

## **Localizing epileptogenic network from SEEG using H2 non-linear correlation, mutual information and graph theory analysis**

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### **Prerequisites**

Download and install the windows version of the MATLAB Runtime (version 9.6) for R2019a, from the following link on the Math Works website: <http://www.mathworks.com/products/compiler/mcr/index.html>.

### **Tool Interface**

EPI-graph tool interface has seven steps, build using MATLAB GUIDE. A) File Upload, B) Frequency range setup and Energy calculation, C) Thresholds to detect IEDs, D) Connectivity parameters, E)  $h^2$  index estimation, F) Mutual Information estimation, G) Launch viewer application, and H) Restart button.

The screenshot displays the EPI-graph software interface with the following components:

- 1. File Upload:** A section for loading a SEEG signal (filename.edf Format). It includes a "Load the SEEG signal" button and a "Loading Done" status indicator. Below this, there are radio buttons for "Avg Reference" (selected) and "Bipolar Derivation".
- 2. Select Frequency Range for Interictals:** A section with input fields for "Lower Frequency" (14 Hz) and "Upper Frequency" (70 Hz).
- 3. Calculate and Plot Normalised Energy Graph:** A section with a "Graph" button.
- 4. Set the Threshold to detect Interictal discharges:** A section with input fields for "Threshold for Normalised Energy" (0.07) and "Threshold for minimum no of Channels" (3).
- 5. Connectivity Parameters:** A section with input fields for "Transmission delay between Channels" (10 ms) and "Window size" (3 Seconds). It also includes an "IED Detection Table" button.
- 6. Calculation of H2 Index (Non linear Correlation):** A section with input fields for "H2 Correlation" (0.7) and "Threshold for H2 Correlation" (0.7). It includes a "Calculate H2" button and a "Types" button.
- 7. Calculation of Mutual Information:** A section with input fields for "Mutual Information" (0.8) and "Threshold for Mutual Information" (0.8). It includes a "Calculate MI" button and a "Types" button.
- 8. Visualize the Graphs in the 3D Brain Viewer:** A section with a "Download" button and an "Open Brain Viewer" button.
- H. RESTART:** A button located at the top right of the interface.

1. Click on the button “Load EDF File” to load an SEEG signal contain recordings from interictal period with a duration of 1-4 hrs.

This close-up screenshot shows the "1. File Upload" section of the EPI-graph software. It includes the following elements:

- 1. File Upload:** A section with a "Load the SEEG signal ( i.e, filename.edf Format)" button and a "Loading Done" status indicator.
- Montages:** A section with radio buttons for "Avg Reference" (selected) and "Bipolar Derivation".

A folder will be created in the current directory, and files obtained from further processes will be added to this folder.

2. The connectivity will be computed for the specified frequency set by the user. By default, SEEG with the frequency of interest 14-70 Hz is set.

EpiGraph

**1. File Upload**

Load the SEEG signal ( i.e, filename.edf Format)  
Minimum 1 hr and Maximum 4 hrs SEEG signal in Interictal Period

Mountages  
☒ Avg Reference ☐ Bipolar Derivation

**2. Select Frequency Range for Interictals.**

Lower Frequency: 14 Hz Upper Frequency: 70 Hz

**3. Calculate and Plot Normalised Energy Graph.** Graph

**4. Set the Threshold to detect Interictal discharges.**

Set the Threshold for magnitude and no of channels  
 Threshold for Normalised Energy: 0.07  
 Threshold for minimum no of Channels: 3

**5. Connectivity Parameters**

Transmission delay between Channels: 10 ms Window size: 3 Seconds IED Detection Table

Total no of IEDs detected (Count)

**6. Calculation of H2 index (Non linear Correlation).**

H2 Index  
 H2 Correlation: Calculate H2  
 Threshold for H2 Correlation: 0.7  
 Calculate Maximum occurrences of IEDs: Types

