referential montage, and a bipolar montage.

Before discussing the differences in these two montages it is important to note that in each montage every recorded channel must be represented. **In other words, if you look at the channels shown in the 'As Recorded' montage, built in to Brain Quick, each of these channels must be represented in the suggested/referential AND bipolar montage, that you build, <u>in the order that is shown in the "as recorded" montage</u>** (HFO Engine/EZ-Detect will not work correctly if either one of the montages is missing any of the recorded channels or if they are out of order). The reason that HFO-Engine/EZ-detect is so strict relates to identifying the appropriate channel names of the TRC file for writing the HFO and spike events to the event file. Developers may find a better solution, but this rule was selected to avoid errors.

For users who are converting EDF files to TRC files using our built-in function, note that the converted TRC file has a built in “Ref Montage” that includes all recorded channels in the order specified by the ‘as recorded’ settings. This saves a lot of trouble for building the montages for HFO-Engine/EZ-detect, because this montage can be simply duplicated and modified. For users who are analyzing native TRC files from Micromed amplifiers please read the next section.

If you are using a EDF derived TRC file begin by duplicating the Ref montage and saving the duplicate as “yourfile suggested”. Selecting the pairing of the channels listed in this suggested/referential montage allows you to choose what channels you would like to exclude, analyze in referential mode, or analyze in bipolar mode.

Analysis in referential mode is ideally suited for recordings from sleep. ICA is applied in this case to 1) create a reference-less band-pass filtered EEG; 2) detect the intervals that exhibit muscle artifact and reject HFO and spike detections during this interval; 3) increase the sensitivity of HFO detections by detecting HFO in individual independent components. Our research has shown that using referential montage and ICA can improve the sensitivity of the detector and improve localization of the seizure onset zone. The main problem with using the referential-ICA approach is that it is computationally and time intensive. It is also not recommended for recordings during the waking state, due to excessive muscle, although it may be effective during the eyes closed resting state. HFO-Engine/EZ-detect has built in functions for determining the ideal channels for referential analysis, however user input can improve performance. We recommend examining the data in Brain Quick with 80-600 Hz band pass filters at a 2 second time speed and denoting the channels in referential montage with excessive or aberrant high-frequency signal or noise as bipolar channels. As will be explained below, HFO-Engine/EZ-Detect can also detect and characterize HFOs using bipolar only montages, and this will not run ICA, thereby saving time and computational power.

Returning to the topic of assigning your channel pairs in the suggested/referential montage the following assignments can be considered: 1) A channel label paired with itself will be considered excluded by HFO-Engine/EZ-detect; 2) A channel label paired with G2 (the reference) will be considered as a candidate for referential (ICA) mode analysis by HFO-Engine/EZ-Detect; 3) A channel label paired with another channel will be considered a bipolar pair and will be analyzed by HFO-Engine/EZ-Detect in bipolar mode by subtracting the pair. Please see the figures section for example montages.

The reason that a bipolar montage is required in addition to the suggested montage is that in the referential case, if a referential channel is deemed unsuitable for referential analysis, then it will be analyzed in bipolar mode instead automatically and its pair must be known. To create your bipolar montage duplicate “yourfile suggested” and save it as “yourfile bipolar” and then enter all the appropriate bipolar pairs.

When you have finished building your montages in Brain Quick for the file you would like to analyze the next step is to **Archive** the montage (press Archive next to create new on the top bar). When you select archive the montage a dialogue box will tell you that your montage is limited to 128 channels. This is the reason that HFO-Engine/EZ-Detect cannot analyze more than 128 channels at a time. If your TRC file has more than 128 channels, the program will automatically delete channels 129 and above since they cannot be analyzed by the detector. In this case, please consider using the tools in edf2trcutils to divide your data in to two separate files for analysis.

