TMSEEG Tutorial

Version 4.0

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For more detail, please see the method article describing the TMSEEG Toolbox:
http://journal.frontiersin.org/article/10.3389/fncir.2016.00078/full

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Introduction

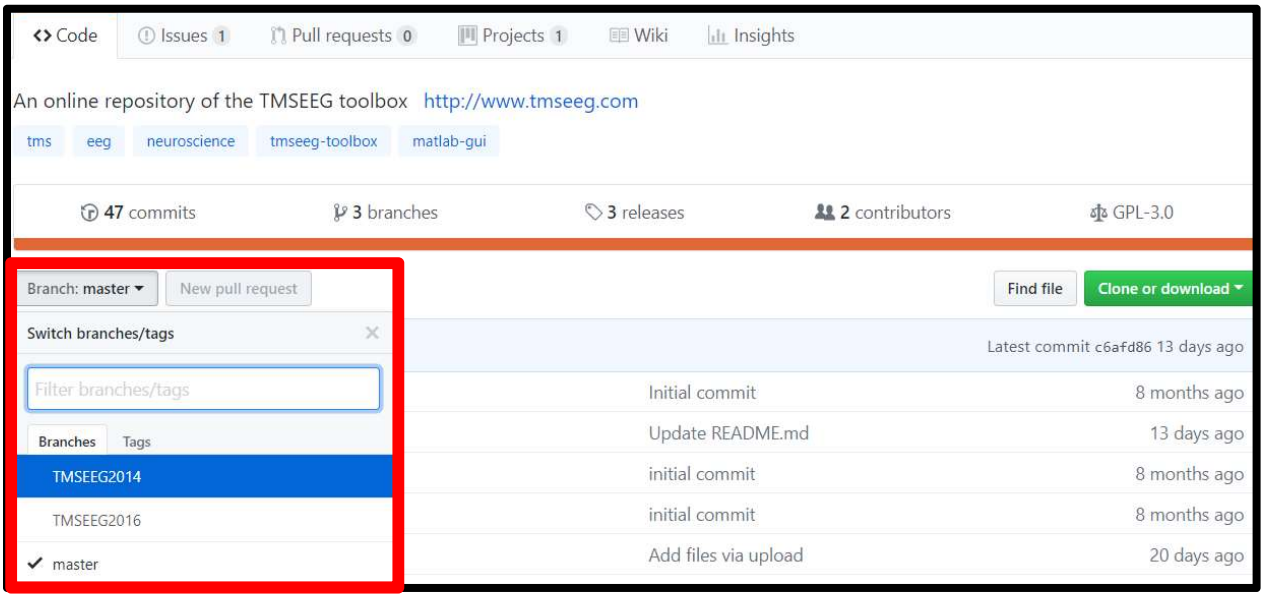
Due to the nature of transcranial magnetic stimulation (TMS) and the sensitivity of electroencephalography signals (EEG), a number of artifacts often mask TMS-evoked potentials (TEP)s. Proper analysis of TMS-EEG data requires the development and standardization of signal processing algorithms to recover TEPs from various sources of artifacts. TMSEEG is a MATLAB App dedicated for processing TMS-EEG data. Implemented with a modular graphical user interface (GUI), TMSEEG provides an interactive and compact platform to process data from various TMS-EEG paradigms. The GUI is designed to guide novice users while the software architecture supports the integration of alternative or additional processing modules for users with experience in TMS-EEG data processing. To simplify and standardize the TMS-EEG signal processing, the toolbox integrates five main novel approaches:

- Focused removal of TMS-induced artifacts from EEG data,
- A streamlined, step-by-step yet modular data processing workflow for ease-of-use and modification flexibility,
- A comprehensive multi-panel display of artifact characteristics for faster and more accurate data removal,
- Integrated quality control using online visualization of the TEP waveforms throughout the data processing steps, and
- Online visualization of component-based artifact removal with capability to label and store a database of artifacts.

Installation

Before loading the electrophysiological dataset into TMSEEG, users must convert their dataset to .set format using the EEGLAB software suite (http://sccn.ucsd.edu/eeglab/downloadtoolbox.php). TMSEEG is highly dependent of EEGLAB for many of its functionalities and therefore the EEGLAB toolbox must be installed prior to data processing.

There are currently three versions of TMSEEG available. The last version works with MATLAB v2013 and higher (**MASTER BRANCH**) and can be found here (https://github.com/EEGSignalProcessing/TMSEEG/). Some issues described in the previous versions have been fixed so we recommend using this last version. If needed, previous versions (**TMSEEG2016 BRANCH)** and (**TMSEEG2014 BRANCH**) can be found respectively here (https://github.com/EEGSignalProcessing/TMSEEG/tree/TMSEEG2016) and here (https://github.com/EEGSignalProcessing/TMSEEG/tree/TMSEEG2014).



TMSEEG requires installation of **EEGLAB v12.0.2.6b** or higher. It also requires:

- MATLAB signal processing toolkit. Make sure to set the MATLAB signal toolbox as a higher path priority than other software such as field trip, as some functions may share common names. Or ideally, remove fieldtrip from your MATLAB path if errors persist.
- FASTICA is the current preferred algorithm for ICA in TMSEEG.
- More detail on the FASTICA algorithm can be found here: (http://research.ics.aalto.fi/ica/fastica/code/dlcode.shtml)

TMSEEG creates multiple intermediate datasets at each processing step to allow easy reprocessing of the data. We highly recommend that each base dataset for processing is placed in its own folder to easily track datasets.

To install TMSEEG:

1. Copy the .mlappinstall file to your current working folder in MATLAB.
2. Right click on the file and select 'Install'.

Dataset Loading and Setup

TMSEEG is initialized by selecting the app from the MATLAB apps toolbar. Users can also open the tool by running the ***tmseeg_main*** function directly in the MATLAB command window (to do this ensure the software folder, under MATLAB -> APPS, has been added to the path). Running the program will display the main GUI of TMSEEG.

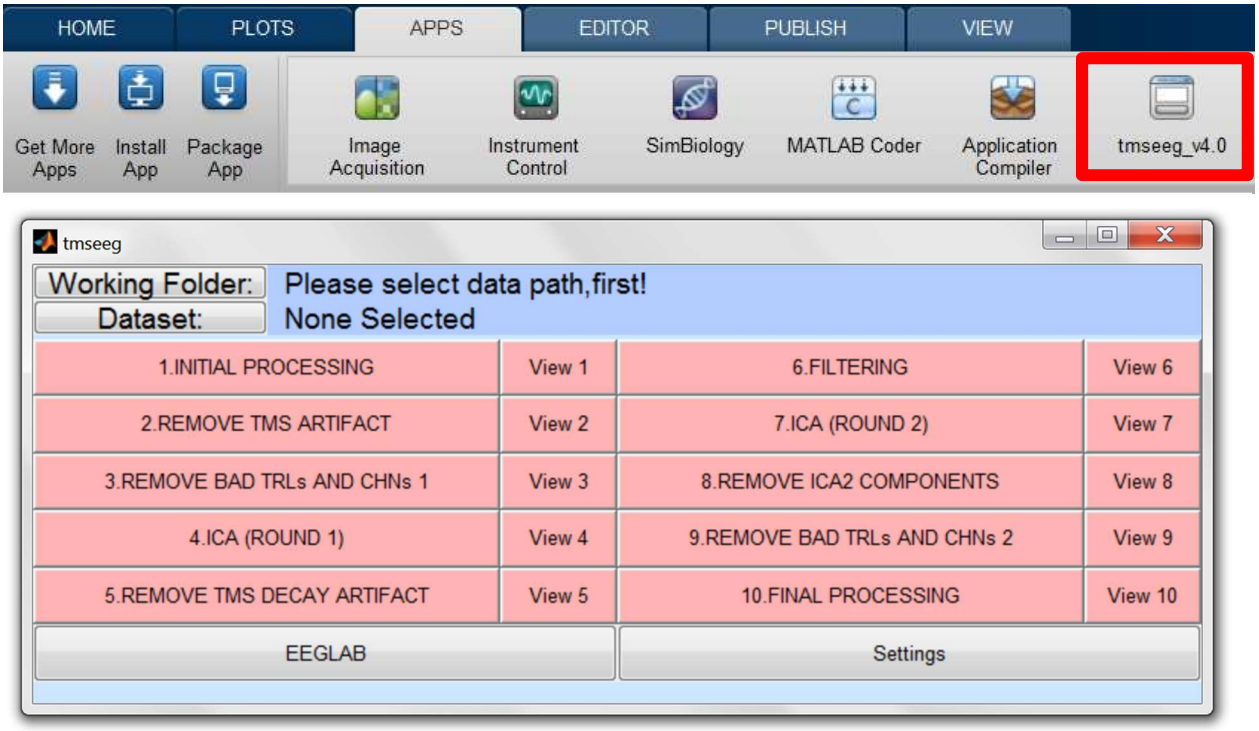


Figure 1: TMSEEG Main GUI

To load a dataset:

