

RIPPLELAB USER'S GUIDE

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Revision Sheet

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1.1	25/02/2016	Inclusion of load data warnings and RIPPLELAB Script section



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los Andes



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1. GENERAL INFORMATION

RIPPELAB is a multi-window GUI developed in MATLAB for the analysis of high frequency oscillations. It is intended to be a user-friendly and intuitive tool, where users with technical and non-technical backgrounds can explore and analyze brain oscillations from different types of electrophysiological data, especially at high frequency ranges.

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1.1. System Overview

RIPPELAB is an MATLAB application, which allows users the manual and automatic detection and validation of cortical High Frequency Oscillations (HFOs). This application loads data from different EEG formats to process, analyze and display HFOs. Its operational status is under development. RIPPELAB operates on Windows, OS and Linux where MATLAB R2012b or later is installed.

1.2. Organization of the Manual

The user's manual consists of eight sections: General Information, System Summary, Getting Started, Using RIPPELAB, HFOs detection, HFOs Validation, RIPPELAB Scripts, Appendixes and References.

General Information section explains in general terms the system and the purpose for which it is intended. System Summary section provides a general overview of the system. The summary outlines the uses of RIPPELAB's software requirements. Getting Started section explains how to get RIPPELAB and the installation process. Using RIPPELAB section provides a detailed description of the software functions for channel load, display and pre-process. HFOs detection section provides a detailed description of the RIPPELAB's options to detect HFOs. HFOs detection section provides a detailed description of the RIPPELAB's options to validate HFOs. RIPPELAB Scripts provides a general description of how the software scripts are organized, and how some features can be modified according to the user requirements. Finally, the Appendixes section presents some supplemental information, and References section presents the cited bibliography.

In this user's manual, the warning icon  indicates information of processes that requires special conditions to operate. The info icon  highlights important information about the functions described in this document.

2. SYSTEM SUMMARY

RIPPLELAB has been released under GNU Public License version 3, and the source code and documentation can be found in <https://github.com/BSP-Uniandes/RIPPLELAB/>.

2.1. System configuration

RIPPLELAB was developed exclusively using MATLAB scripts, so the compilation of native libraries or external functions is not required. This multi-platform tool can be used on OS X, Linux and Windows 32 and 64-bit architectures, and it can be installed as a MATLAB App in versions equal or later to R2012b.

3. GETTING STARTED

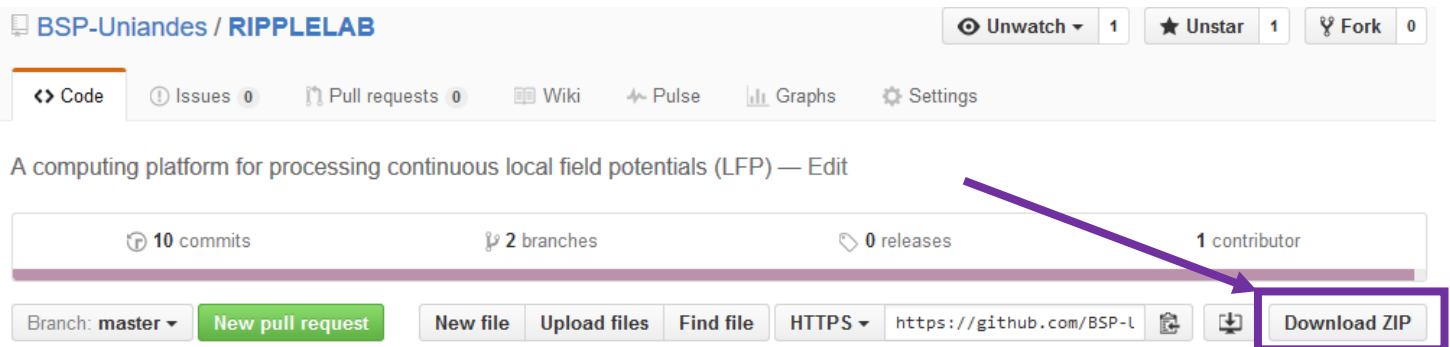
RIPPLELAB was developed in MATLAB version 7.12 (R2011a), and it has been tested in versions 8 (R2012b) and 8.5 (R2015a). To reduce dependency of proprietary MATLAB toolboxes, we integrated some low level functions from BioSig (Vidaurre et al. 2011) and FiledTrip (Oostenveld et al. 2011) toolboxes for specific signal processing and statistical analysis tasks. Even so, if present, RIPPLELAB identifies the MATLAB Signal Processing Toolbox and implements it in order to achieve faster signal processing algorithms.

All the RIPPLELAB images in this manual correspond to the GUI display using MATLAB 8.5 (R2015a)

3.1. Installing the software

RIPPLELAB scripts are found in <https://github.com/BSP-Uniandes/RIPPLELAB/>.

- In the GitHub webpage, please select the [Download ZIP] option:



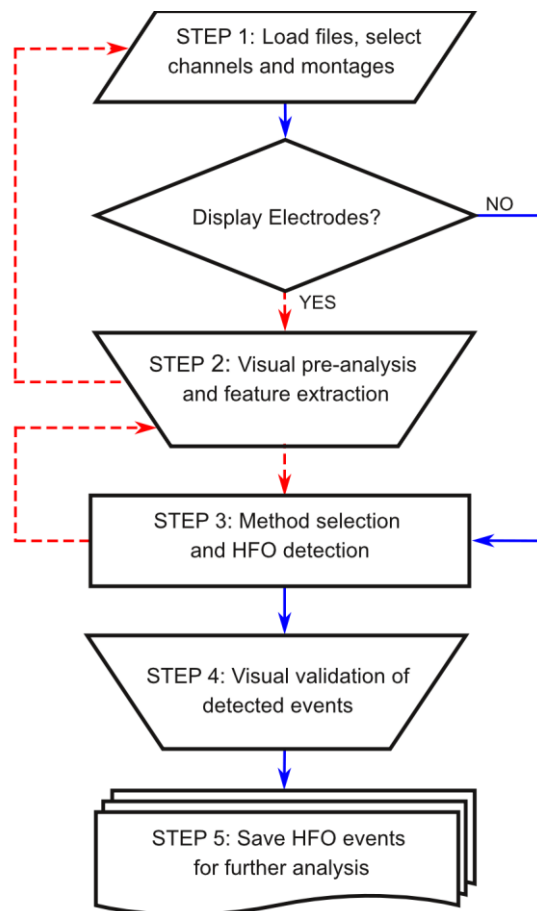
- Select a location to unzip the RIPPLELAB files.
- If you wish, you can add the RIPPLELAB files to the MATLAB path: [Home> Set Path> Add with subfolders]
- Start to use RIPPLELAB

4. USING RIPPLELAB

The complete procedure for detection and analysis of HFOs through RIPPLELAB consists of several steps that are presented in the following subsections and are summarized in **Fig 1**. The steps to use the RIPPLELAB interface are:

- Step 1: Import Files to read
- Step 2: Pre-processing
- Step 3: HFO detection
- Step 4: HFO validation by visual inspection
- Step 5: Save analysis

Figure 1. Steps for HFO detection using the RIPPLELAB software

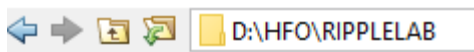


To open RIPPLELAB main GUI, several options are available:

- a. If RIPPLELAB files are in the MATLAB path, write the script name on the workspace.