General properties

# Lines	Base time	Reference	Master gain	Master high pass	Master low pass	
51	10 sec	G2	400 µV/cm	off	600.0 Hz	☑ Master notch

Montage lines

Derivation				Gain		Filter						Trace properties		
#	Input -	Input +	Comment	Value	Linked to master gain	Type	High pass	Linked to master HP	Low pass	Linked to master LP	Linked to master notch		Line type	Clipping
default														
1	GA1	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
2	GA2	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
3	GA3	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
4	GA4	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
5	GA5	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
6	GA6	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
7	GA7	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
8	GA8	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
9	GA9	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
10	GA10	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
11	GA11	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
12	GA12	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
13	GA13	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
14	GA14	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
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51	GA51	G2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None

Figure 1: example Ref montage generated by TRC file

General properties

# Lines	Base time	Reference	Master gain	Master high pass	Master low pass	Master notch
51	10 sec	G2	400 µV/cm	off	600.0 Hz	✓

Montage lines

Derivation				Gain		Filter							Trace properties		
#	Input -	Input +	Comment	Value	Linked to master gain	Type	High pass	Linked to master HP	Low pass	Linked to master LP	Linked to master notch		Line type	Clipping
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46	GA46	G2		400 µV/cm	✓	IIR	off	✓	600.0 Hz	✓	✓	■	Lines	None
47	GA47	G2		400 µV/cm	✓	IIR	off	✓	600.0 Hz	✓	✓	■	Lines	None
48	GA48	G2		400 µV/cm	✓	IIR	off	✓	600.0 Hz	✓	✓	■	Lines	None
49	GA49	GA49		400 µV/cm	✓	IIR	off	✓	600.0 Hz	✓	✓	■	Lines	None
50	GA50	GA50		400 µV/cm	✓	IIR	off	✓	600.0 Hz	✓	✓	■	Lines	None
51	GA51	GA51		400 µV/cm	✓	IIR	off	✓	600.0 Hz	✓	✓	■	Lines	None

Figure 2: Example user defined suggested/referential montage for HFO-Engine/EZ-Detect derived from copying montage in Figure 1

General properties

# Lines	Base time	Reference	Master gain	Master high pass	Master low pass	Master notch
51	10 sec	G2	400 µV/cm	off	600.0 Hz	☑

Montage lines

Derivation				Gain		Filter						Trace properties		
#	Input -	Input +	Comment	Value	Linked to master gain	Type	High pass	Linked to master HP	Low pass	Linked to master LP	Linked to master notch		Line type	Clipping
default														
1	GA1	GA2		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
2	GA2	GA3		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
3	GA3	GA4		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
4	GA4	GA5		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
5	GA5	GA6		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
6	GA6	GA7		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
7	GA7	GA7		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
8	GA8	GA8		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
9	GA9	GA9		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
10	GA10	GA10		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
11	GA11	GA11		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
12	GA12	GA12		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
13	GA13	GA13		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
14	GA14	GA14		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
15	GA15	GA15		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
16	GA16	GA17		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
17	GA17	GA18		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
18	GA18	GA19		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
19	GA19	GA20		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
20	GA20	GA21		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
21	GA21	GA22		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
22	GA22	GA23		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
23	GA23	GA24		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
24	GA24	GA25		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
25	GA25	GA26		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
26	GA26	GA26		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
27	GA27	GA27		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
28	GA28	GA28		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
29	GA29	GA29		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
30	GA30	GA30		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
31	GA31	GA31		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
32	GA32	GA33		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
33	GA33	GA32		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
34	GA34	GA34		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
35	GA35	GA35		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
36	GA36	GA36		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
37	GA37	GA37		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
38	GA38	GA38		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
39	GA39	GA40		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
40	GA40	GA40		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
41	GA41	GA41		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
42	GA42	GA42		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
43	GA43	GA43		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
44	GA44	GA44		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
45	GA45	GA45		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
46	GA46	GA47		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
47	GA47	GA48		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
48	GA48	GA48		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
49	GA49	GA49		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
50	GA50	GA50		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None
51	GA51	GA51		400 µV/cm	☑	IIR	off	☑	600.0 Hz	☑	☑	■	Lines	None

Figure 3: Example of user defined bipolar montage for HFO-Engine/Ez-Detect. Note handling of bad electrodes in Figure 2.