**7. Calculation of Mutual Information.**

Mutual Information  
 Mutual Information: Calculate MI  
 Threshold for Mutual Information: 0.8  
 Calculate Maximum occurrences of IEDs: Types

**8. Visualize the Graphs in the 3D Brain Viewer.**

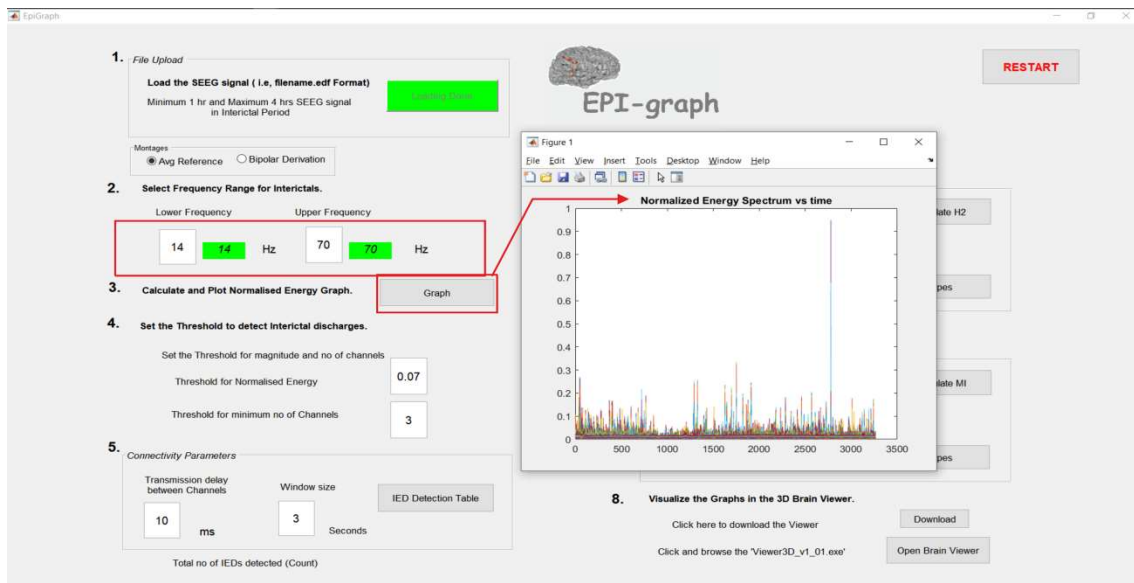
Click here to download the Viewer  
 Click and browse the "Viewer3D\_v1\_01.exe"

Download Open Brain Viewer

RESTART

EPI-graph

- Click on the button "Graph" to compute the normalized energy plot. The x-axis represents time and the y-axis represents normalized energy.



- Set the thresholds to detect interictal discharges.

**4. Set the Threshold to detect Interictal discharges.**

Set the Threshold for magnitude and no of channels

Threshold for Normalised Energy

Threshold for minimum no of Channels

**5. Connectivity Parameters**

Transmission delay between Channels

Window size

IED Detection Table

Total no of IEDs detected (Count)

- Set connectivity parameters such as transmission delay between channels and window size. The default values for window size and delay were 3 seconds and 10 ms respectively.

EpiGraph

**1. File Upload**

Load the SEEG signal ( i.e. filename.edf Format)

Minimum 1 hr and Maximum 4 hrs SEEG signal in Interictal Period

Montages

☒ Avg Reference ☐ Bipolar Derivation

**2. Select Frequency Range for Interictals.**

Lower Frequency

Upper Frequency

14 Hz 70 Hz

**3. Calculate and Plot Normalised Energy Graph.**

Graph

**4. Set the Threshold to detect Interictal discharges.**

Set the Threshold for magnitude and no of channels

Threshold for Normalised Energy

Threshold for minimum no of Channels

**5. Connectivity Parameters**

Transmission delay between Channels

Window size

IED Detection Table

Total no of IEDs detected (Count)