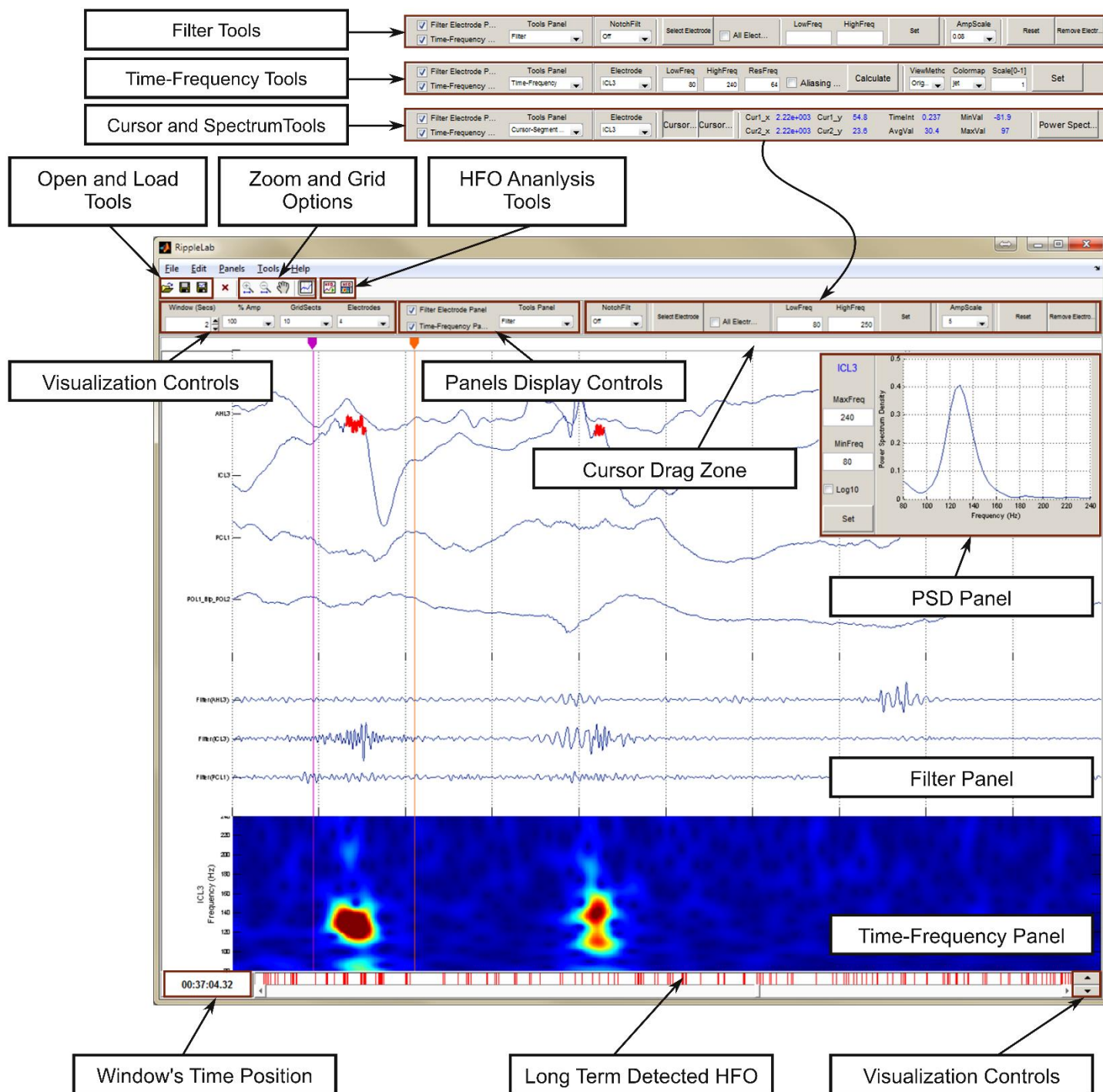
Command Window
`p_RippleLab`

- b. If files are not in the MATLAB path, you must select the RIPPLELAB location on the MATLAB current Folder. For instance:



- c. Starting the application will bring the main window figure (Fig 2).

Figure 2. RIPPLELAB's main window




4.1. Importing Files

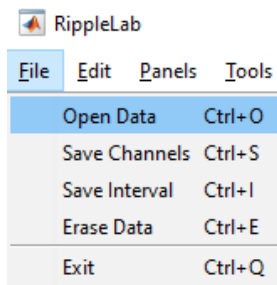
The user can select one or several files for the analysis of long-term recordings. Available and tested EEG formats are:

- Generic standard formats (*.rec, *.edf)
- Nicolet Files (*.eeg)
- EPILEPSIAE file format (*.data)
- Neuralynx Files (*.ncs)
- Plexon Files (*.plx)
- Axon binary Files (*.abf)
- EEGLAB files (*.set)
- Micromed files (*.trc)
- Customized MATLAB Files (*.mat)

Furthermore, RIPPLELAB includes the open source FieldTrip (Oostenveld et al. 2011) scripts to open EEG formats. However, not all the formats listed by FieldTrip have been tested.

4.1.1. Including a new file

- a. To include a new file to RIPPLELAB select the Open Data icon in the toolbar menu  or go to File > Open Data on the RIPPLELAB's main figure [Fig 2: Open and Load Tools Box]:



- b. Then, the Select Channels Window is displayed (Fig 3)
- c. Go to the *+Files* button in the Select Channels Window
- d. Select the file or files to open. Only select files of the same format when selecting multiple files.



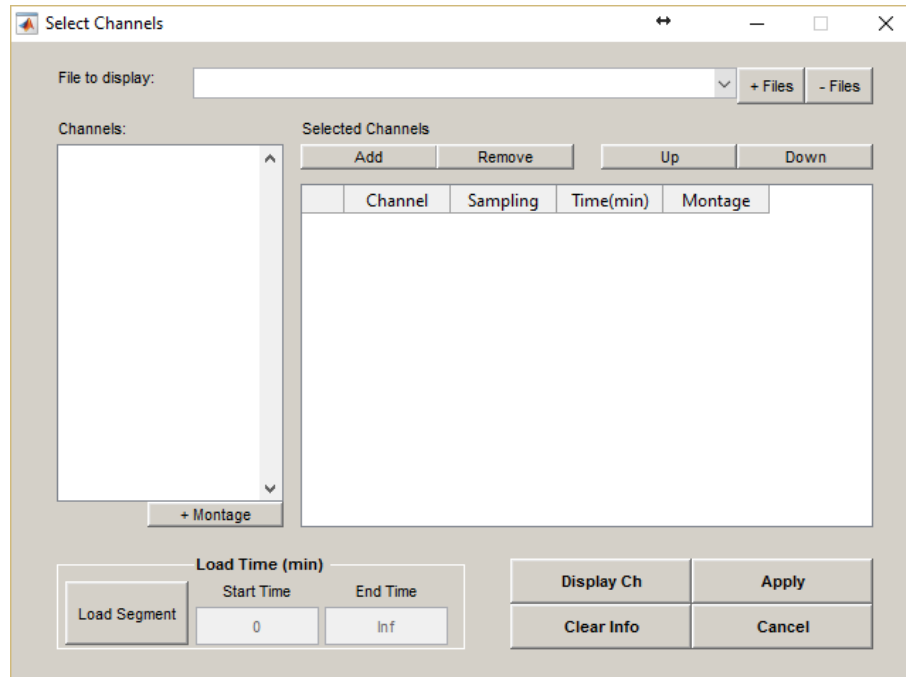
When more than one file has been selected, only the common electrodes will be visible. If there is not common electrodes, the *Channels* list will be empty.

- e. The selected file will be displayed in the *File to display* popup menu in the Select Channels Windows


4.1.2. Removing a File

- f. If multiple files have been selected and you want to remove one file of the list, then click on the *-Files* button in the Select Channels Window and select the file to remove.
- g. If you want to remove all the files or the file selected, then click the *Clear Info* button in the Select Channels Window.

Figure 3. Select Channels window



4.1.3. About the customized MATLAB Files

 RIPPLELAB have the possibility to open customized MAT files, but this files need to be organized in the appropriate structure to be correctly opened.

The correct File MAT file structure required by RIPPLELAB to be opened is:

- The custom MATLAB File (*.mat) for RIPPLELAB is a structure with two fields: Header and Data.
- The **Data** field is an nxm matrix with n samples and m channels.
- **Header** is another structure with four fields:
 - **Sampling**, a vector of sampling rates in Hz for each channel,
 - **IniTime** which is a vector of the initial time of the register ([HH mm SS.ms]),
 - **Samples** representing the number of samples in a channel,
 - **Labels** which is a cell vector of strings with the channel names.

Nevertheless, when a MAT file with different file structure is selected, then the *Convert *.mat files* window is opened to convert MAT files to the appropriate format (**Fig 4**).

In this window, you can select the variable corresponding to data, scale, sampling rate and labels. Also, you can add this information manually for the scale, sampling rate, labels and start time. Each parameter includes a help button for specific information.

After selecting the appropriate parameters, three options are available:

- **Load MAT file Button:** When this option is selected, the data is loaded in the *Select Channels* window once. However, the file structure is not retained for future sessions. Thus, the next time RIPPLELAB opens this file, the file parameters must be introduced again.
- **Save MAT file Button:** When this option is selected, the system ask to save a new file with the customized MAT file structure. This option do not load the data info into the *Select Channels* window, and it must be selected as a new file again. However, the file structure is retained for future sessions. Thus, the next time RIPPLELAB opens this file, the file parameters do not must be introduced again.
- **Cancel Button:** This option ignores all the parameters and returns to the previous window.

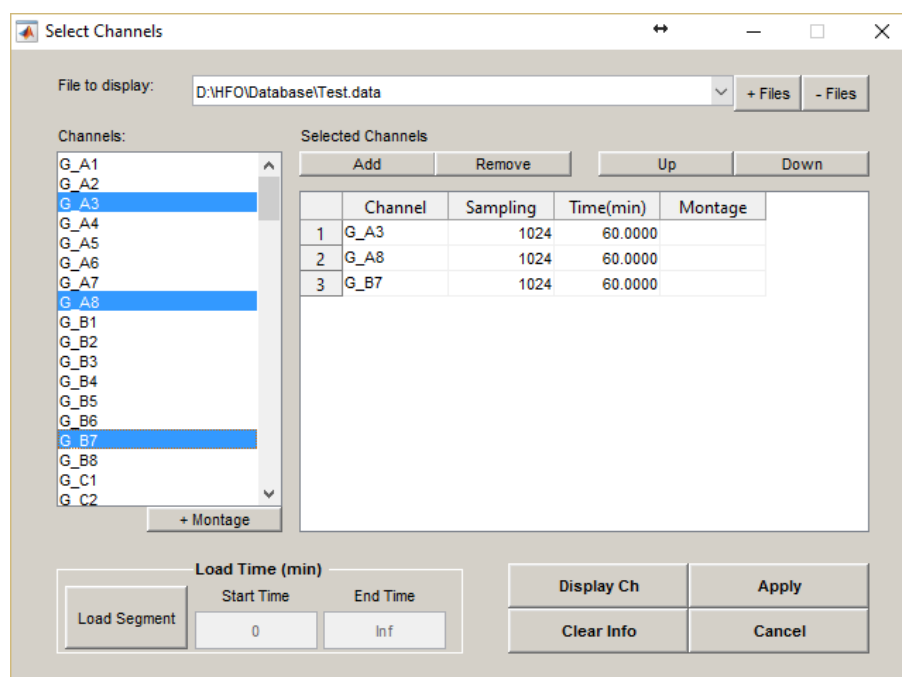
Figure 4. Convert *.mat files window

4.2. Channel Selection

After file selection, the respective electrodes are going to be presented in the *Channels* List (**Fig 5**). One or multiple electrodes can be selected for further analysis.

- To include channels to process, select them from the *Channels* list and click on the *Add* button.
- To remove a selected channel, click on the electrode in the *Selected Channels* table and click on the *Remove* button.
- The order in which the electrodes are displayed on the *Selected Channels* table is the order in which the electrodes are going to be visualized or processed. If you want to change this order, then click on the respective electrode and click on the *Up* or the *Down* buttons.