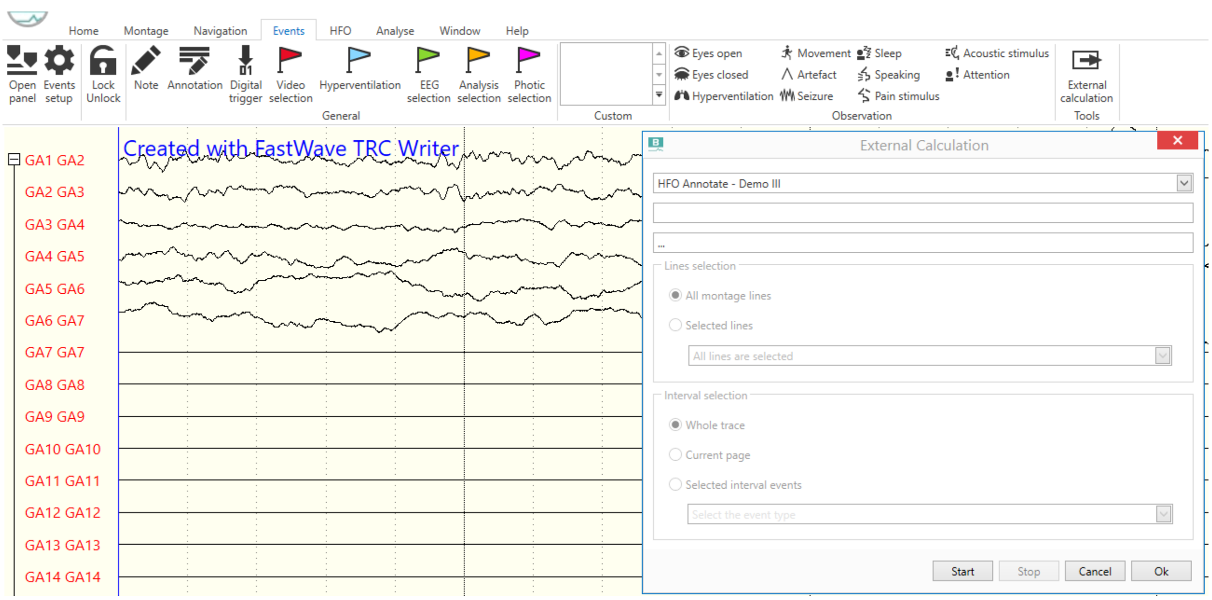
Using Native TRC files

HFO-Engine/EZ-Detect can process native TRC files recorded from Micromed amplifiers. However, it encounters several problems. One problem relates to duplication of the as recorded montage, which may need to be performed manually. Another problem relates to non-EEG channels (EKG, EMG) being mishandled by the detector introducing error. After beta testing native TRC file data, it is suggested that the simplest solution is to export the TRC file within Brain Quick to a raw EDF file. The raw EDF file, created by Brain Quick, can then be reconverted to a TRC file, using our converter, and this will result in a “Ref montage” that makes building your analysis much easier. This extra step would also be required if you have more than 128 recording channels since the file will need to be separated in to two.

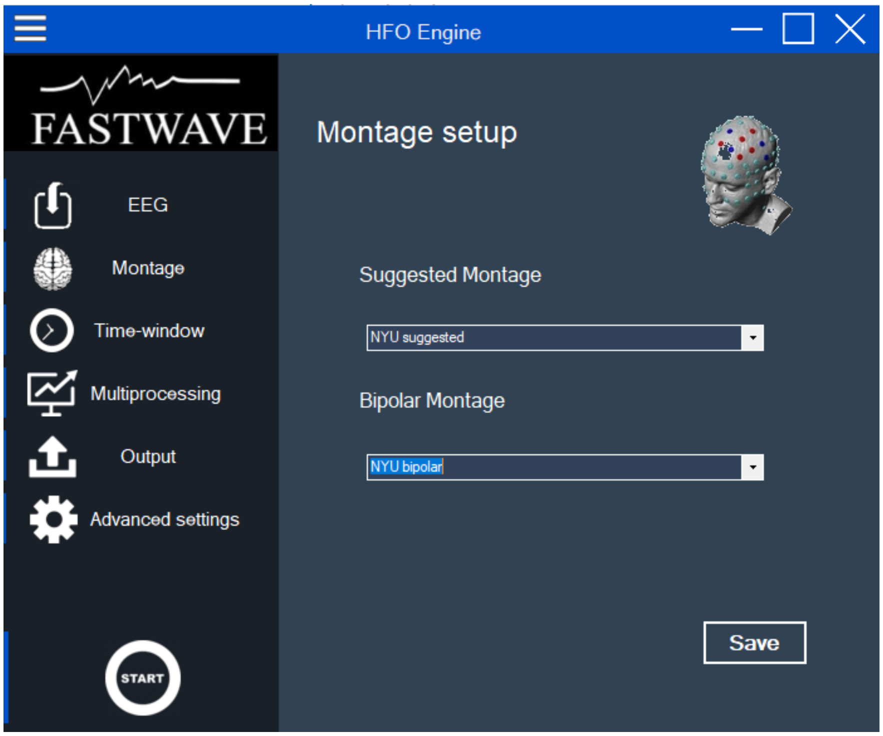
Brain Quick also allows the user to make clips of TRC files. HFO-Engine/EZ-Detect can analyze clips if the clip begins at the same time as the parent TRC file. However, if the clip occurs later the annotations will be incorrect. To overcome this problem the TRC clip can be exported as a raw EDF and then reconverted to a TRC file.