1. Select the **Working Folder** button, calling a 'select working folder' window. Using the pathing tool, select the folder you have created containing your base .set file
2. After selecting the folder, select the **Dataset** button and choose your .set file in the working folder

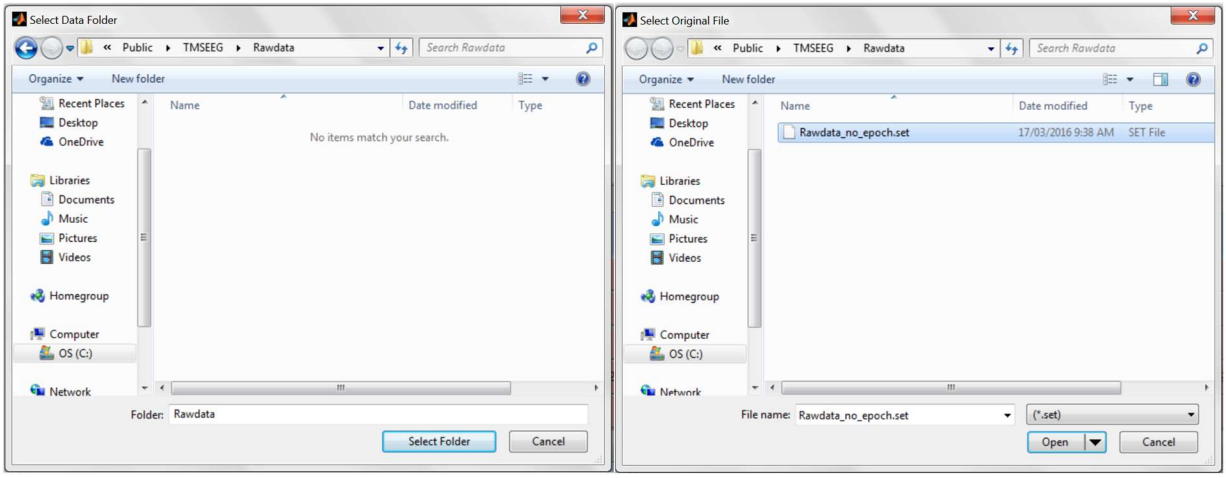


Figure 2: Selecting folder (Left) and File (Right)

If you have previously processed the dataset in the working folder, the TMSEEG GUI will indicated a completed dataset by colouring the step green (see **Figure 3** below)

Figure 3: Main GUI displaying previous work and settings

The **Settings** button in the main GUI brings up a smaller window, allowing the user to select and change the processing parameters of the toolbox. Users can also access main GUI of EEGLAB main GUI at any time during data processing through the **EEGLAB** button.

Settings

Parameters for data processing can be changed in the settings tab. Settings are currently available for:

- Step 1 – Initial processing
- Step 2 – TMS Artifact removal
- Steps 3 and 9 – Removal of bad trials and channels
- Steps 7 and 8 – Rejecting artifacts using ICA (round 2)
- View Data – Graphing options for View Data feature at each step

Due to the sequential nature of the TMSEEG workflow, if the settings are changed for a specified step, the workflow will reset to that step (i.e., all data processing from the specified step and onwards will be erased). We highly recommend users to specify all parameters in the setting tab before processing the data to avoid unnecessary resets of the processing workflow.

Step 1 – Initial Processing

After completing the loading steps, select the **Initial Processing** button on the main GUI to initiate the first processing step, which guides the user with a series of pop-ups through the following processes:

1. Epoching and Baseline Removal

If the dataset was not previously epoched, TMSEEG will prompt the user with a list of events in the input dataset to epoch around. The default setting for epoching is -1000ms to 1000ms. After epoching the dataset, the user is prompted for baseline removal based on a user-selected time range (default is set relative to the selected pre-stimulus range).

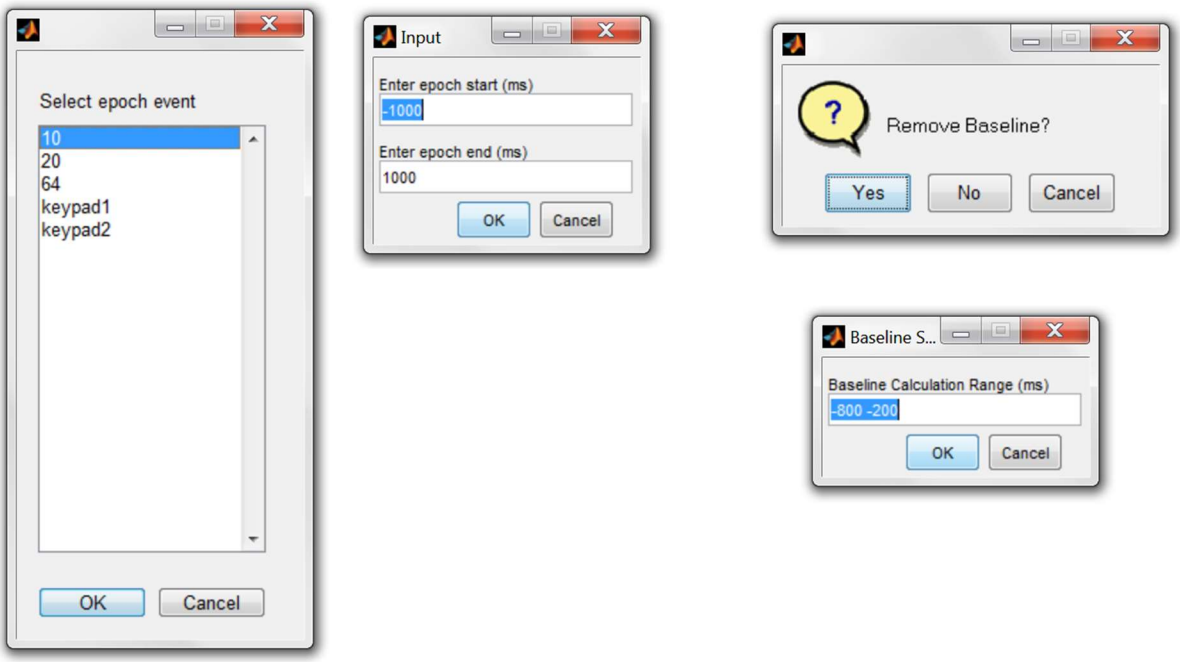


Figure 4: Epoching and Baseline Process

2. Resampling

Resampling is recommended to improve toolbox performance and reduce data storage requirements. TMSEEG will prompt the user to resample if data sampling frequency is greater than 1000Hz.