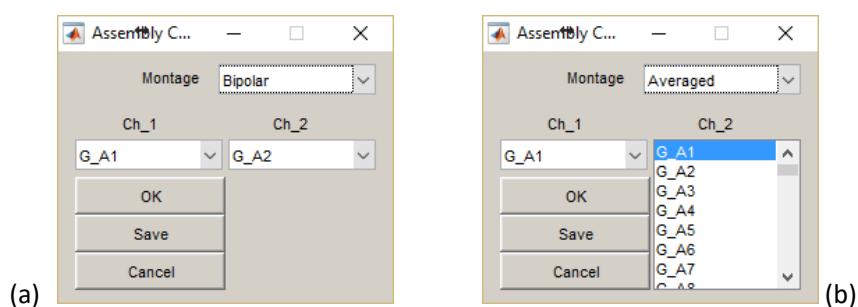
Figure 5. Channel selection in the Select Channels window

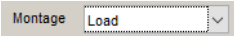


4.2.1. Montage selection

Electrode montages can be included in RIPPLELAB's channel list. For this, click on the *+Montage* button in the *Select Channels* window (**Fig 5**) and the *Assembly Channels* Window will be displayed (**Fig 6**).

Figure 6. Assembly Channels window options



- In the *Assembly Channels* Window you can select the Bipolar (**Fig 6.a**) or average (**Fig 6.b**) montages on the *Montage* popup list. Whereas the *Bipolar* option only gives the possibility to select two channels, the *Average* option give the chance to select multiples electrodes to build the average reference.
- An additional option on the *Montage* popup list is to load a previous built montage selecting the *Load* option . This will open the file explorer to search for a *.rmtg file with the montage configuration.
- Click on the *OK* button to include the new montage on the *Channels* List.

- Click on the *Save* button to save the new montage. This will open the file explorer to save a *.rmtg file with the montage configuration.
- Click on the *Cancel* button to return to the previous window ignoring any selection.

4.3. Channel's Load

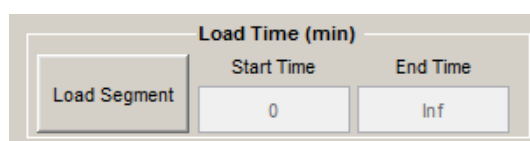
Selected electrodes can be further processed by displaying the signals for pre-analysis or by processing the HFO detection without previous visualization.

- To display the signals, click on the *Display Ch* button in the *Select Channels* window (**Fig 5**).
- To save Channel information and load the channels only when HFO analysis is performed, click on the *Apply* button in the *Select Channels* window (**Fig 5**).

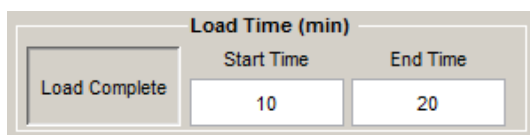


It is important to note that RIPPLELAB is set to load all the selected data into memory to further processing. Hence, with working with large files is recommended to select only specific time segments of the focus channels to analyze.

- To load only a signal segment, click on the *Load Segment* button to enable the segment controls of the *Load Time* Box. You can select the start and the end time of the signals to be loaded. Please take in account that start and end time are set in minutes.

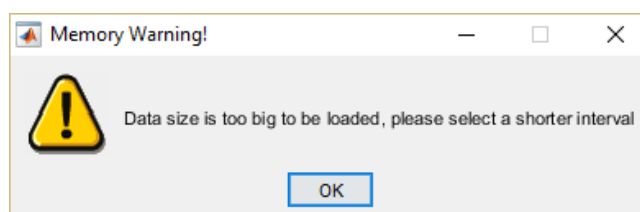


- If a segment is selected and you want to load the complete signal, then click on the *Load Complete* Button to set the start and end times to the first and last sample of the data.

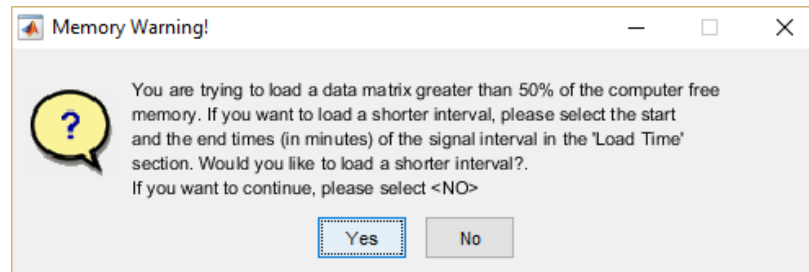


The data size which RIPPLELAB is capable to load depends on the free memory of the system.

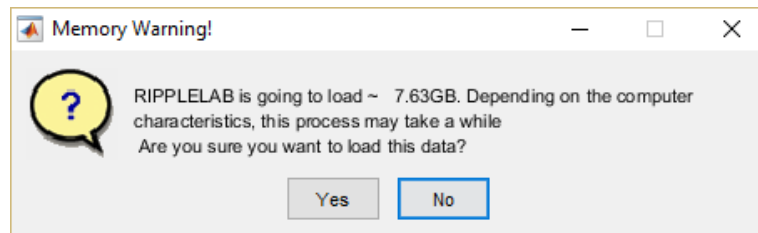
- If data size is larger than 95% of the free memory available, then RIPPLELAB aborts the load and displays a warning message:



- If data size is larger than 50% of the free memory available, then RIPPLELAB displays a warning message indicating this fact and suggest to reduce the data length. To select a shorter data segment click <Yes> in this Message; if you want to continue, then select <No>



- If you have selected to continue the load, a warning message indicating the data size to load is presented. You can abort the load by selecting <No> if the data is too big for the required process.



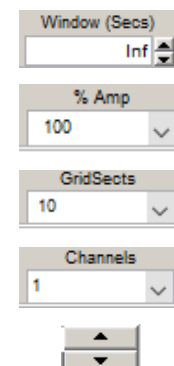
i The time required to load the selected channels varies depending on the characteristics of the EEG format to load, the RAM memory of the computer and the number of channels and samples of the data. This time fluctuates between some milliseconds and some minutes if data is too large.

4.4. Data pre-processing

If data have been selected to be displayed, the RIPPLELAB's main window (**Fig 2**) allows you to visually explore the raw data and to compute different measures to better tune the HFOs detection algorithms.

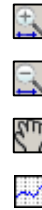
- Visualization controls include [**Fig 2: Visualization controls Box**]:

- Axis management: time window length
- Amplitude scale.
- The number of grids per window.
- Determining the number of channels to be visualized.
- Up/Down Selection



- Zoom and Grid [**Fig 2: Zoom and Grid Options Box**]:

- Horizontal Zoom in
- Horizontal Zoom out
- Panning
- Grid On/Off



- Alternation between relative time (reference to the initial time of the recording) and absolute time (real date and time if present) of the displayed segment of data. [**Fig 2: Window's Time Position Box**]:

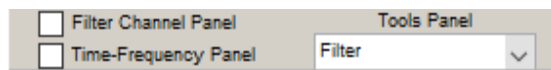
00:00:00.00

- Fast time navigation through the horizontal slider bar

To enable the Filter, Time-Frequency and PSD Panels, the Filter and Time-Frequency analysis must be performed. This is done using the *Panel Display Controls* [**Fig 2: Panel Display Controls box**]. In the *Tools Panel* popup list the option Filter, Time-Frequency and Cursor-Segment Analysis enables the specific options for each of these analyses.

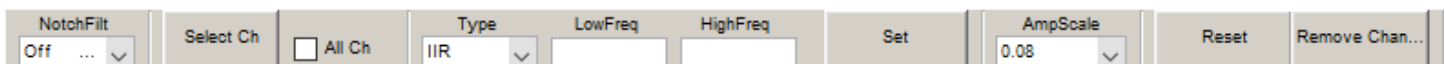
4.4.1. Filtering

The *Filter* option enables the Filter Tools (**Fig 7**).



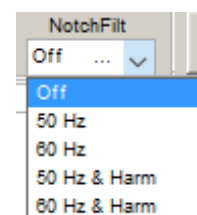
i RIPPLELAB executes the filter analysis over all the signal time of the selected channels. Hence, if the data is large, the time required to complete the filter analysis will take some time.

Figure 7. Filter Tools





- NotchFilter Button:** This popup list selects a notch filter, which applies an fft/fft filter removing the selected frequencies with a smoothed decay in the frequency domain. Specifically, this filter is only computed on all the channels in memory.

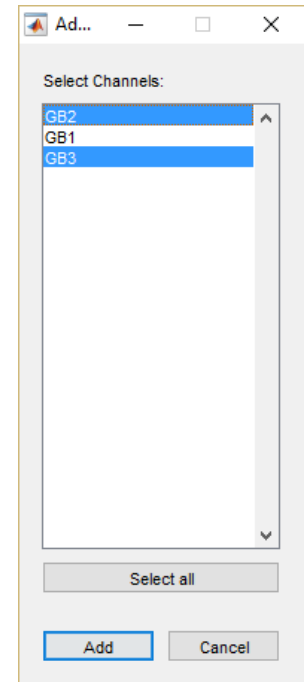
i The filtered data will replace the original data in the main axes.




- **SelectCh Button:** This button opens a list to select the specific channels to filter with custom frequencies.

 The filtered data of the channels selected in this window will be visualized in a parallel panel to the original signal. [Fig 2: Filter Panel]:

 The filtered data will not replace the original data in the main axes.




- **All Ch Checkbox:** When this option is checked, the filter specifications are applied on all the channels in memory.

 The filtered data will replace the original data in the main axes.