Activating and using the plug-in

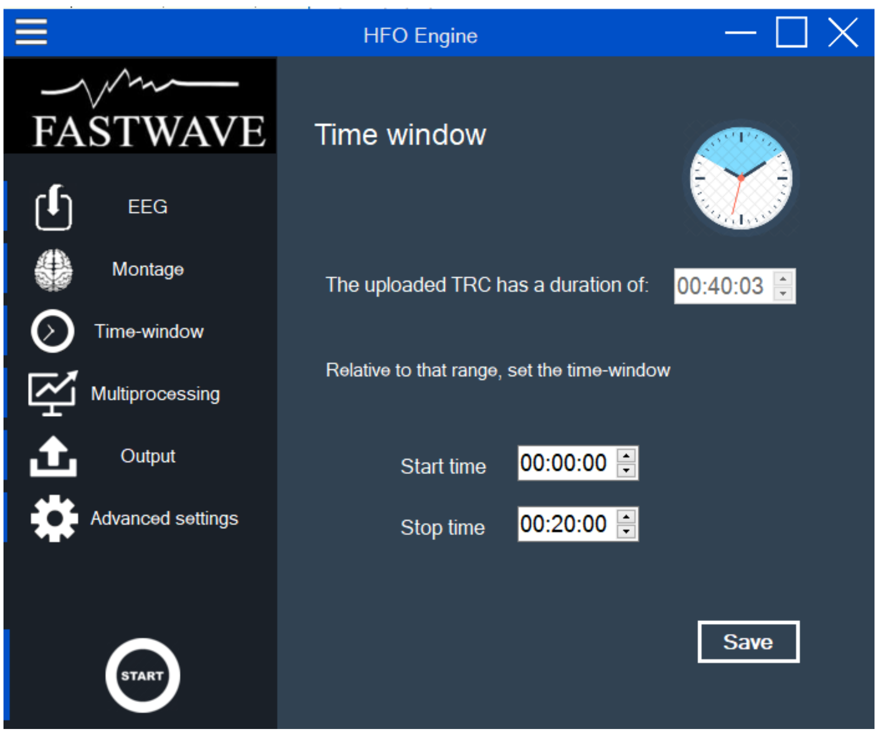
After archiving your TRC file montages and thereby saving them to the TRC file you are ready to start the plug-in. The plug-in can be found under the events menu and clicking on the external calculation tools. This will bring up the external calculation dialogue box. Be sure to choose HFO Annotate – Demo III and click start.



After pressing start HFO-Engine client will open automatically. Look on the dock for the dialogue box that Grito cannot be found and click OK. The next step is to go to advanced settings of the client and connect the HFO-Engine client with the server. After a connection has been established click on EEG in the HFO Engine client. A window appears with a preselected TRC file, make no changes, and click save and then the file will be uploaded to the server. After the upload completes click on montage and choose your suggested and bipolar montages and click save. If you want to analyze in bipolar only mode then choose the bipolar montage for your suggested montage and bipolar montage.



Next click on time window and edit the time-window for the duration of your analysis. HFO-Engine/EZ-Detect processes the iEEG in 10-minute blocks to avoid over consumption of memory. We suggest denoting 10-minute intervals in the time-window dialogue box. The example below will analyze the first 20 minutes of data from a 40-minute file. Be sure to click save.



You **DO NOT** need to click on multiprocessing or output. After entering the time-window, you can now click **start**. While EZ-Detect is running, you can monitor output and progress on the HFO-Engine server side. As a side note, parallel processing and GPU processing are implemented in the current Matlab DSP pipeline. This release of HFO-Engine/EZ-Detect does not run multiple DSPs as separate threads because of Matlab and memory restrictions. You are welcome to make changes to the code for cluster computing purposes. In our version, the single DSP can easily utilize 16-32 cores on its own.