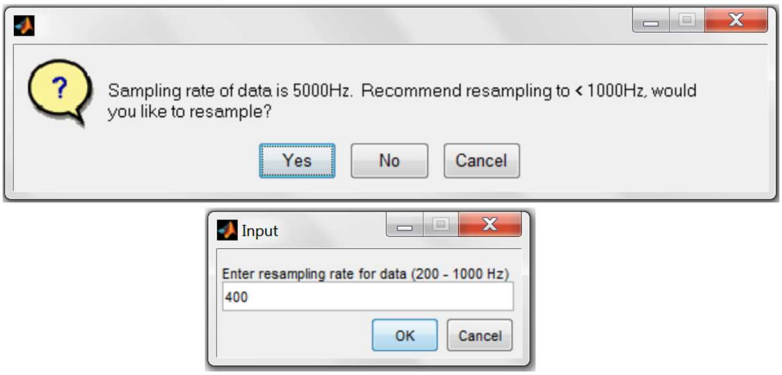


Figure 6: Resample Prompt and Input

3. Channel location lookup

After resampling, the user is prompted to select a channel location file using EEGLABS pop_chanedit() function or load default locations using a database of 385 defined channel labels from the 'Standard-10-5-Cap385.elp' file originally from the EEGLAB distribution.

If the user decides to keep channels without channel locations, a warning is provided. It is highly recommended to delete channels without channel locations in Step 1 or alternatively in Step 3. Channels without any location information cannot be interpolated and therefore may cause issues if trials within these channels are marked for deletion. Non-EEG channels should also be removed before ICA. Future versions will allow the user to select channels for ICA.

An automatic pop-up window shows the channel locations (if available) in a topographic display, with a scrolling list for the user to select channels for removal. If the channel locations cannot be found, a pop-up window will alert the user.

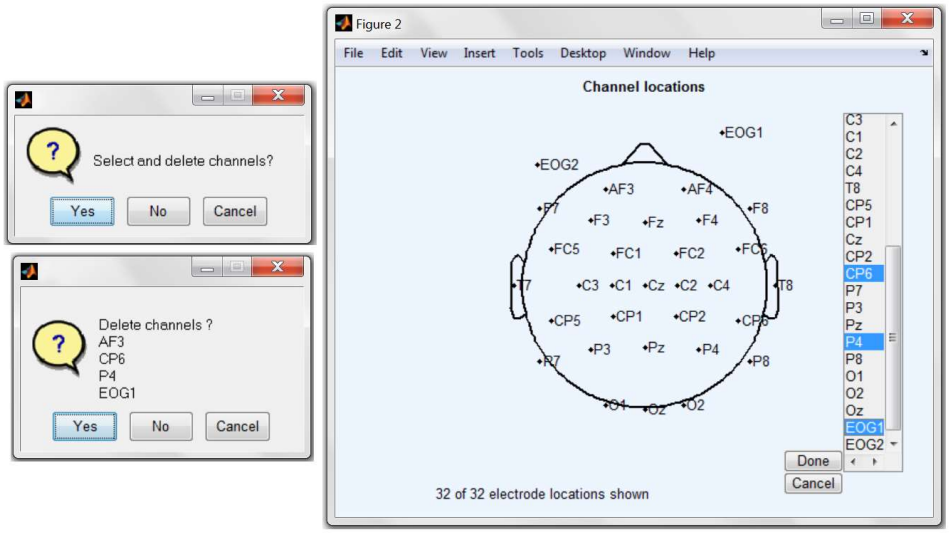


Figure 7: Channel Removal Display

Step 2 – TMS Artifact Removal

TMS artifact removal consists of an interactive GUI that allows the user to visualize the range of data removal relative to the dataset. This allows the user to delete the TMS pulse artifact while retaining the TMS decay artifact for later removal in Step 4-5.

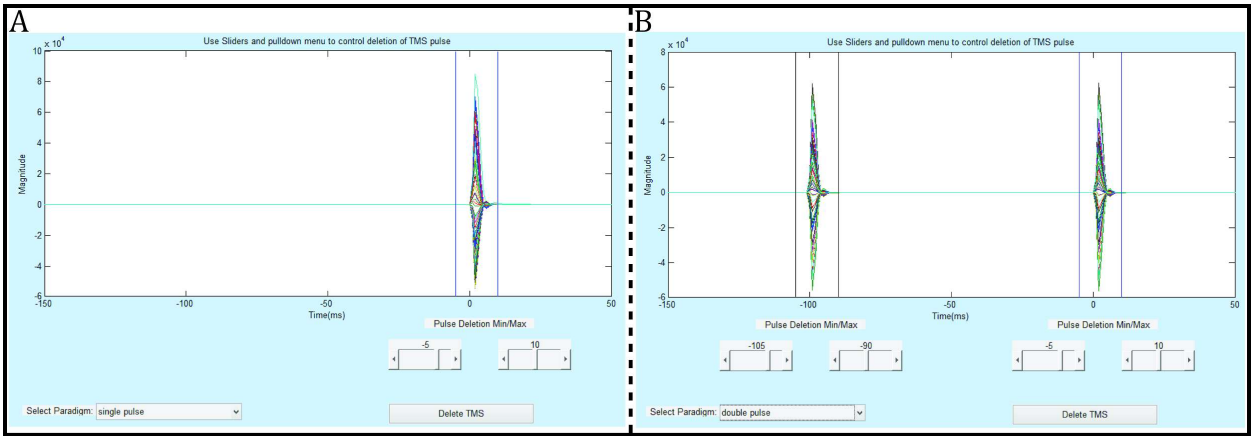


Figure 8: TMS Pulse Removal – A) Single Pulse Paradigm, B) Double Pulse paradigm. Adjusting the sliders below each pulse will change the range of deletion.

1. Selecting Pulse Paradigm

The user selects the **TMS Paradigm**, currently between single and double pulse. The inter-stimulus interval and pulse duration can both be adjusted in the settings function from the main GUI. **Figure 8** shows the Step 2 display for both single and paired-pulse paradigms.

2. Adjusting Removal Period

Adjusting the **sliders** will change the range of data removal. This selected data will be removed from the dataset and the surrounding data is concatenated before saving the dataset. For visualization in the toolbox, the removed data interval is represented with NaN values (i.e., a gap). Pulse duration can be adjusted through the **Settings** tab to allow removal of large blocks of data (ex., for repetitive TMS data).

Step 3 – Removal of Bad Trials and Channels

1. Select Attribute for Display

TMSEEG displays data through the **Plot Trials** and **Plot Channels** GUI with a user-selected attribute. In the Plot Trials display, trials are displayed based on the chosen attribute extracted over all channels. In the Plot Channels option, a subplot is generated for each channel to display the **ATTRIBUTE** value at each trial for the specified channel.