- **Type:** This popup list selects the filter type to be applied: IIR (*non-causal filter*) or FIR (*causal filter*). The *causal filter* implements a Hamming-windowed FIR digital filter of 50th order and a cutoff attenuation specified at -6dB (Widmann et al. 2014). The *non-causal filter* employs a type-II Chebyshev IIR forward-backward digital filter, which has a passband ripple of no more than 1 dB and a stopband attenuation of at least 20dB, a cutoff attenuation specified at -3dB, and a second-order section implementation to maintain stability.

- **LowFreq and HighFreq:** Frequency cutoffs of the filter to be implemented. According the values, a filter category is implemented:

- Low Pass Filter: LowFreq = Blank & HighFreq = Numeric value.
- High Pass Filter: LowFreq = Numeric value & HighFreq = Blank.
- Band Pass Filter: LowFreq = Numeric value & HighFreq = Numeric value & LowFreq < HighFreq

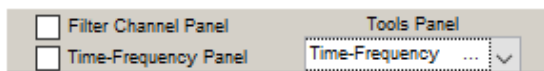
 Non-valid options:

- LowFreq > HighFreq
- LowFreq = Blank & LowFreq = Blank
- Any numeric value > Nyquist Frequency (Sampling frequency / 2)

- **Set Button:** Applies the specific filter depending on the selected parameters
- **AmpScale Popoup List:** When the filter panel is visualized, this option controls the amplitude of the filtered signals.
- **Reset Button:** When the original data has been replaced by the filtered data. This option returns to the original signals.
- **Remove Channels Button:** This button displays a list to select the channels to be removed from the filter panel.

4.4.2. Time Frequency analysis

The *Time-Frequency* option enables the Time-Frequency Tools (**Fig 8**).




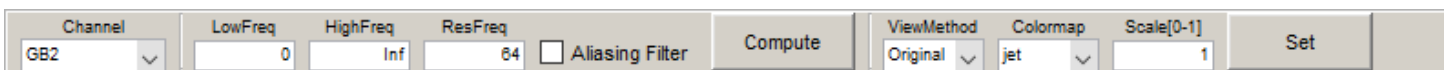

 RIPPLELAB executes the filter analysis only on the displayed segment of the signal. Hence, if the displayed signal is large, the time required to complete the filter analysis will take some time. For each time the displayed segment is computed, the Time-Frequency analysis is computed

Figure 8. Time-Frequency Tools

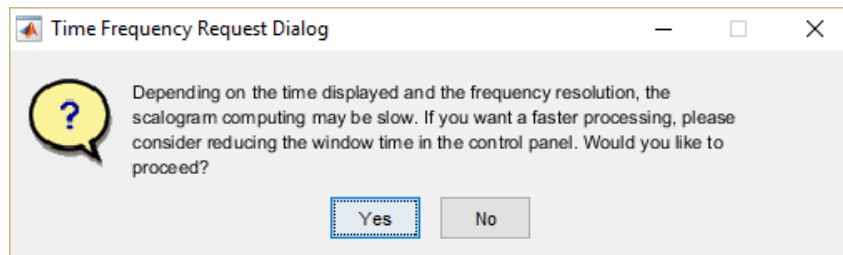


- **Channel list:** This control allows you to select the channel to compute the Time-Frequency analysis.
- **LowFreq and HighFreq:** Frequency boundaries for the Time-Frequency analysis. Frequencies must be $\text{LowFreq} < \text{HighFreq} < \text{Nyquist Frequency (Sampling frequency / 2)}$
- **ResFreq:** This control allows you to select the Frequency resolution. The numeric value corresponds to the number of frequency steps between the low frequency boundary and the high frequency boundary.
- **Aliasing Filter checkbox:** When this option is checked, an antialiasing filter is computed before the Time-Frequency analysis.
- **Compute button:** Computes the Time-Frequency analysis.

 The Time-Frequency analysis of the selected channel will be visualized in a parallel panel to the original signal.

[Fig 2: Time-Frequency Panel]:

 A warning message will be displayed:



- **ViewMethod list:** When the Time-Frequency panel is displayed, this option allows you to change the equalization of the Time-Frequency coefficients.
- **Colormap list:** When the Time-Frequency panel is displayed, this option allows you to change the colormap of the visualized Time-Frequency.
- **Scale:** This control requires a numeric value in the interval $[0,1]$ which scales the Time-Frequency coefficients amplitude.
- **Set button:** Clicking in this button applies any changes established in the *ViewMethod*, *Colormap* and *Scale* controls.

4.4.3. Cursors measures

The *Cursor-Segment Analysis* option enables the Cursor and Spectrum Tools (**Fig 9**).

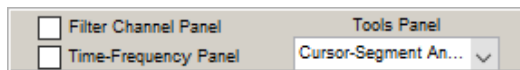


Figure 9. Cursor and Spectrum Tools



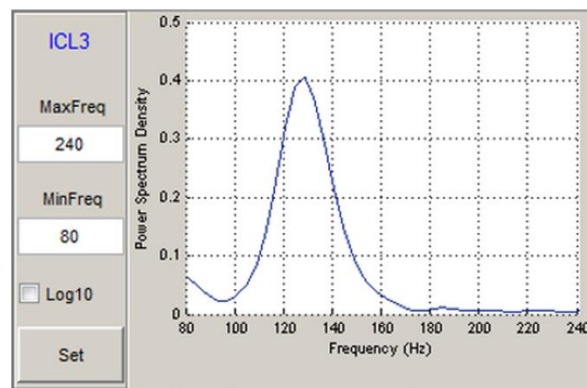
- **Channel list:** This control allows you to select the channel to compute cursor measures and power spectrum.
- **Cursor_1 and Cursor_2 buttons:** These buttons enables and disables the cursors 1 and 2.
- **Cursor Measures:** These controls display different measures depending on the cursors position.
 - **Cur1_x, Cur_2x, Cur1_y, Cur_2y:** Display the cursors positions in the x and y axes.
 - **TimeInt:** Time interval between cursors in seconds.
 - **AvgVal:** Average amplitude value of the signal segment between cursors.
 - **MinVal, MaxVal:** Minimum and Maximum amplitude values of the signal segment between cursors.

- **Power Spectrum button:** Computes the power spectrum of the signal segment between cursors, and it displays the analysis on the PSD Panel [Fig 2: PSD Panel].

4.4.4. Power spectrum

The PSD panel (Fig 10) allows the user to set basic display options of the power spectrum graph.


Figure 10. The PSD Panel



- **MinFreq and MaxFreq:** Frequency boundaries for the power spectrum analysis. Frequencies must be $\text{MinFreq} < \text{MaxFreq} < \text{Nyquist Frequency (Sampling frequency / 2)}$.
- **Log10 checkbox:** Visualize Logarithmic or linear Frequency axis.
- **Set Button:** Clicking in this button applies any changes established in the *MinFreq*, *MaxFreq* and *Log10* controls
- Move the cursors by grabbing the triangles on the cursor bars



5. HFOs DETECTION

To detect HFOs, click on the *HFO Detection Methods* icon  [Fig 2: HFO Analysis Tool Box], or you can go the menu *Tools>HFO Detection Methods*. This will open the *HFO-Detection Methods* window (Fig 11).

To process an automatic HFO detection, it is not necessary that the signals to analyze had been previously displayed. If you click on the *Apply* button in the *Select Channels* window (Fig 3), the signals are going to be loaded only when required by the HFO detection process

5.1. General Controls

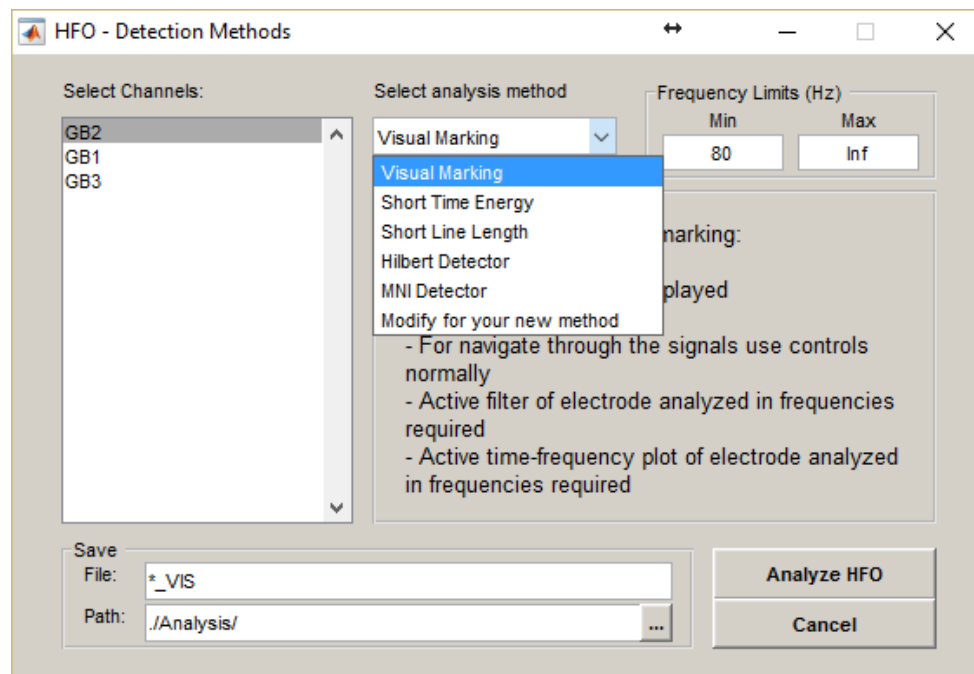
- **Select Channels list:** This control allows you to select the channels to analyze using the HFO detection methods



Multiple electrodes can be selected for automatic detection of HFOs, but only one electrode is possible when selecting the visual marking analysis. [Fig 2: Time-Frequency Panel]:

- **Select analysis method list:** This control allows you to select the HFO detection method.
- **Frequency Limits:** This control allows you to select frequency interval in which the HFO detection is developed. Frequencies must be $\text{Min} < \text{Max} < \text{Nyquist Frequency (Sampling frequency / 2)}$.
- **Save Controls:** These controls allow you to select the Name and the Path for the results file for the HFO analysis. The sign '*' acts as a wildcard character which matches the original file name.
- **Analyze HFO:** This button starts the HFO detection process.
- **Cancel Button:** This option ignores all the parameters and returns to the previous window.