It may take 30-120 minutes for a 10-minute block of data to complete (see benchmarks in installation instructions). Once the analysis is finished the progress bar will advance to 100% the event (EVT) file will be downloaded, and a dialogue box will open that says 'analisis complete'. Click OK on this dialogue box. **Next, you must close HFO Engine for the plug-in process to complete.** After that, the progress bar on external calculation will have advance to 100% and click on the ok box. Finally, change your montage in Brain Quick to the montage suggested to HFO Engine/EZ-Detect and all of your annotations will appear on the iEEG.

Inspecting HFO detection results

After the long wait the detections are ready for review. A couple of tips for reviewing your detections: 1) you must be in the montage specified to the client as suggested to view all the annotations; 2) you will not be able to see the HFOs accurately unless you use a sweep speed of 1-2 seconds; 3) Brain Quick uses IIR filters by default. These filters are nice for inspecting the activity coinciding with HFOs. However, to best inspect the detectors accuracy we recommend an FIR filter. The FIR filter can be specified in the montage settings within Brain Quick. Very often, detections that seem questionable in the IIR settings will be apparent in the FIR settings.

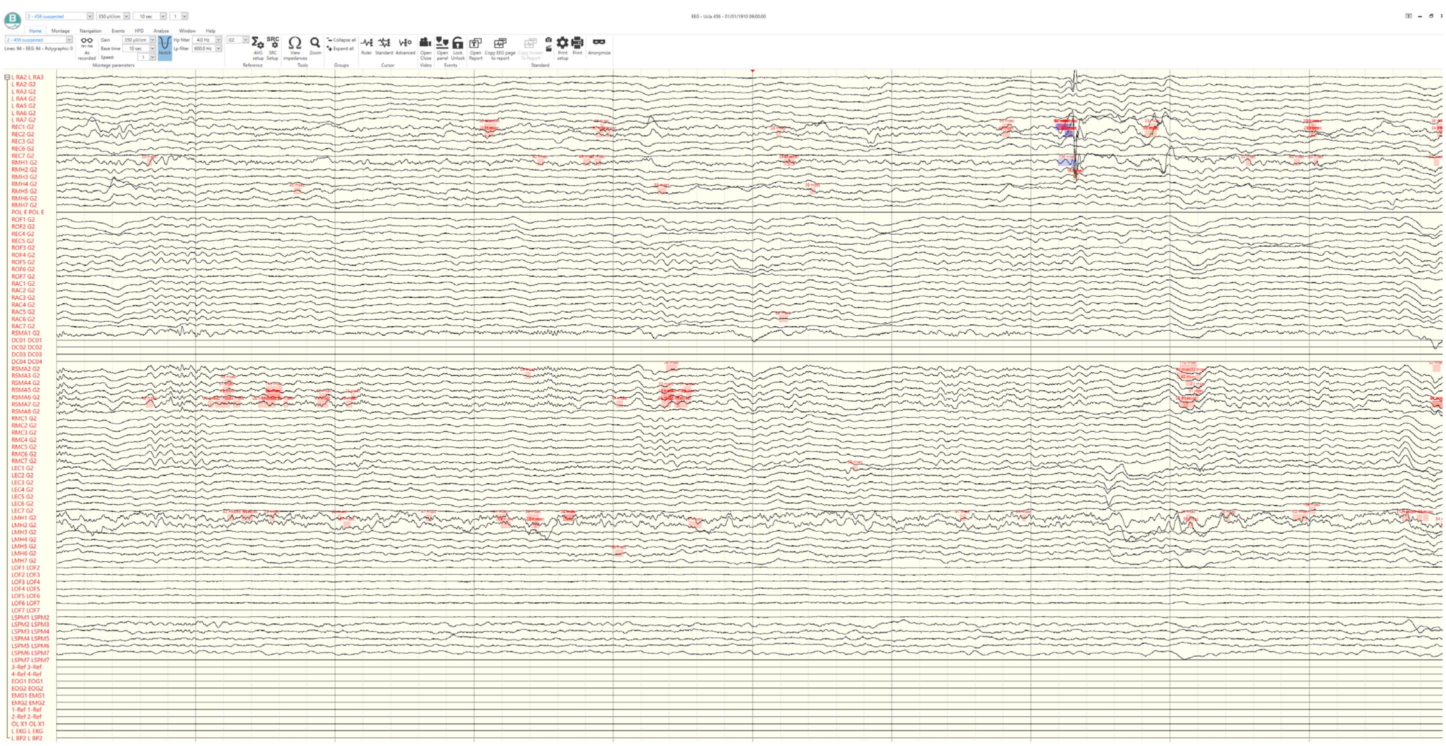


Figure 4 10 second sweep speed of unfiltered annotated SEEG. Red indicates ripples, green indicates fast ripples, and blue indicates spikes.