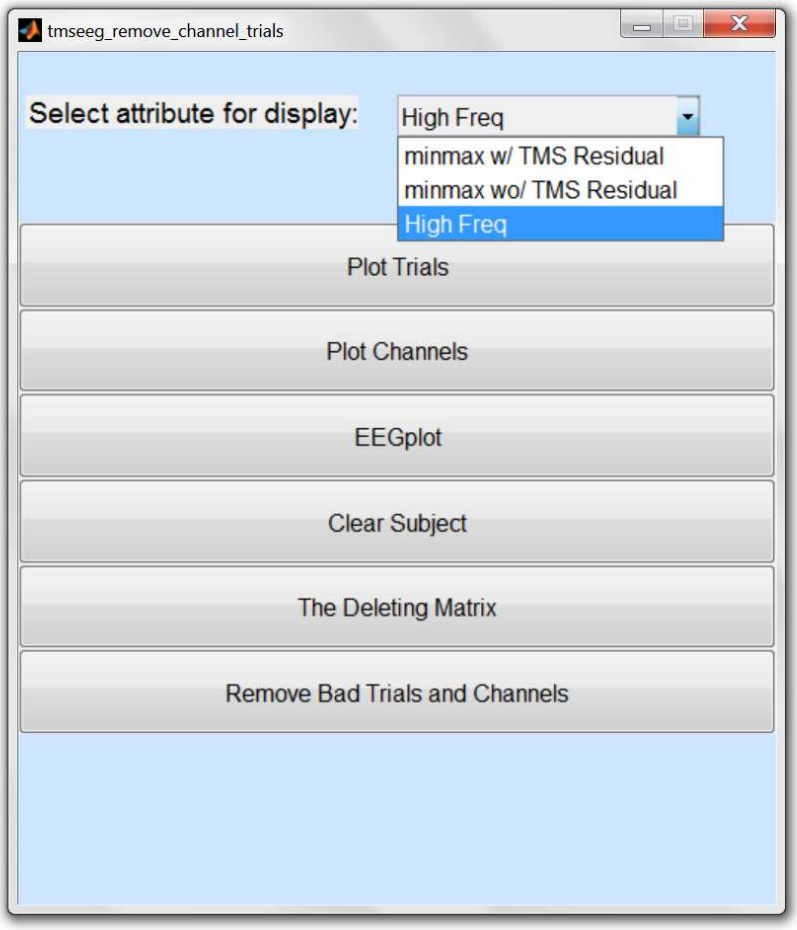


Figure 9: Main GUI for Trial/Channel Removal with ATTRIBUTE Selection

2. Plot Trials

Plot Trial uses the selected **ATTRIBUTE** to calculate an attribute value for each trial. This is displayed through a scatterplot **(Figure 10)**. By clicking these dots, the relevant trial data is displayed through a new GUI, allowing the user to delete selected channels in the trial, or the whole trial.

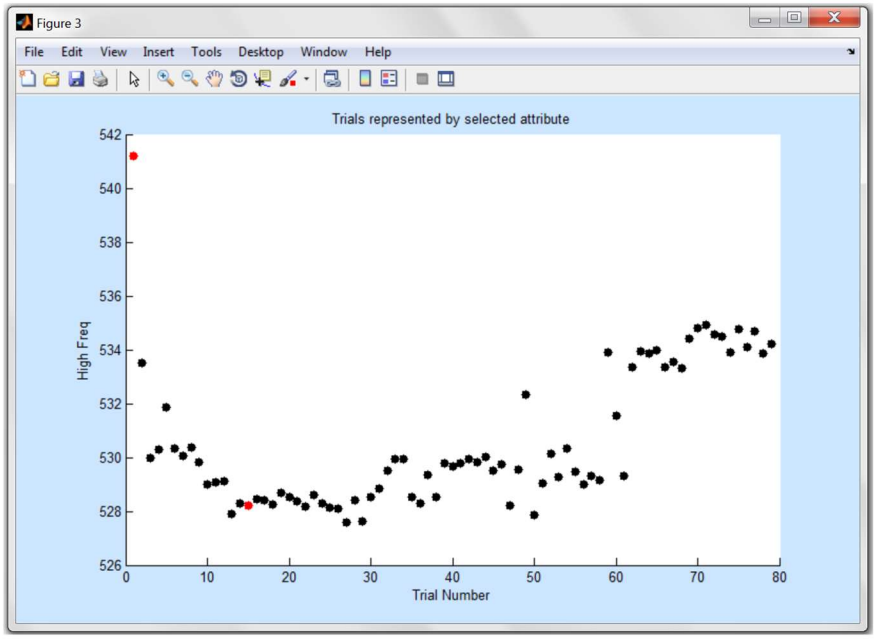


Figure 10: Plot Trials GUI – Trials that have been marked for deletion are shown in red. Clicking a dot with the mouse brings up the display shown in Figure 11 below.

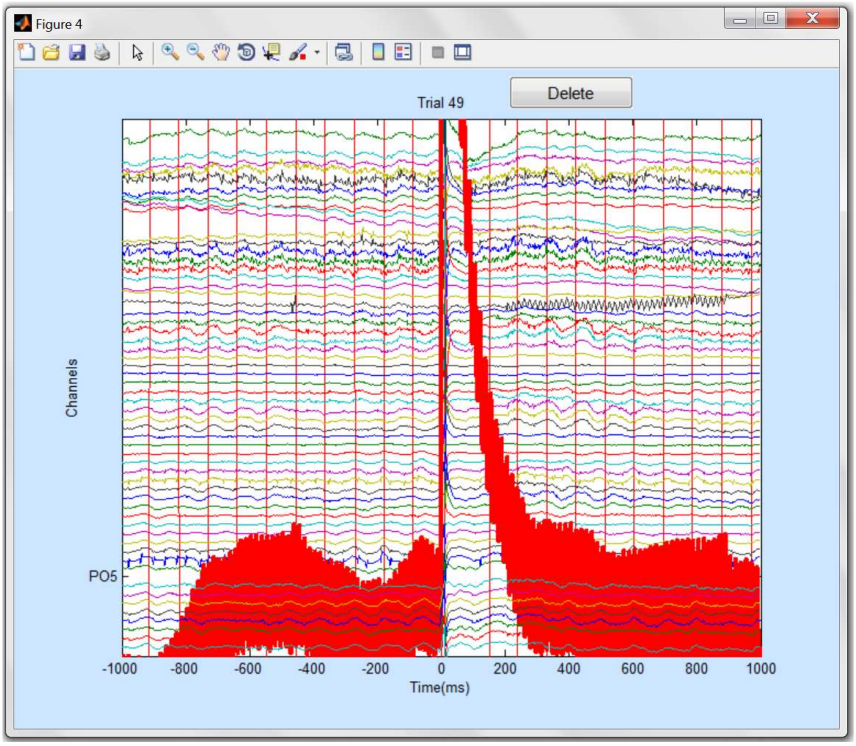


Figure 11: Trial Deletion GUI – Called by clicking on the corresponding dot in the Plot Trials GUI. Channel data is displayed for the selected trial (in this case trial 49). The red channel (PO5) has been selected for deletion in the above display and will be removed for the duration of trial 49 by clicking the Delete button.

In this **Trial Deletion GUI**, channels can be selected for deletion for the duration of the trial using the **Delete** button. Alternatively, if the user clicks on the **Delete** button without selecting any channels then the whole trial is deleted.

3. Plot Channels

TMSEEG offers easy visualization so that the user can assess data for removal with the **Plot Channels** GUI. Plot Channels creates a subplot for each channel in the dataset as seen in **Figure 12**. This scatterplot displays the ATTRIBUTE value of each trial within the channel (**Figure 12**). Selecting these subplots will bring up the **Channel Removal GUI** (**Figures 13-14**), while selecting the dots in the subplots will bring up the **plot Trial GUI** as seen as **Figure 10** for that channel from where you can access the **Trial Deletion GUI** as seen in **Figure 11** by selecting again one of the dots.