Figure 11. HFO-Detection Methods window



5.2. Manual detection of HFOs

- To perform a manual detection of HFOs, please select the *Visual Marking* option on the Select Analysis method list (Fig 11).



Manual detection can only be performed for a single electrode, which must be first displayed according to the procedure described in the 4.2 and 4.3 sections.

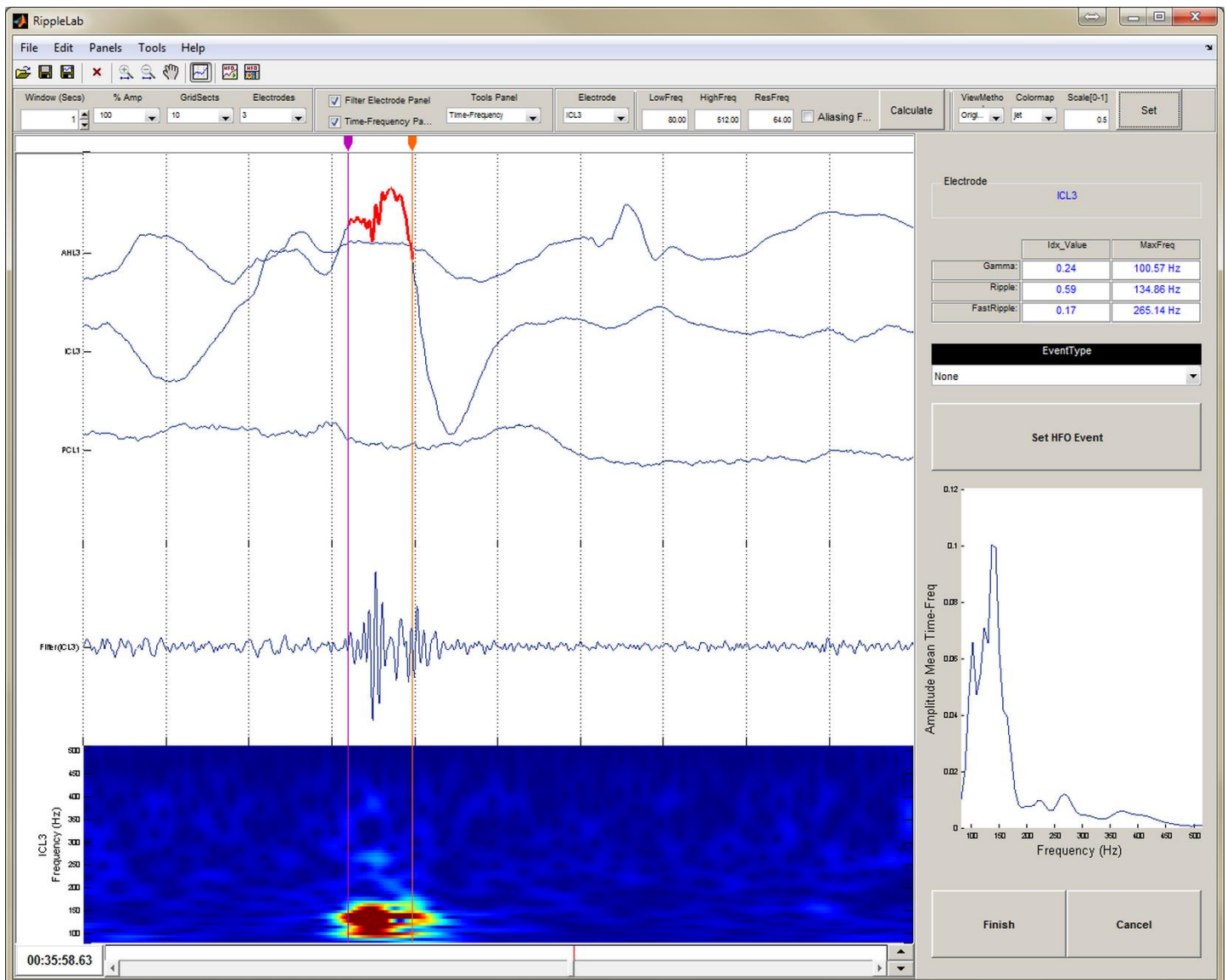
- b. In the *Frequency Limits* panel, select the frequency range where the visual detection will be performed.
- c. Select the name and path of the results file in the *Save* panel.
- d. Click on the Analyze HFO button. Then, the main figure is set to manually mark HFOs as displayed in **Fig 12**.



As the Time-Frequency analysis is developed in the selected frequency range, then the warning message of 4.4.2 section is displayed.

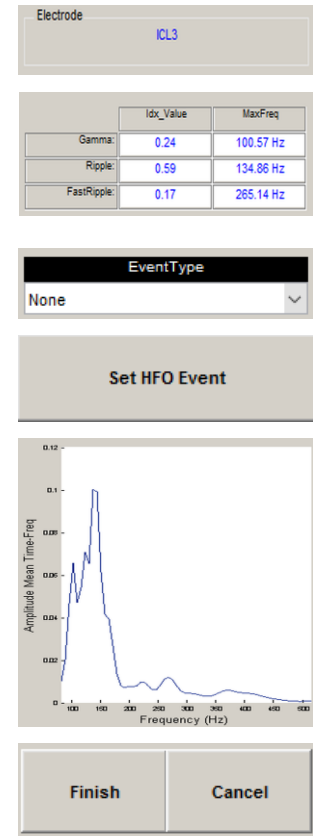
- e. If you need, you can add as many filtered plots in the desired frequencies as described in section 4.4.1.
- f. Look for HFOs. When a HFO is found, set the event limits with the cursors and click on the *Set HFO Event* button.

Figure 12. RIPPLELAB's main figure set to develop the HFO visual marking



- HFO visual marking controls include (**Fig 12**)

- Channel/Electrode: Label of the electrode to be analyzed
- The gamma, ripple and fast ripple indexes (Ibarz et al. 2010)
- Set Event Type for detailed classification of the selected event as Gamma, Ripple or Fast Ripple.
- Set HFO Button, when a HFO is found
- Use the power spectrum density to have more frequency information about the signal between cursors
- Click on the finish button to save the HFO marks, or click on the cancel button to exit the visual marking mode



5.3. Automatic detection of HFOs

Four automatic methods for HFO detection were implemented in RIPPLELAB: the Short Time Energy detector (Staba et al. 2002), the Short line length detector (Gardner et al. 2007), the Hilbert detector (Crépon et al. 2010) and the MNI detector (Zelmann et al. 2012). Each of these methods have their own specific parameters (**Fig 13**) and default values are established as published by each work. A brief description of each method is stated at next.

- The **Short Time Energy (STE)** is the algorithm proposed by Staba et al., 2002. Setting parameters are displayed in **Fig 13.b**. In brief, the wideband EEG signal is band-pass filtered in the high frequency range (*Frequency Limits* parameter). The energy from the filtered signal is then computed using the root mean square (RMS) defined by the equation

$$E(t) = \sqrt{\frac{1}{N} \sum_{k=t-N+1}^t x^2(k)}$$

Figure 13. Automatic detection parameters

a) **HFO - Detection Methods**

Select Electrodes: AHL3, AHL6, ICL1, ICL3

Select analysis method: Visual Marking

Frequency Limits (Hz): Min 80, Max Inf

Detection Parameters:

Considerations for visual marking:

- Electrodes must be displayed
- Select only an electrode
- For navigate through the signals use controls normally
- Active filter of electrode analyzed in frequencies required
- Active time-frequency plot of electrode analyzed in frequencies required

Save File: *_VIS Path: /Analysis/ Analyze HFO Cancel

b) Select analysis method: Short Time Energy

Frequency Limits (Hz): Min 80, Max Inf

Detection Parameters:

Epoch (Sec)	RMS_Window (ms)	RMS SD_Threshold
180	3	5
	MinWindow (ms)	Min GapTime (ms)
	6	10
	Min Oscillations	Peak SD_Threshold
	6	3

c) Select analysis method: Short Line Length

Frequency Limits (Hz): Min 80, Max Inf

Detection Parameters:

Epoch (Sec)	Filter Window (ms)
180	5
	Threshold Percentil
	97.5
	Event MinTime (ms)
	80

d) Select analysis method: Hilbert Detector

Frequency Limits (Hz): Min 80, Max Inf

Detection Parameters:

Epoch (Sec)	SD Threshold	Min EventTime (ms)
180	5	10

e) Select analysis method: MNI Detector

Frequency Limits (Hz): Min 80, Max Inf

Detection Parameters:

Epoch (Sec)	MinWindow (ms)	Baseline Segment (Sec)
10	10	125
CHF_Epoch (Sec)	Min GapTime (ms)	Shift
1	10	0.5
CHF_Percentil	Threshold Percentil	Threshold
95	99.9999	0.67
		minBaseline
		5

within a N= 3-ms window (*RMS_Window* parameter), and successive RMS values greater than 5 standard deviations (SD) above the overall RMS mean (*RMS SD_Threshold* parameter) are selected as putative HFO events if they last more than 6 ms (*Min_Window* parameter). Finally, only events containing more than 6 peaks (*Min Oscillations* parameter) greater than 3 SD above the mean value of the rectified band-pass signal are retained (*Peak SD_Threshold* parameter). In addition, events separated by 10 ms or less are marked as a single oscillation (*Min Gap Time* parameter). In the original paper, the energy threshold was established to be set depending to the complete analyzed segment, which had a duration of 10-min. Hence in RIPPLELAB, the energy threshold can be computed for the entire signal, as originally proposed by Staba, or shorter segments can also be used, as suggested by Gardner et al. (2007) (*Epoch* parameter).