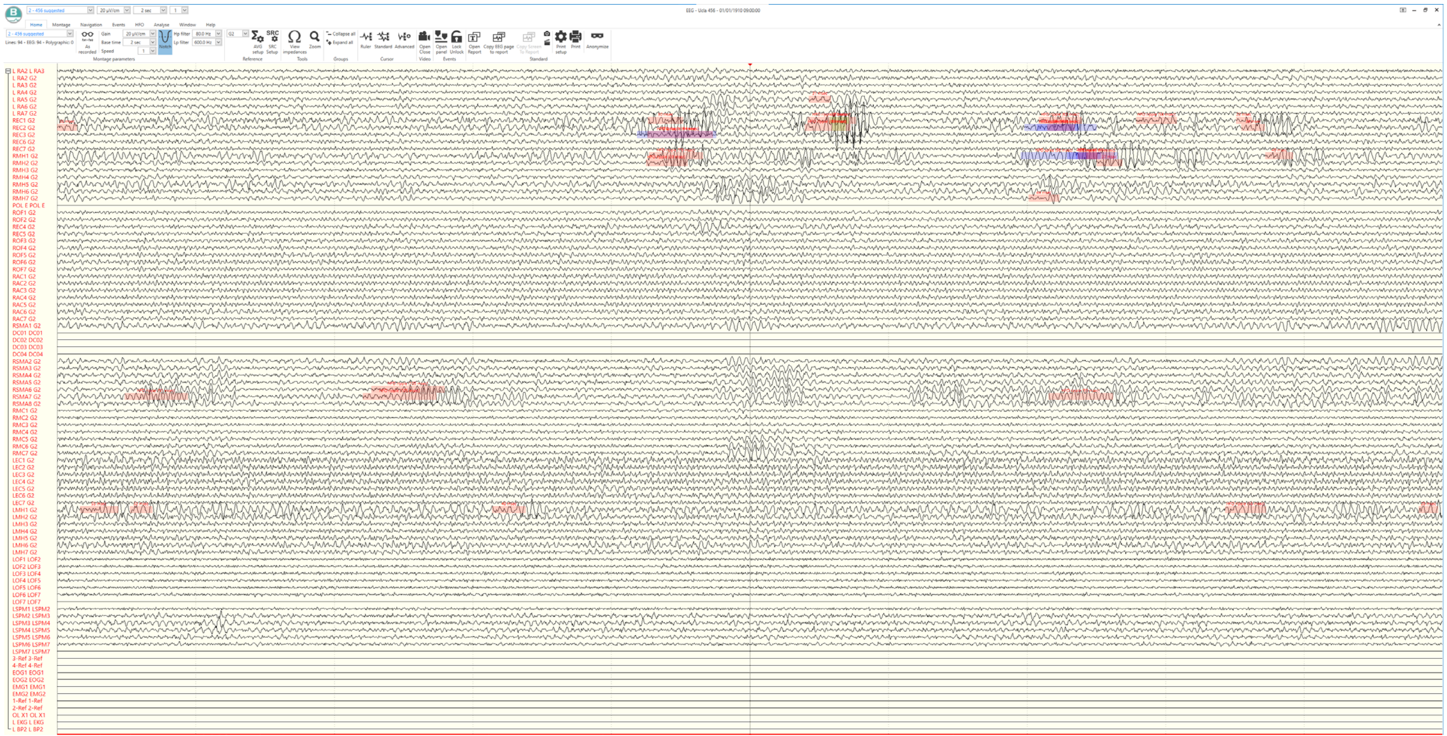


Figure 5 two second sweep speed of the same file after band-pass filtering 80-600 Hz using the Brain Quick FIR filter