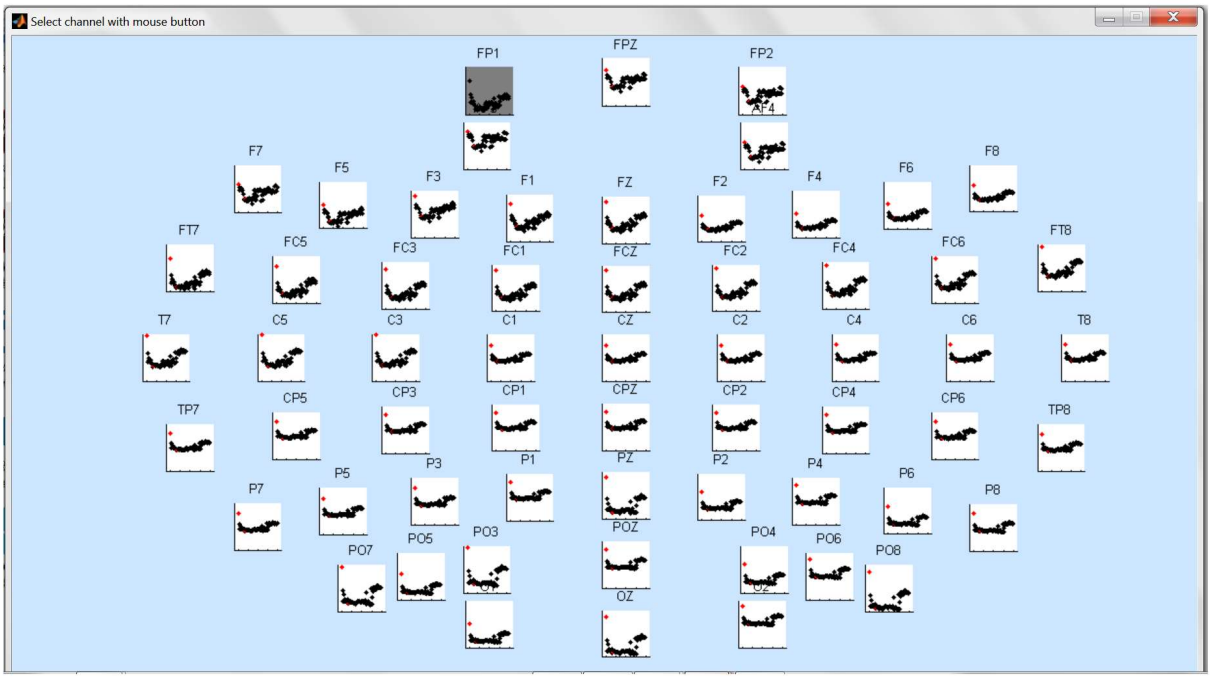


Figure 12: Plot Channels GUI – The position of the scatterplot for each channel is based on the loaded channel co-ordinates file. Dots in each channel subplot indicate the ATTRIBUTE value of each trial, and a blacked-out channel indicates that it has been set for removal.

IMPORTANT NOTE: Users are highly recommended to delete channels without co-ordinates at this step. Alternatively, if users want to retain these channels they can make sure they do not delete any trials within these channels. Deleted trials within channels will be interpolated (if below the user-specified threshold) at the end of step 3 and channels with no channel co-ordinates cannot be interpolated. It will result in an error.

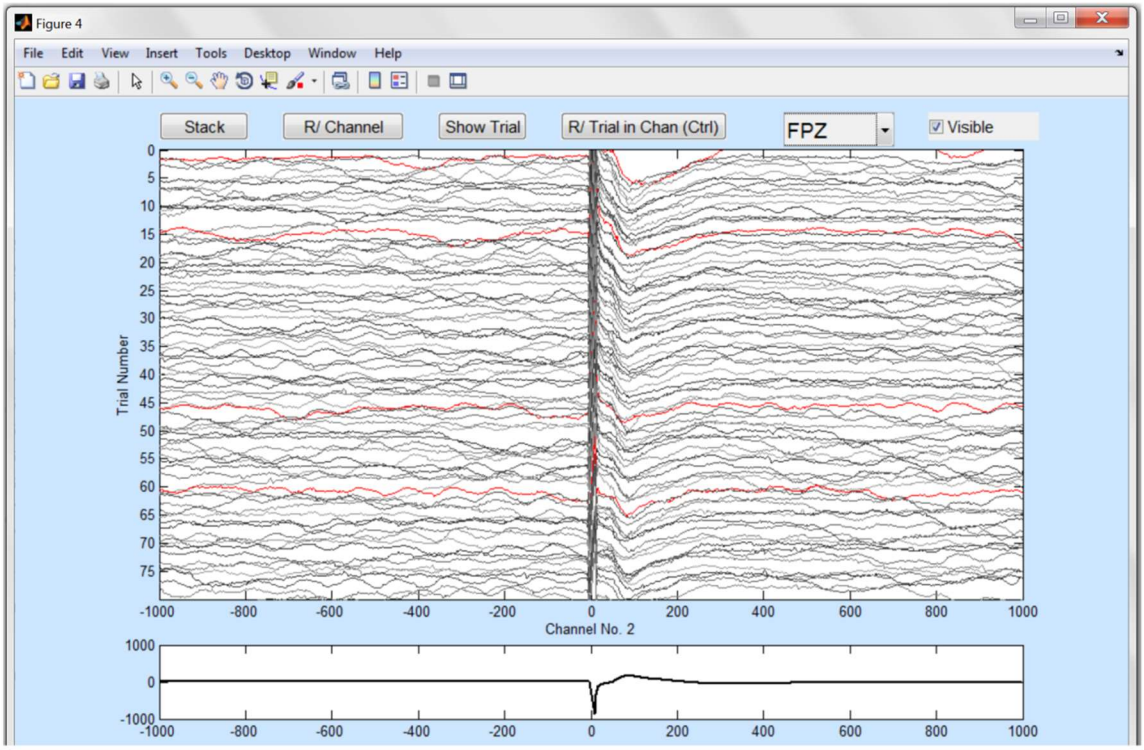


Figure 13: Channel Removal GUI – Spread Mode

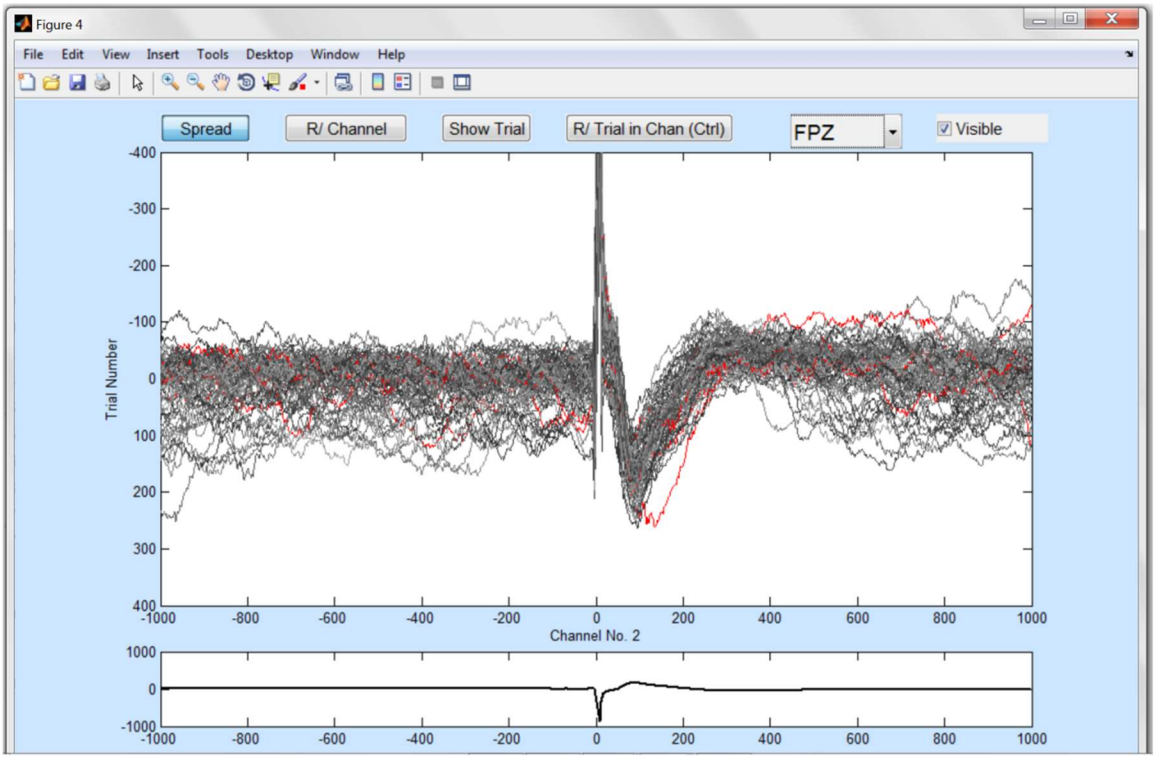


Figure 14: Channel Removal GUI – Stacked Mode

Figure 13 and **Figure 14** show the Channel Removal GUI in its two display modes: Stacked and Spread. The spread display plots the channels in a more traditional offset format, while the stacked display plots all traces on the same baseline for comparison. Three options exist for deleting data in this window:

a. **Removal of Trial in Channel –** Delete an individual trial-channel pair, by right-clicking the data segment or by selecting the data segment and clicking the "**R/ Trial in Channel**" button.
b. **Remove Channel –** Using the "**R/ Channel**" option, mark all trials in the channel for deletion.
c. **Trial Deletion –** Select a trial and use the "**Show Trial**" button to open the Trial Deletion GUI to delete the entire trials or selected channels within the trial (**Figure 11**).