- The **Short Line Length detector (SLL)** was developed by Gardner et al. (2007) and Worrell et al. (2008); setting parameters are displayed in **Fig 13.c**. In this approach, a preprocessing stage is done with a derivative filter in order to equalize the spectrum of the signal. Next, a band-pass filter is applied (*Frequency Limits* parameter). Then, the energy of the signal is calculated by a short time line length measure (Esteller et al. 2001) defined by

$$E(t) = \sum_{k=t-N+2}^i |x(k) - x(k-1)|$$

with window N = 5 ms (*Filter Window* parameter). An event is valid if its amplitude is greater than the 97.5th percentile of the empirical cumulative distribution function (*Threshold Percentile* parameter) for each 3-min epoch (*Epoch* parameter) and if it has a minimum duration (*Event Min Time* parameter). This duration is set in 80 ms in Gardner et al. (2007), but it is ignored in Worrell et al. (2008). We set this parameter as 12 ms by default in order to accept events larger than 6 oscillations at 500Hz.

- The **Hilbert Detector (HIL)** was proposed by Crépon et al., (2010). Setting parameters shown in **Fig 13.d**. In this method, the signal is first filtered between a selected frequency range (*Frequency Limits* parameter), and the envelope is then

computed with the Hilbert transform. For an event to be considered valid, two conditions must be met: first, for each event, the local maximum must exceed a threshold of 5 SD of the envelope (*SD Threshold* parameter) calculated originally over the entire recording or from a time interval (*Epoch* parameter). Second, each detected HFO must have a minimal time length of 10 ms (*Min EventTime* parameter). As in the STE detector case, we included the possibility to analyze the threshold by epochs specified by the user.

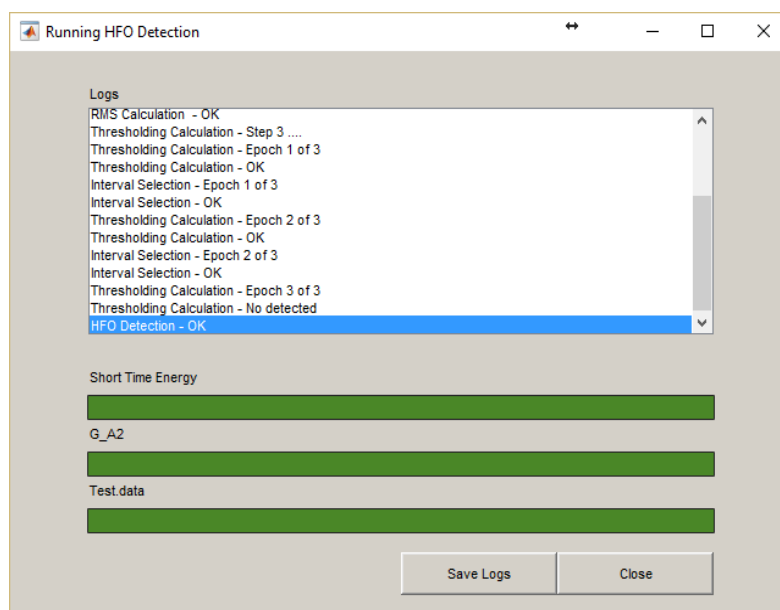
- **The MNI detector (MNI)** was developed by Zelmann et al. (2012). Setting parameters are observed in **Fig 13.e**. In this method the signal is first band-pass filtered (*Frequency Limits* parameter). Then, a baseline detection procedure based on the wavelet entropy is applied (Zelmann et al. 2010). For this, the signal is divided into segments of 125 ms (*Baseline Segment* parameter) with 50% overlap (*Baseline Shift* parameter). Next, for each segment, the normalized wavelet power of the autocorrelation function is computed using the complex Morlet wavelet (Morlet et al. 1982). Subsequently, the maximum theoretical wavelet entropy from the segment is obtained for the white noise (Rosso et al. 2001), and the segment is considered as a baseline interval when the minimum entropy is larger than a threshold (*Baseline Threshold* parameter). If a “sufficient amount” of baseline exists, HFOs candidates are detected in accordance with the energy, defined as the moving average of the RMS amplitude of the filtered signal. Segments with energy above a threshold (*Threshold Percentile* parameter) and lasting more than 10 ms (*MinWindow* selection) are considered as HFO. Similar to other methods, events located less than 10 ms apart are considered as single events (*Min GapTime* option). If a sufficient amount of baseline is not present in the signal, an iterative procedure is carried out where the threshold is computed for the band-passed signal. Originally, this detection methodology was implemented with 1-min segments of EEG signal. Therefore, we included the possibility to process the data thresholds in epochs of time specified by the user.


5.4. HFO detection process and logs

To start an automatic HFO detection process, click on the *Analyze HFO* button in the *HFO-Detection Methods* window (**Fig 11**). This selection launch the *Running HFO Detection* window (**Fig 14**), which indicates the progress of the HFOs detection process.

After the detection process ends, you can save the detection logs in a text file by clicking on the **Save Logs** button. Click on the Close button to return to the main window

Figure 14. Running HFO detection window



 After any detection process is finished and the signals have been previously displayed, a group of red marks will appear upon the horizontal slider bar [Fig 2. Long Term Detected HFO Box]. Each mark is a shortcut to each detected event, so if you click on these marks, the time position skips to the selected HFO event.

6. HFOs VALIDATION


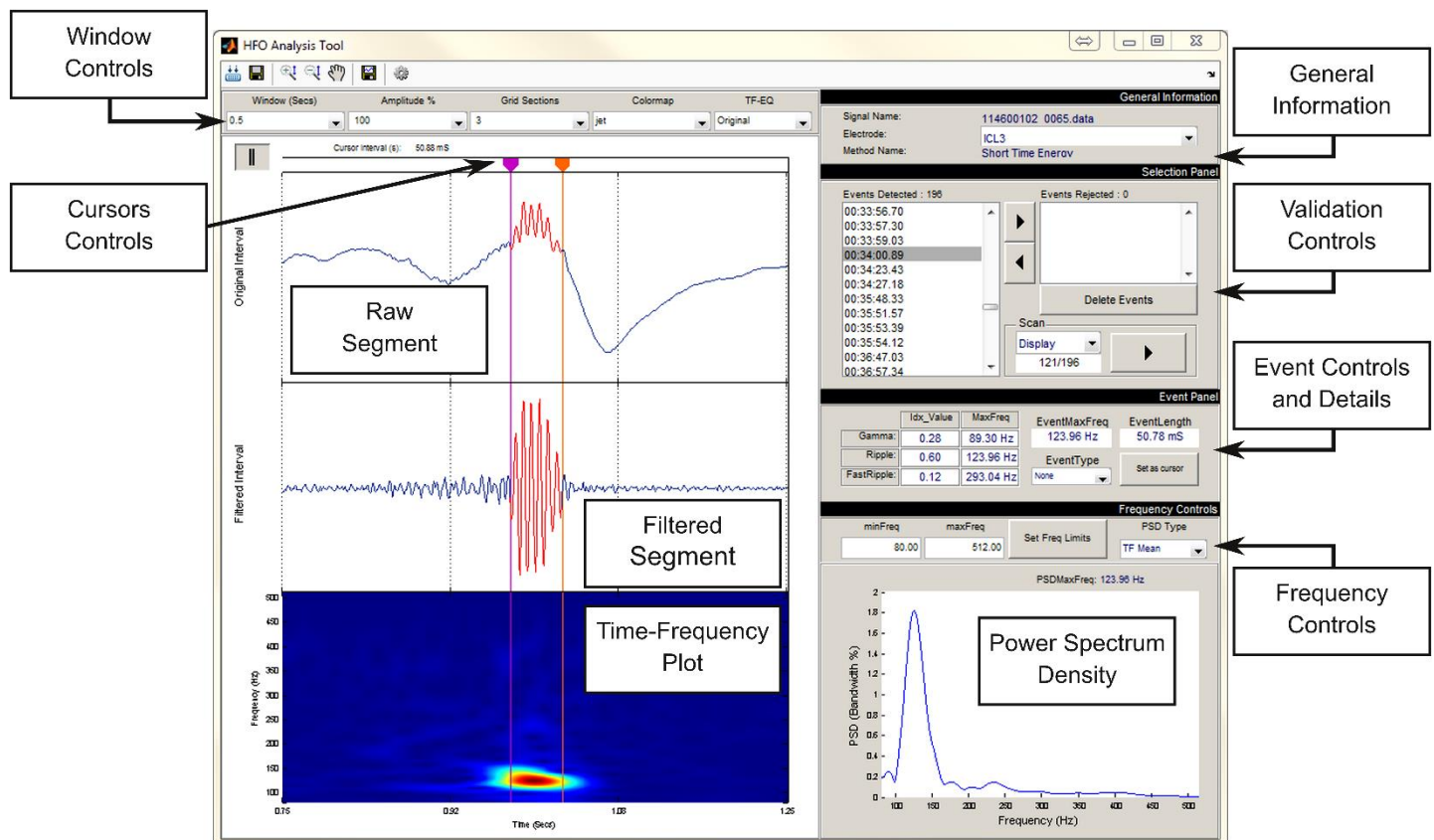
To open the tool for HFO validation, click on the *HFO Analysis Tool* icon  [Fig 2: HFO Analysis Tool Box], or you can go the menu Tools>HFO Analysis Tool. This will open the HFO Analysis Tool interface (Fig 15).