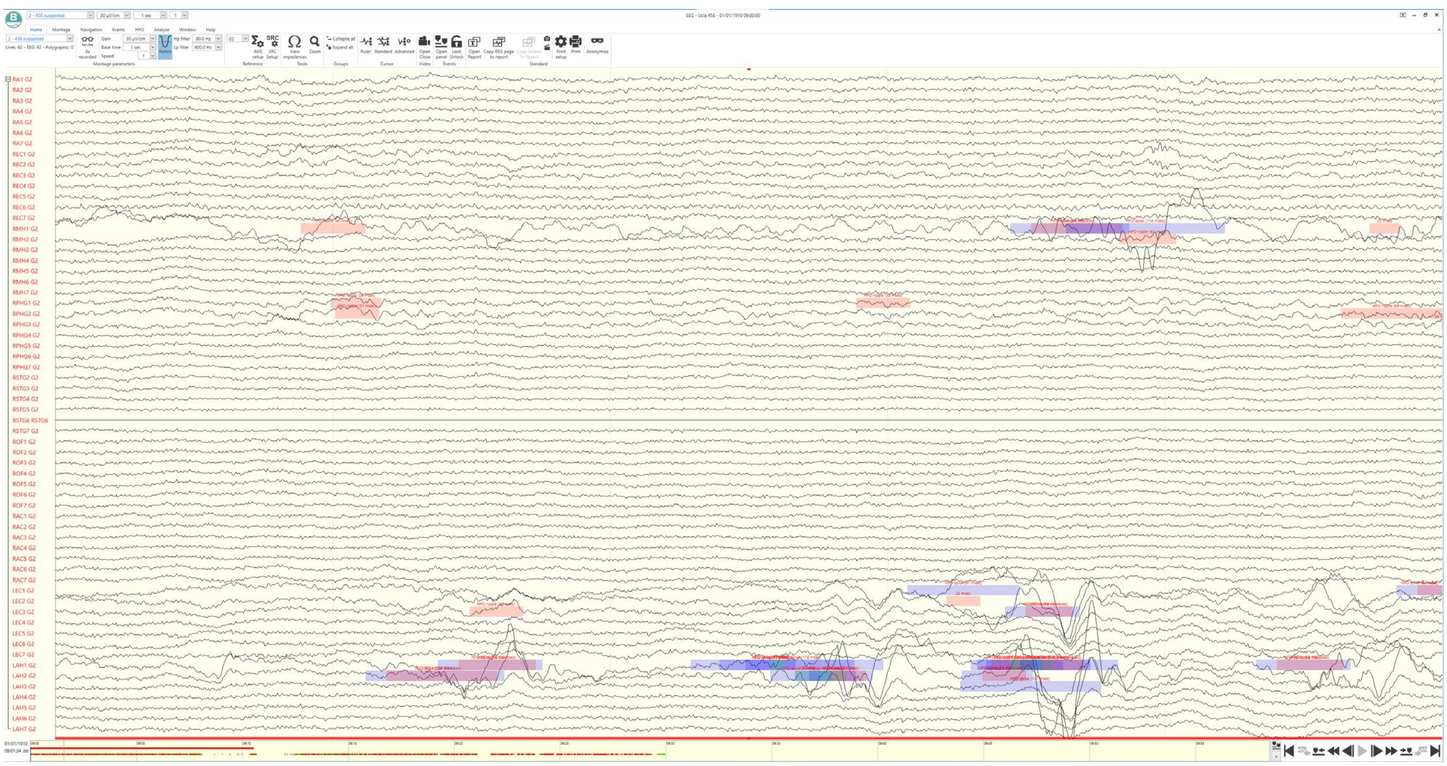


Figure 6 two second sweep speed of another file after band-pass filtering 80-600 Hz using the Brain Quick IIR filter. Note that HFO on spike events can be better differentiated using these filter settings.

MATLAB output

The EZ-Detect DSP does a lot more than annotate the onset and offset of the events. To utilize the full analytic power of this software you need to examine the final output of the HFO detections and quantifications which is stored in the ~/ez-detect/disk_dumps/ez_pac_output folder as .MAT files. These files store all the parameters for each event detection. The ezmongo repository on this github site contains 1) example scripts for editing these files, after manually redacting HFOs in Brainquick; and 2) example scripts for uploading the contents of these data files to a MongoDB for further analysis.