**6. Visualize the Graphs in the 3D Brain Viewer.**

Download

Open Brain Viewer

**Table1** Location of IEDs referenced with seconds.

	1	2	3	4	5	6	7
1							

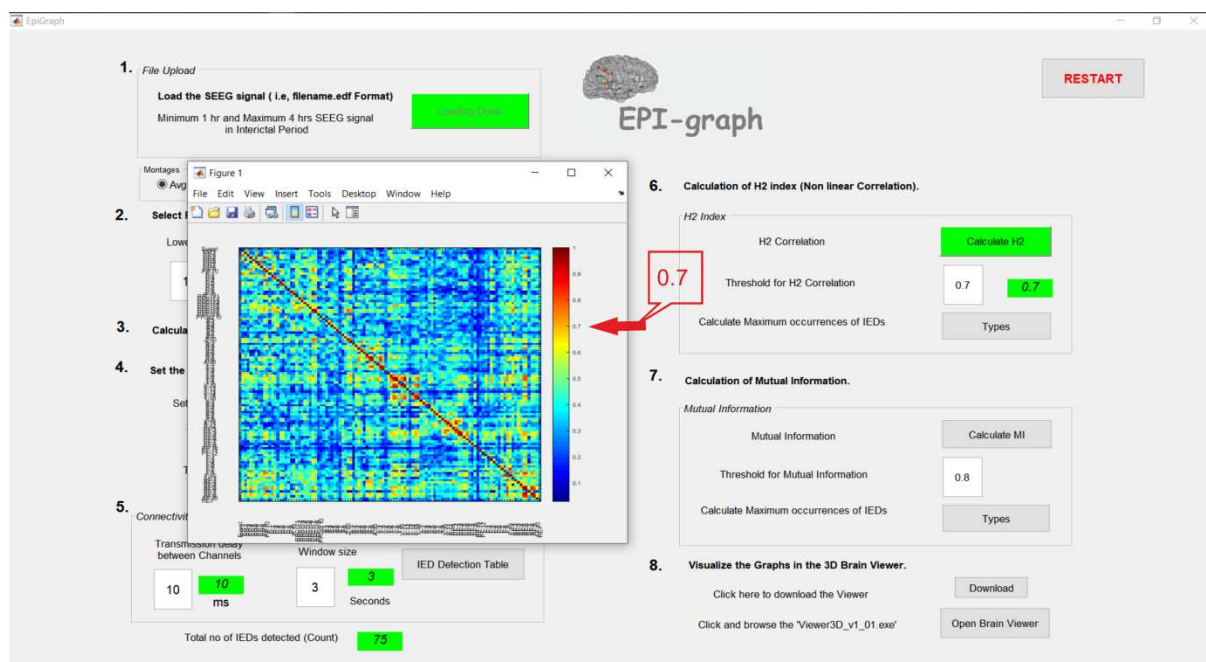
**Table2** Location of IEDs referenced without time.

	69	70	71	72	73	74	75
1	01:38:24	01:40:25	01:40:47	01:40:49	01:41:09	01:42:23	01:42:49