Trials marked for deletion will be seen as red in the Channel Removal GUI if the "Visible" option is selected. The channel drop down menu allows quick scrolling through the channels and can be operated using the up and down arrows on the keyboard.

4. EEGPLOT

For users familiar with the ***eegplot*** function in EEGLAB, we have included this function directly linked to TMSEEG:

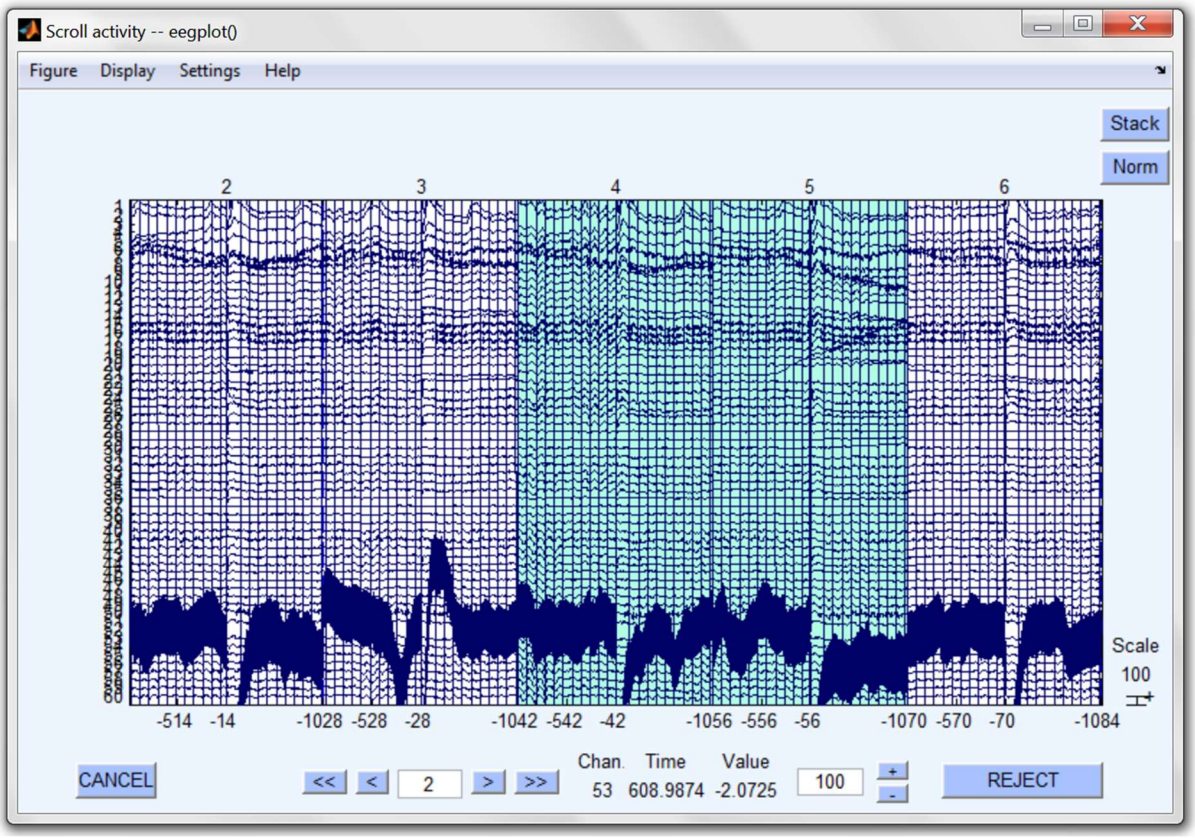


Figure 14 – EEGPlot Option – Called using the EEGplot option from the remove trials and channels GUI. Selected trials (highlighted in blue) are removed by pressing the REJECT button.

5. Clear Subject

If the user needs to restart the cleaning process, the trials/channels marked for deletion can be quickly cleared using the **Clear Subject** button.

6. Deletion Matrix

The **Deletion Matrix** button offers an efficient quality control on the deletion process by plotting the trials and channels currently selected for deletion in a matrix (Trials vs Channels) format:

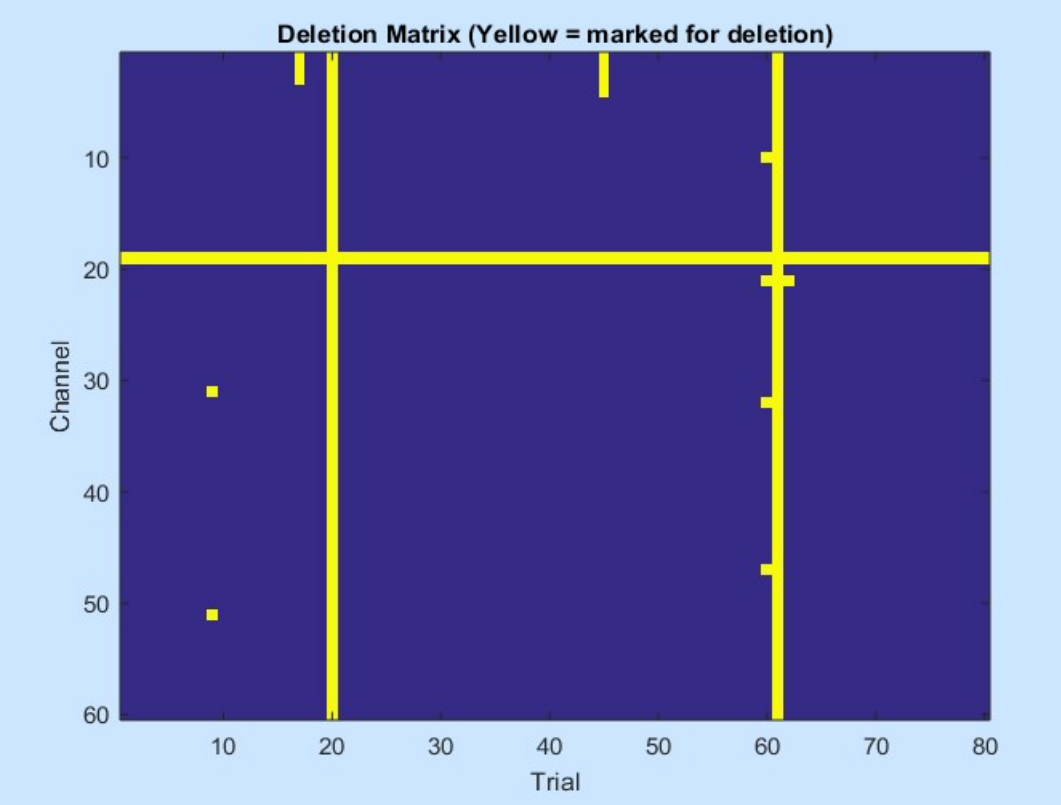


Figure 15: The Deletion Matrix

Step 4 – Round 1 of ICA

TMSEEG uses the ***pop_runica*** function from EEGLAB to run ICA, currently using the **FASTICA** algorithm (see introduction for downloading link). Assuming FASTICA has been downloaded and is on the MATLAB path, selecting the ICA1 button will run ICA on the latest dataset (post removal of channels and trials selected in step 3) to extract the maximum number of components (i.e., the number of channels in the dataset). Users can specify the channels that should be used with ICA.. If non-EEG channels are present in the data, please unselect them before ICA.