Figure 15. HFO Analysis Tool interface



- Window controls include [Fig 15: Window controls Box]:
 - Window (Sec):** time window length
 - Amplitude** scale in %.
 - Grid Sections** changes the number of grids per window.
 - Colormap** changes the Time-Frequency scale of colors

Window (Secs)

0.5

Amplitude %

100

Grid Sections

5

Colormap

jet

- **TF/EQ** changes the equalization of the Time-Frequency coefficients
- General Information Panel [Fig 15: General Information Box]:
 - It presents the name of the analyzed file, the selected method for detection and the currently selected channel
- Selection Panel [Fig 15: Validation Controls Box]:
 - **Events detected** displays the time moments where events were detected. By clicking each row, the corresponding event is selected and displayed.
 - **Events Rejected** displays the time moments where events were manually rejected.
 - **Accept/Rejected controls** shift the events as rejected or accepted depending on the selection.
 - **Delete Events button** clears all the rejected events
 - **Scan** offers three different possibilities.
 - *Display* allows you to automatically visualize all detected events.
 - *Auto-Classify* lets an event classification based on its spectral characteristics. Thus, they can be labeled as *Gamma*, *Ripple*, *Fast Ripple*, *Spikes*, *Artifacts* or *Others*.
 - *Remove Others* allows you to delete those events classified as *Others*.
- Event Panel [Fig 15: Event Controls and Details Box]:
 - The gamma, ripple and fast ripple indexes (Ibarz et al. 2010)
 - **EventMaxFreq** Maximum frequency of the signal for the segment between cursors.
 - **EventLength** Time in seconds of the selected event.
 - **EventType** allows you define the event type according to the classification: *Gamma*, *Ripple*, *Fast Ripple*, *Spike*, *Artifact* or *Other*.

TF-EQ

Original

General Information

Signal Name: 114600102_0065.data

Electrode: ICL3

Method Name: Short Time Energy

Events Detected : 196

00:35:51.57

00:35:53.39

Events Rejected : 0



Delete Events

Scan

Display

130/196

	Idx_Value	MaxFreq
Gamma:	0.27	83.44 Hz
Ripple:	0.73	127.91 Hz
FastRipple:	0.00	Hz

EventMaxFreq

127.91 Hz

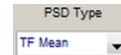
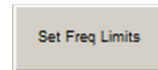
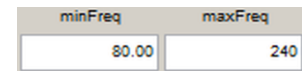
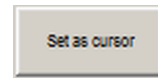
EventLength

45.90 mS


EventType

None

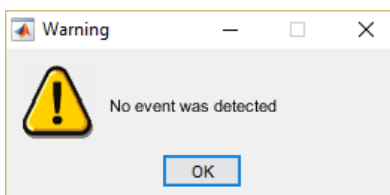
- **Set as a cursor** Time in seconds of the selected event.
- Frequency Controls Panel [Fig 15: Validation Controls Box]:
 - **minFreq/maxFreq** allows the user to change the frequency limits for both the filtered signal and the time-frequency plot.
 - **Set Freq Lims button** establishes any change in the frequency limits
 - **PSD Type** determines the computation type of the power spectrum for the segment between cursors.
- The left panel presents a short segment of individual events.
 - **Clip to event button** sets automatically the cursors to the detected event segment.
 - In the top panel, the raw signal is plotted highlighting the HFO in red. The equivalent filtered signal and the time-frequency plot are presented in middle and bottom panels, respectively.



6.1. Load a HFO analysis


After starting the HFO Analysis Tool Interface, click on the Import *Analysis Icon*  to load a HFO analysis file (*.rhfe).

If the HFO analysis file contains detected events, they will be automatically presented. Conversely, if no events were detected, a warning message will be displayed




6.2. Review a HFO analysis

- a. You can visually validate each of the detected events by selecting the different events in the *Events Detected* list. Move throughout the events by clicking on them or with the arrow keys.
- b. Reject a selected event by clicking on the remove button (Right Arrow Button) [Fig 15: Validation controls Box].
- c. Delete the rejected events by clicking the *Delete Events* button [Fig 15: Validation controls Box].
- d. Accept a rejected event by selecting it in the *Events Rejected* list and clicking on the accept button (Left Arrow Button) [Fig 15: Validation controls Box]
- e. Classify the event type as *Gamma*, *Ripple*, *Fast Ripple*, *Spike*, *Artifact* or *Other* using the *EventType* control [Fig 15: Event Controls and Details Box]

 To speed up the validation process, some keyboard shortcuts have been implemented:

- Shift + arrow left or Shift + arrow right: controls the position of the left cursor.
- Ctrl + arrow left or Ctrl + arrow right: controls the position of the right cursor.
- Alt + Enter: event limits are resized to the position limited by the cursors.
- D key: moves the selected event to the Events Rejected list.
- A key: moves the last event in the Events Rejected list to the Events Detected list.

6.3. Save a HFO analysis

After the review process, save the HFO analysis file by clicking on the save analysis button 

7. RIPPLELAB SCRIPTS

This section is related to specific characteristics of RIPPLELAB programming. This information is not relevant for the usage of the RIPPLELAB interface, but it gives useful material for the understanding of RIPPLELAB scripts and organization.

7.1. Scripts overview

RIPPLELAB GUI is completely written programmatically without the use of MATLAB GUIDE. Consequently, all the figures included in the RIPPLELAB interface are not previously created as .fig objects.

RIPPLELAB's programming establishes a variable prefix code which indicates the variable type as described at next:

- *s_VariableName*: The (s_) prefix states the variable use as a scalar (*single numeric value*).
- *v_VariableName*: The (v_) prefix states the variable use as a vector (*mx1 or 1xn array*).
- *m_VariableName*: The (m_) prefix states the variable use as a matrix (*mxnrx... array*).
- *st_VariableName*: The (st_) prefix states the variable use as a structure or MATLAB object.
- *str_VariableName*: The (str_) prefix states the variable use as a character string.
- *f_FunctionName*: The (f_) prefix states the name of a function or nested function.
- *p_ProgramName*: The (p_) prefix states the name of a function used as the main script of a code (program).

The scripts are written in MATLAB sections named according to the functionality of the code, and the object handles are stored in MATLAB structures.

To facilitate the process of edition, the sections to modify when a new method is included are marked with the comment: `[**INSERT!**]`, and an example is provided for each case.

7.2. Including a new EEG format

To include a new EEG format load script, two features functions must be modified: `f_GetHeader()` for EEG header reading and `f_GetData()` for EEG samples data reading.

- For `f_GetHeader` find the `[**INSERT!**]` comment and follow the example. A new case section referenced to the file extension must be included. For Instance, for a new EEG format with file extension `*.new` and header loader script named `"newformatreadheader()"`, the case section may be established as:

```
function st_Info = f_GetHeader(pst_SigPath)
% Reads header information from header or eeg files
% INPUT:
% pst_SigPath.name: Name of Signal file
% pst_SigPath.path: Path of Signal File
% OUTPUT
% st_Info.SigPath      = Full Path of signal file
% st_Info.SigName      = Signal Name;
% st_Info.SigExt       = File extension for signal type;
% st_Info.str_FileType = File Type
% st_Info.Start        = Absolute start time
% st_Info.Time         = Time length of record in mins;
% st_Info.SampleRate   = Sample rate for signal;
% st_Info.NumbRec      = Number of records;
% st_Info.Labels       = Label of records;
% st_Info.Scale        = Amplitude scale;
% st_Info.error        = Reading Error;
% st_Info.AmpScaleRec  = Amplitude scale for record;
% st_Info.MinMaxRec    = min value and max value per record;
% st_Info.Custom       = Structure with custom information according with type

% Script
(...)

case 'new'
    st_Info = newformatreadheader(str_FullPath);

    st_Info.s_Start      = st_Info.a;
    st_Info.s_Time       = st_Info.b;
    st_Info.s_Samples    = st_Info.c;
    st_Info.v_SampleRate = st_Info.d;
    st_Info.s_NumbRec    = st_Info.e;
    st_Info.v_Labels     = st_Info.f;
    st_Info.s_Scale      = st_Info.g;
    st_Info.st_Custom    = st_Info;

% Script
(...)
```

- For `f_GetData` find the `[**INSERT!**]` comment and follow the example. A new case section referenced to the file extension must be included. For Instance, for a new EEG format with file extension `*.new` and data loader script named `"newformatreaddata ()"`, the case section may be established as:

```

function st_Data = f_GetData(pst_Info,pv_TimeLims,pv_Selected)
% Reads channels data from eeg files
% INPUT:
% pst_Info = Information structure
%
% st_Info.SigPath = Full Path of signal file
% st_Info.SigName = Signal Name;
% st_Info.SigExt = File extension for signal type;
% st_Info.str_FileType= File Type
% st_Info.Start = Absolute start time
% st_Info.Time = Time length of record in mins;
% st_Info.SampleRate = Sample rate for signal;
% st_Info.NumbRec = Number of records;
% st_Info.Labels = Label of records;
% st_Info.Scale = Amplitude scale;
% st_Info.error = Reading Error;
% st_Info.AmpScaleRec = Amplitude scale for record;
% st_Info.MinMaxRec = min value and max value per record;
% st_Info.Custom = Structure with custom information according with
% type
%
% pv_TimeLims = Time limits of channels to load
% pv_Selected

% OUTPUT
%
% st_Data = Data structure
%
% st_Data.v_Labels = Labels of selected channels;
% st_Data.s_Sampling = Frequency sample;
% st_Data.v_TimeLims = Time limits of channels to load;
% st_Data.m_Data = mxn matrix of channels samples m: samples, n:channels
% st_Data.v_Time = Time vector;
% st_Data.s_TotalTime = Total time in seconds;

% Script
(...)

case 'new'

% f_AskSamplesLims() gives the sample position of the selected start and end
% time

[s_Start,s_End] = f_AskSamplesLims(st_Data.s_Sampling,...
    pst_Info.s_Time,pv_TimeLims);

if isempty(s_End)
    s_Start = ... % Stablish here the start condition for reading the first
    sample
end

if isempty(s_End)
    s_End = ... % Stablish here the start condition for reading the last
    sample
end

st_Data.m_Data = newformatreaddata(pst_Info.str_SigPath,...
    'channels',pv_Selected,...