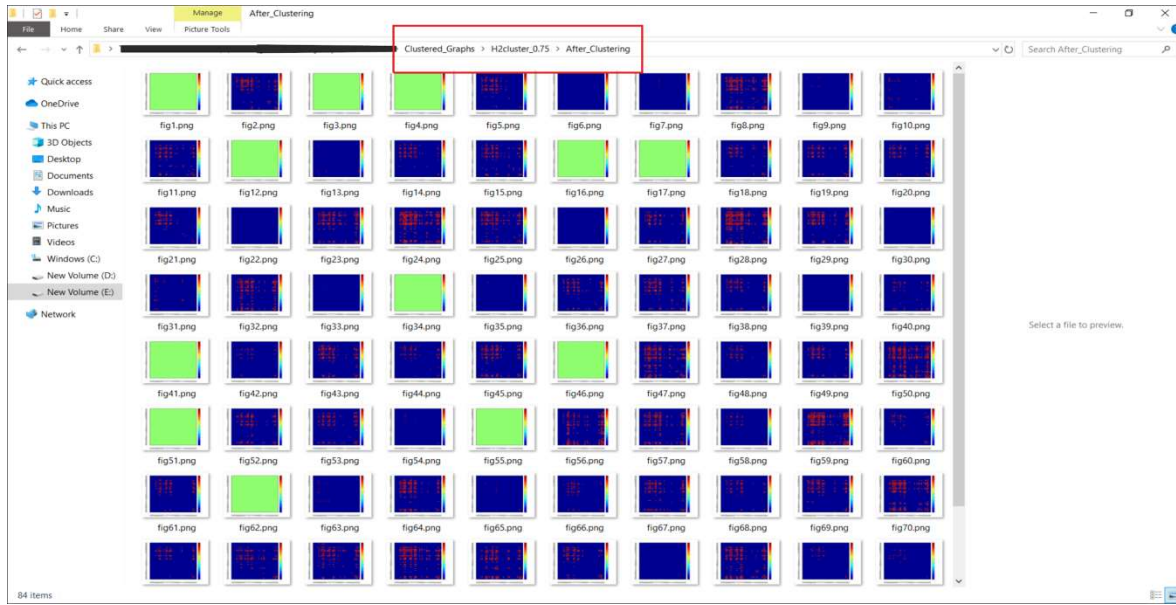
Click on the button “IED Detection Table”, a window will pop up which has two tables with IEDs locations. The first table has all the IED locations with respect to time. A count will be displayed (in step5 red box) which will give the total number of interictal discharges detected from the uploaded SEEG.

## 6. Estimation of $h^2$ index.

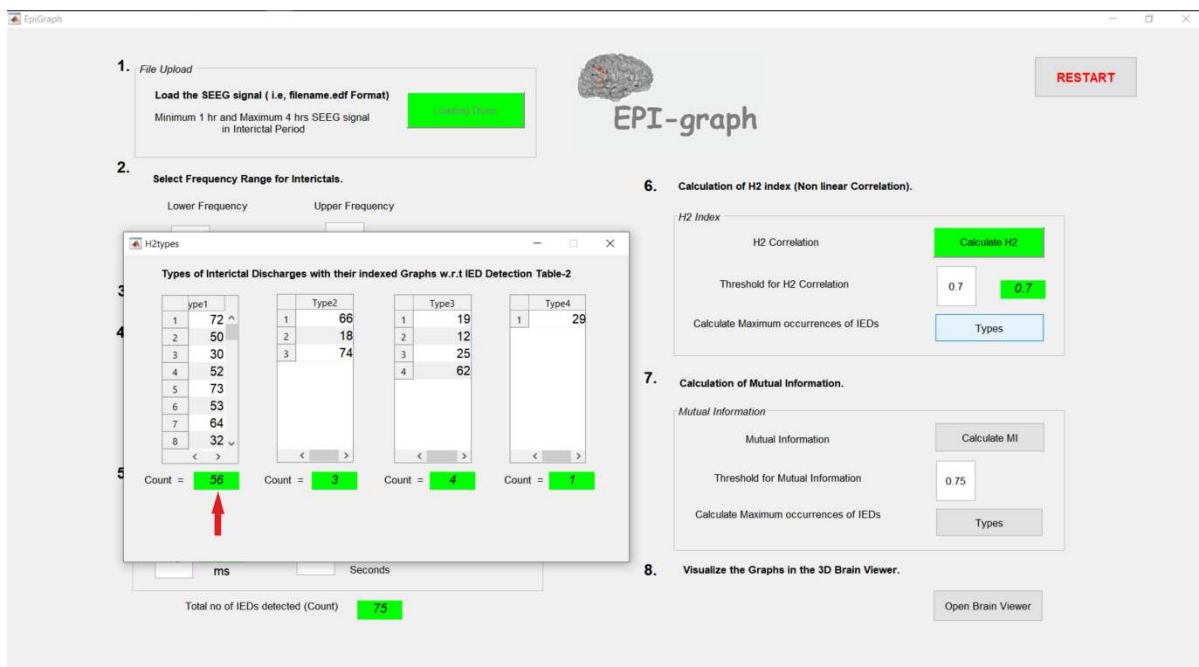
**6.1.** On clicking the button “Calculate  $h^2$ ”,  $h^2$  index i.e. nonlinear correlation will be computed for all the detected IEDs and graphs for all the detected IEDs will be saved in this path *Patient\_Name/Normal\_Graphs/Graphs\_H2*.