Step 5 - Remove TMS Decay with ICA (Round1)

After running ICA in Step 4, Step 5 calls the **TMS Decay Removal GUI**, to assist users in the process of removing the optimal combination of components associated with the TMS decay artifact:

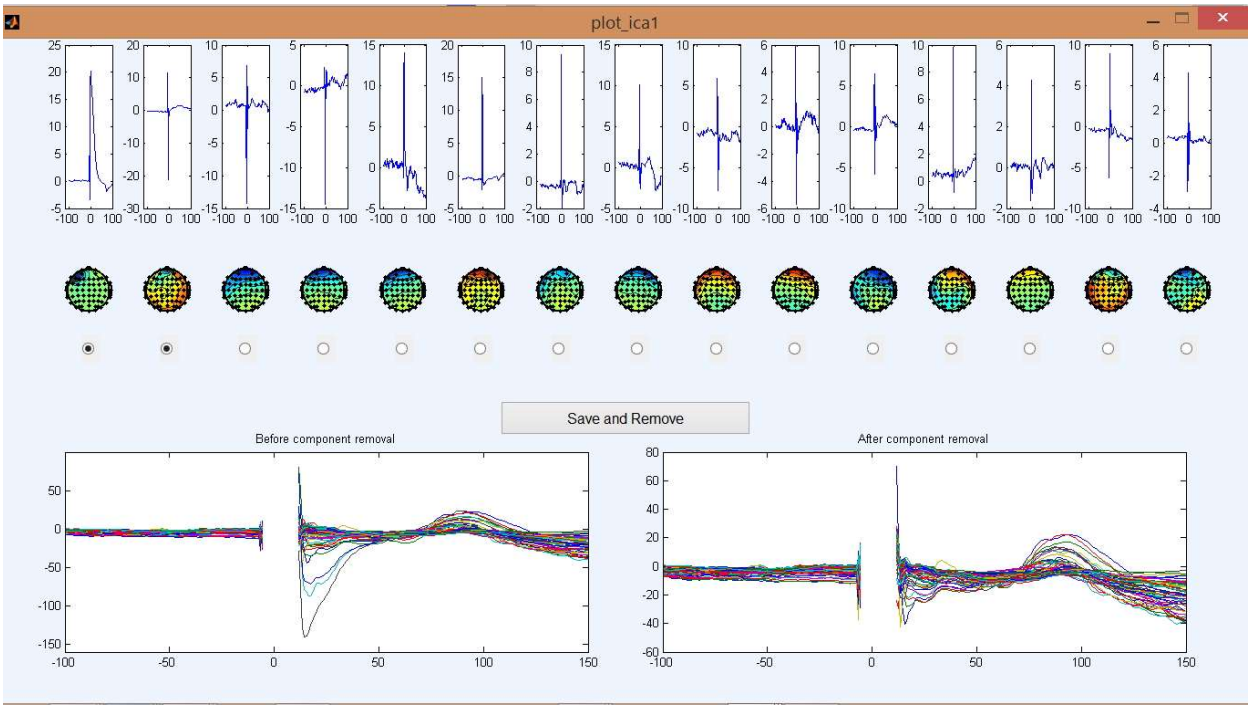


Figure 16: TMS Decay Artifact Removal

Step 5 GUI displays the 15 largest components in terms of magnitude, with both the direct component plots and the topographic displays. The bottom left display shows a butterfly plot of the data before removal of components, while the bottom right display is updated to show the data after selected components have been removed.

Step 6 – Filtering

After removing the TMS Decay Artifact, selecting Step 6 from the main GUI brings up the filtering GUI (**Figure 17**). TMSEEG currently offers two options:

- **FIR filtering** – filtering with a basic FIR filter (recommended 1-55Hz) to remove unwanted frequencies and avoid power line noise. The user can adjust the filter order using the filter order button.
- **IIR Filtering** – Bandpass filtering using a butterworth filter, with a notch filter centred at 60Hz for removal of power line noise. Currently, the user can adjust the frequency bands of the filter, and the order of the butterworth filter by selecting the filter order button.

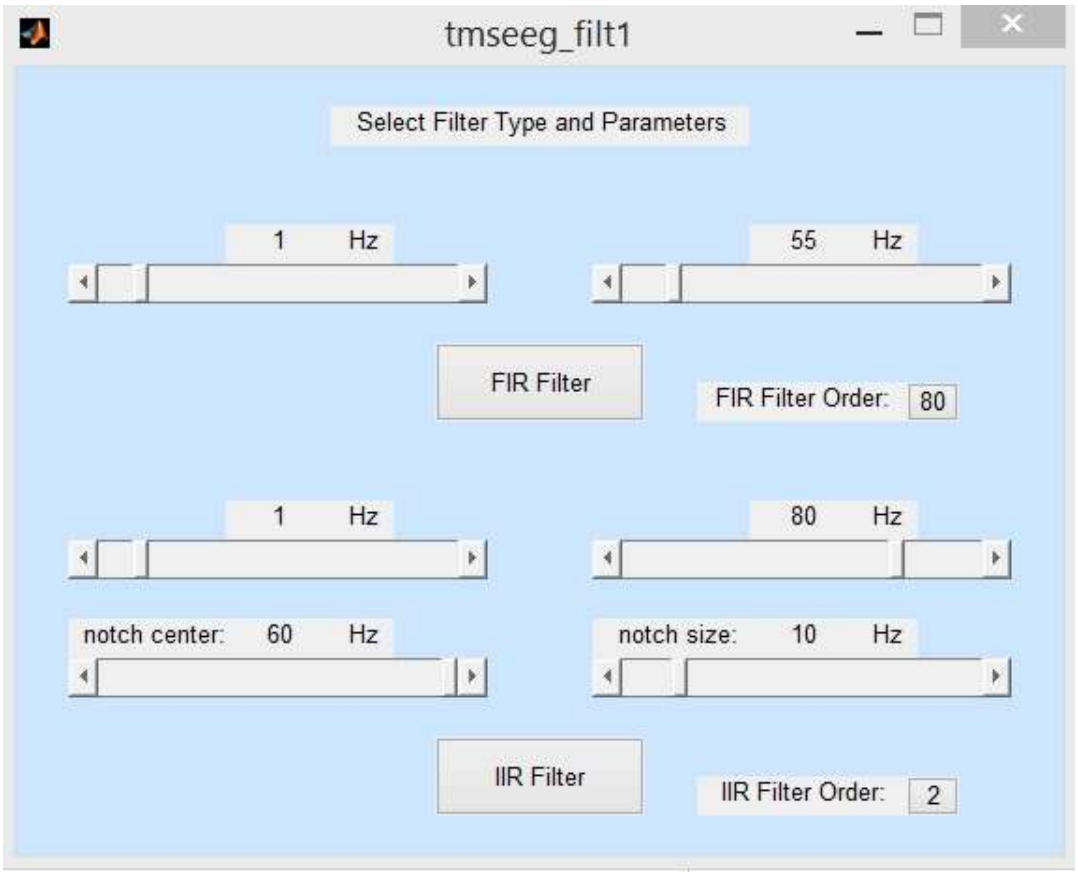


Figure 17: Filtering GUI

Step 7 – Round 2 of ICA

Step 7 runs ICA once again with the ***pop_runica*** function and the **FASTICA** algorithm. The number of components extracted is dependent on a percentage of remaining channels (default 90%) that can be adjusted in the step 7/8 settings.