```

```

        'start',s_Start,...
        'stop',s_End);

    if find(size(st_Data.m_Data) == numel(pv_Selected)) == 1
        st_Data.m_Data = st_Data.m_Data';
    end

% Script
(...)

```

7.3. Including a new detection method

To include a new detection method, the following two features must be set: the visualization of the panel that allows the configuration of different parameters associated with the new method and the selection of the new method for further processing.

In order to access and visualize the new method settings, the cell array `v_HFOMethodsList` containing the HFO detection options must be modified as follows:

```

v_HFOMethodsList = [{'Visual Marking'}, {'Short Time Energy'},...
                    {'Short Line Length'}, {'Hilbert Detector'},...
                    {'MNI Detector'}, {'Modify for your new method'}];

% Example:
% v_HFOMethodsList = [{'Visual Marking'}, {'Short Time Energy'}, ...
%                    {'Short Line Length'}, {'Hilbert Detector'},...
%                    {'MNI Detector'}, {'XXX Detector'}];

```

If some new selection controls for the method to implement are desired, a new panel must be enabled in the section “%% - [Controls] << Auxiliary Figures >> - (HFO Detection Methods)”, and the handle objects corresponding to HFO settings should be saved in the structure named `st_HFOMethod` (e.g. `st_HFOMethod.XXX_Epoch`, `st_HFOMethod.XXX_Threshold`, `st_HFOMethod.XXX_Window`, etc). The corresponding parameter controls should be defined in the section identified as “%% - [Controls] || HFO DETECTION - PANEL || New Method Objects ||”, and the new panel visibility must be set in the `f_HFOSelectMethod()` nested function under the section “%% [Functions] Auxiliary Figure - Select and Run HFO Methods”.

To set the selection of the method for processing, the user must include the new detection case in the switch block defined inside the `f_HFORunMethod()` function. This block calls the nested functions to set the algorithm parameters of each method. A new nested function must be created, and it can be named as desired (e.g. `f_HFOSet-XXX`). The goal of this new nested function is to establish all the parameters required specifically for the new implemented algorithm and to call the external function that performs the detection method. This nested function is placed in the section “%% [Sub-Functions] HFO Methods: New Method” and an example is stated as follows:

```

function f_HFOSet-XXX()
%Function to read the settings for the new implemented method XXX
st_HFOSettings.s_Epoch      = eval(get(st_HFOMethod.XXX_Epoch,'string'))
st_HFOSettings.s_Thresh     = eval(get(st_HFOMethod.XXX_Threshold,'string'));

```

```

st_HFOSettings.s_Window      = eval(get(st_HFOMethod.XXX_Window, 'string'));
st_HFOAnalysis.str_DetMethod = 'Method XXX';

st_HFOAnalysis.m_EvtLims = f_findHFOxXXX(...
    str_TempFile, ...
    st_HFOControl.s_CurrElecIdx, ...
    st_HFOSettings, ...
    st_HFOAnalysis.s_Sampling);

end

```

In the previous example, the structure `st_HFOSettings` contains the specific settings for the XXX method, which also includes the frequency band for the analysis, and `f_findHFOxXXX()` corresponds to the external function where the detection algorithm is implemented. The values for `str_TempFile`, `st_HFOControl.s_CurrElecIdx` and `st_HFOAnalysis.s_Sampling` are already set by the system, and they correspond respectively to the path where the data is stored, the index of the channel to be analyzed and the sampling frequency of the data. The `f_findHFOxXXX()` function must return the detected events in a `mx2` matrix where each row is a putative event, the first column corresponds to the first index of the detected event and the second column corresponds to the last index of the detected event. It is important to note that the function output must be called `st_HFOAnalysis.m_EvtLims` for subsequent processing in RIPPLELAB. An example of the external function implementing the detection algorithm is presented in the pseudocode as follows:

```

function m_HFOEvents = f_findHFOxXXX(pstr_SignalPath, ps_SignalIdx, ...
st_HFOData, s_SampleFrec)

m_Data      = [];
load(pstr_SignalPath)
v_Signal    = m_Data(:,ps_SignalIdx);
clear m_Data

v_Freqs     = [st_HFOData.s_FreqIni st_HFOData.s_FreqEnd]; % Filter freqs
s_Epoch     = st_HFOData.s_Epoch; % Epoch Time
s_Thresh    = st_HFOData.s_Thresh; % Threshold
s_Window    = st_HFOData.s_Window; % Window Time
clear st_HFOData

% Preprocessing Filter
(...)
% Thresholding Process
(...)
% Event detection
(...)

if Events Detected
    m_HFOEvents = [v_IdxIni(:) v_IdxEnd(:)];
else
    m_HFOEvents = [];
end

% v_IdxIni: vector with the initial indexes of the detected events
% v_IdxEnd: vector with the final indexes of the detected events

end

```


8. Appendixes

8.1. GNU GENERAL PUBLIC LICENSE

Version 3, 29 June 2007

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9. REFERENCES

- Crépon, B., Navarro, V., Hasboun, D., Clemenceau, S., Martinerie, J., Baulac, M., et al. (2010). Mapping Interictal Oscillations Greater than 200 Hz Recorded with Intracranial Macroelectrodes in Human Epilepsy. *Brain : A Journal of Neurology* 133 (Pt 1): 33–45. doi:10.1093/brain/awp277.
- Esteller, R., Echauz, J., Tcheng, T., Litt, B., and Pless, B. (2001). Line Length: An Efficient Feature for Seizure Onset Detection. *2001 Conference Proceedings of the 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society* 2.
- Gardner, AB., Worrell, GA., Marsh, E., Dlugos, D., and Litt, B. (2007). Human and Automated Detection of High-Frequency Oscillations in Clinical Intracranial EEG Recordings. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology* 118 (5): 1134–43. doi:10.1016/j.clinph.2006.12.019.
- Ibarz, JM., Foffani, G., Cid, E., Inostroza, M., and Menendez de la Prida, L. (2010). Emergent Dynamics of Fast Ripples in the Epileptic Hippocampus. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience* 30 (48): 16249–61. doi:10.1523/JNEUROSCI.3357-10.2010.
- Morlet, J., Arensz, G., Fourgeau, E., and Giard, D. (1982). Wave Propagation and Sampling Theory: Sampling Theory and Complex Waves. *Geophysics* 41 (2): 222–36. doi:10.1190/1.1441329.
- Oostenveld, R., Fries, P., Maris, E., and Schoffelen, J-M. (2011). FieldTrip: Open Source Software for Advanced Analysis of MEG, EEG, and Invasive Electrophysiological Data. *Computational Intelligence and Neuroscience* 2011 (January): 156869. doi:10.1155/2011/156869.
- Rosso, O., Blanco, S., Yordanova, J., Kolev, V., Figliola, A., Schürmann, M., et al. (2001). Wavelet Entropy: A New Tool for Analysis of Short Duration Brain Electrical Signals. *Journal of Neuroscience Methods* 105 (1): 65–75. <http://www.ncbi.nlm.nih.gov/pubmed/11166367>.
- Staba, RJ., Wilson, CL., Bragin, A., Fried, I., and Engel, J. (2002). Quantitative Analysis of High-Frequency Oscillations (80-500 Hz) Recorded in Human Epileptic Hippocampus and Entorhinal Cortex. *Journal of Neurophysiology* 88 (4): 1743–52. <http://www.ncbi.nlm.nih.gov/pubmed/12364503>.
- Valderrama, M., and Le Van Quyen, M. (2011). High-Frequency Oscillations and Interictal Spikes in Partial Epilepsy: Joining the Benefits. *Clinical Neurophysiology* 122 (1). International Federation of Clinical Neurophysiology: 3–4. doi:10.1016/j.clinph.2010.06.006.
- Vidaurre, C., Sander, TH., and Schlögl, A. (2011). BioSig: The Free and Open Source Software Library for Biomedical Signal Processing. *Computational Intelligence and Neuroscience* 2011: 935364. doi:10.1155/2011/935364.
- Widmann, A., Schröger, E., and Maess, B. (2014). Digital Filter Design for Electrophysiological Data - a Practical Approach. *Journal of Neuroscience Methods* 250. Elsevier B.V.: 34–46. doi:10.1016/j.jneumeth.2014.08.002.
- Worrell, GA., Gardner, AB., Stead, SM., Hu, S., Goerss, S., Cascino, GJ., et al. (2008). High-Frequency Oscillations in Human Temporal Lobe: Simultaneous Microwire and Clinical Macroelectrode Recordings. *Brain : A Journal of Neurology* 131 (Pt 4): 928–37. doi:10.1093/brain/awn006.
- Zelmann, R., Mari, F., Jacobs, J., Zijlmans, M., Chander, R., and Gotman, J. (2010). Automatic Detector of High Frequency Oscillations for Human Recordings with Macroelectrodes. *Conference Proceedings : ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference* 2010 (January): 2329–33. doi:10.1109/IEMBS.2010.5627464.
- Zelmann, R., Mari, F., Jacobs, J., Zijlmans, M., Dubeau, F., and Gotman, J. (2012). A Comparison between Detectors of High Frequency Oscillations. *Clinical Neurophysiology* 123 (1): 106–16. doi:10.1016/j.clinph.2011.06.006.