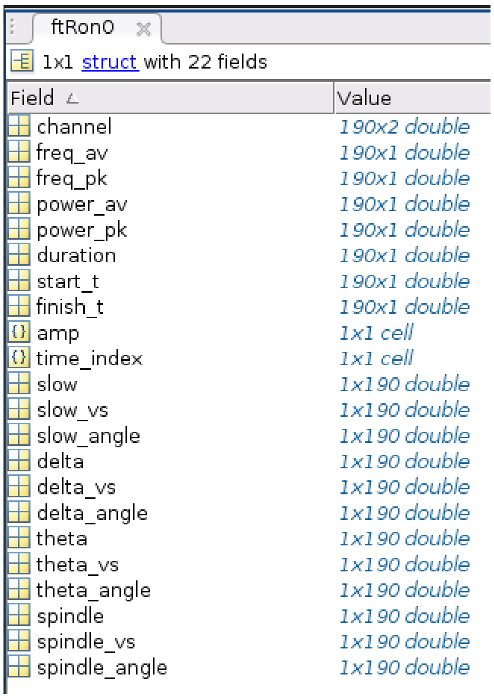


Figure 7 Detailed information of each fast ripple on oscillation detection for a single patient in the ez_pac this data can be uploaded to a MONGODB using the tools in the ezmongo repository.

Appendix

1) HFO Detector and independent component analysis:

a. CUDAICA: GPU optimization of Infomax-ICA EEG analysis. Raimondo F, Kamienkowski JE, Sigman M, Fernandez Slezak D. Comput Intell Neurosci. 2012;2012:206972. doi: 10.1155/2012/206972.

b. Utilization of independent component analysis for accurate pathological ripple detection in intracranial EEG recordings recorded extra- and intra-operatively. Shimamoto S, Waldman ZJ, Orosz I, Song I, Bragin A, Fried I, Engel J Jr, Staba R, Sharan A, Wu C, Sperling MR, Weiss SA. Clin Neurophysiol. 2018 Jan;129(1):296-307. doi: 10.1016/j.clinph.2017.08.036.

c. Visually validated semi-automatic high-frequency oscillation detection aides the delineation of epileptogenic regions during intra-operative electrocorticography. Weiss SA, Berry B, Chervoneva I, Waldman Z, Guba J, Bower M, Kucewicz M, Brinkmann B, Kremen V, Khadjevand F, Varatharajah Y, Guragain H, Sharan A, Wu C, Staba R, Engel J Jr, Sperling M, Worrell G. Clin Neurophysiol. 2018 Oct;129(10):2089-2098. doi: 10.1016/j.clinph.2018.06.030.

2) Topographical Method of HFO categorization and quantification:

a. A method for the topographical identification and quantification of high frequency oscillations in intracranial electroencephalography recordings. Waldman ZJ, Shimamoto S, Song I, Orosz I, Bragin A, Fried I, Engel J Jr, Staba R, Sperling MR, Weiss SA. Clin Neurophysiol. 2018 Jan;129(1):308-318. doi: 10.1016/j.clinph.2017.10.004.

3) HFO Phase-amplitude coupling (phasor method):

a. Ripples on spikes show increased phase-amplitude coupling in mesial temporal lobe epilepsy seizure-onset zones. Weiss SA, Orosz I, Salamon N, Moy S, Wei L, Van't Klooster MA, Knight RT, Harper RM, Bragin A, Fried I, Engel J Jr, Staba RJ. Epilepsia. 2016 Nov;57(11):1916-1930. doi: 10.1111/epi.13572.

b. Bimodal coupling of ripples and slower oscillations during sleep in patients with focal epilepsy. Song I, Orosz I, Chervoneva I, Waldman ZJ, Fried I, Wu C, Sharan A, Salamon N, Gorniak R, Dewar S, Bragin A, Engel J Jr, Sperling MR, Staba R, Weiss SA. Epilepsia. 2017 Nov;58(11):1972-1984. doi: 10.1111/epi.13912. Epub 2017 Sep 26.

c. Ripples Have Distinct Spectral Properties and Phase-Amplitude Coupling With Slow Waves, but Indistinct Unit Firing, in Human Epileptogenic Hippocampus. Weiss SA, Song I, Leng M, Pastore T, Slezak D, Waldman Z, Orosz I, Gorniak R, Donmez M, Sharan A, Wu C, Fried I, Sperling MR, Bragin A, Engel J Jr, Nir Y, Staba R. Front Neurol. 2020 Mar 24;11:174. doi: 10.3389/fneur.2020.00174. eCollection 2020. PMID: 32292384