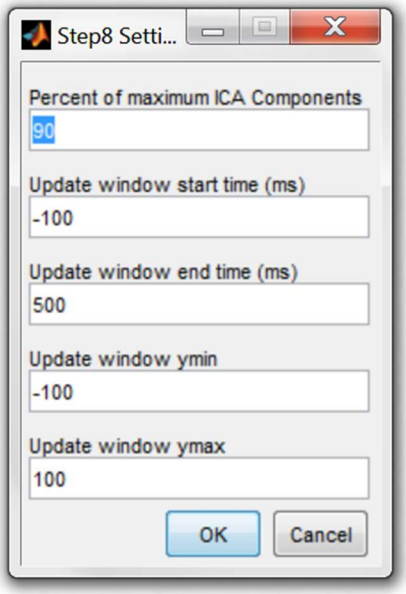


Figure 18: Step 7/8 Settings

Step 8 – Remove Artifacts with ICA (Round 2)

Using the calculated ICA components in step 7, step 8 calls the component removal GUI to facilitate tagging and removal of common TMS-EEG related artifacts:

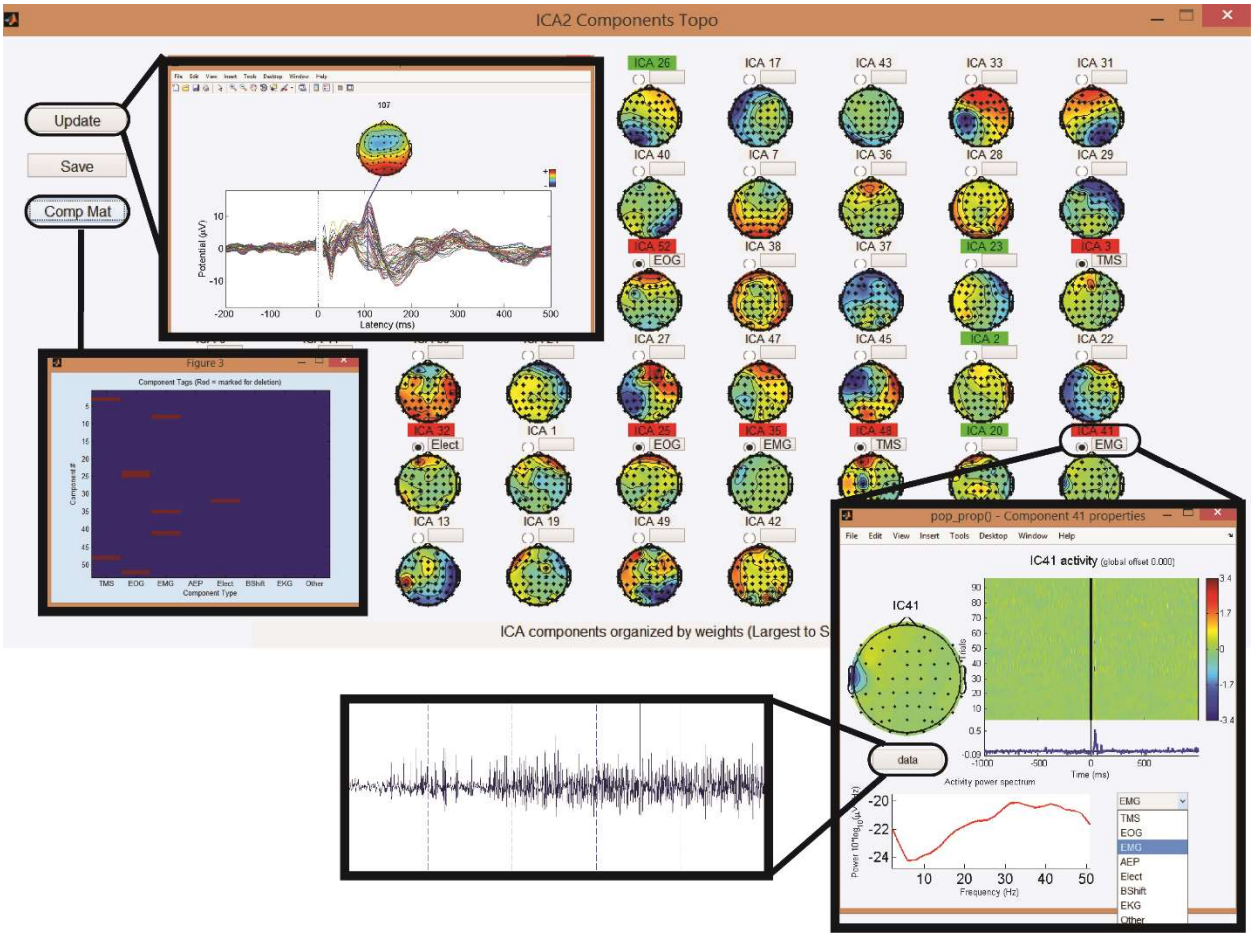


Figure 18: ICA Round 2 Component Removal Display

The main component removal GUI shows topographic plots of the ICA components, sorted in decreasing order of magnitude. Selecting the button of the relevant ICA component brings up a custom display showing information on topography, frequency content, and trial/channel amplitude information (**Figure 18**). Using this display, components can be marked using the drop-down menu as a specific artifact type or viewed more closely using the '**data**' button. Once a component is marked as an artifact for deletion, the ICA component label turns red, while viewing (not marking) a component will mark the label as green. In the top-left corner of the GUI, the user can view the butterfly waveform before and after the removal of the marked components by clicking on the **Update** button. However, these marked components are not removed until the user decides to **Save** the workspace. Finally, for quality control, the user can visualize the number of deleted components and the type of artifacts deleted through the **Comp Mat** button.

Step 9 – Remove Channels and Trials 2

Step 9 includes a second round of trial and channel removal, targeting any residual noise or artifacts introduced in the processing workflow. Please refer to the Step 3 instructions as the noise removal process is identical. The parameters of this step can be modified as needed through the **Settings** button in the main GUI of TMSEEG.

Step 10 – Final Processing

TMSEEG performs three tasks during the final processing step: (i) interpolation of channels deleted in Steps 3 and 9, (ii) re-referencing of channel data, and (iii) the addition of a buffer space for time period(s) deleted in Step 2. Re-referencing and the addition of a buffer space are optional. Interpolation is performed using the ***pop_interp*** function from EEGLAB. By default, the function is specified to use the spherical method. This step concludes the processing of EEG data from raw TMS-EEG signals to clean TEPs. At any given step during the workflow, users can visualize the progressive removal of artifacts through the averaged TEP butterfly plot by clicking on the "**View Step**" button in the main GUI (**Figure 19**) or continue data processing in EEGLAB using the **EEGLAB** button.

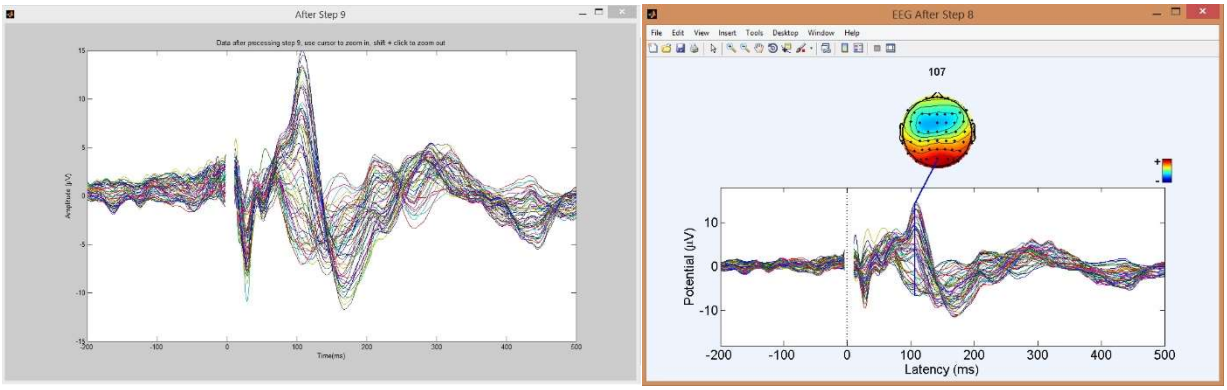


Figure 19: Butterfly plots shown when selecting the View Step button (with and without topographical map)