**6.2.** Set the correlation threshold for the graphs. The threshold and clustered graphs will be saved in separate folders.



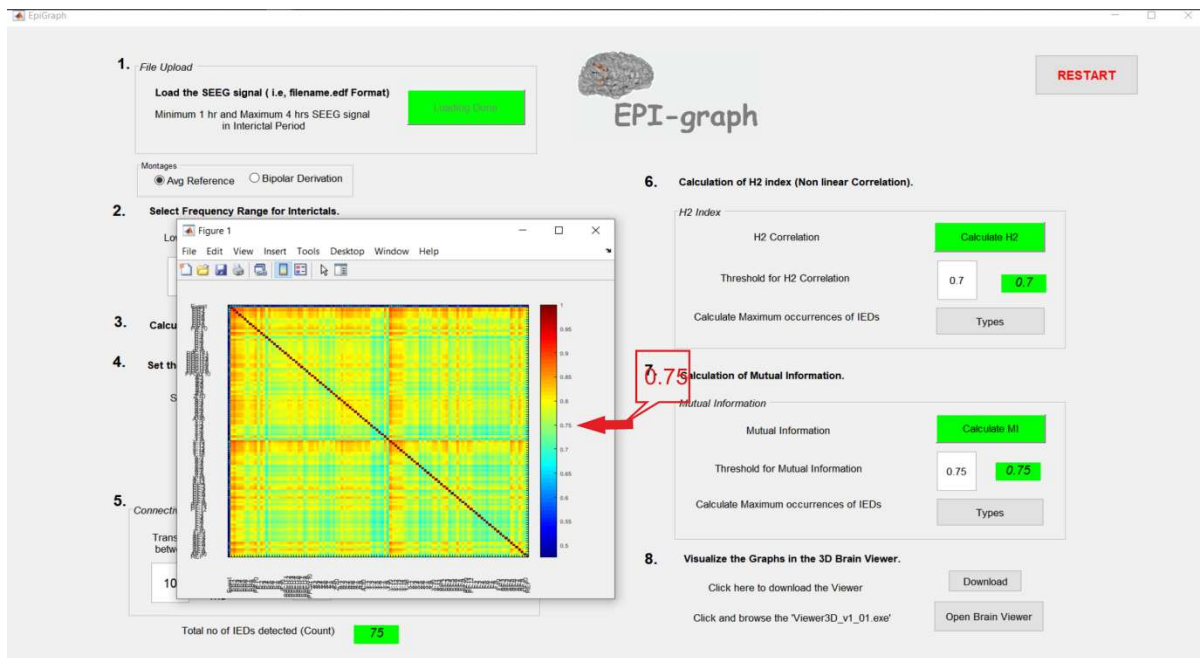
**6.3.** Click on the button “Types”, and it will group all the interictal discharges into different types. A table will pop up having respective IED numbers under each type.



All the necessary files which are required for the 3D Brain Viewer will be saved in this path *Patient\_Name/Types/H2\_0.7*.

## 7. Estimation of Mutual Information.

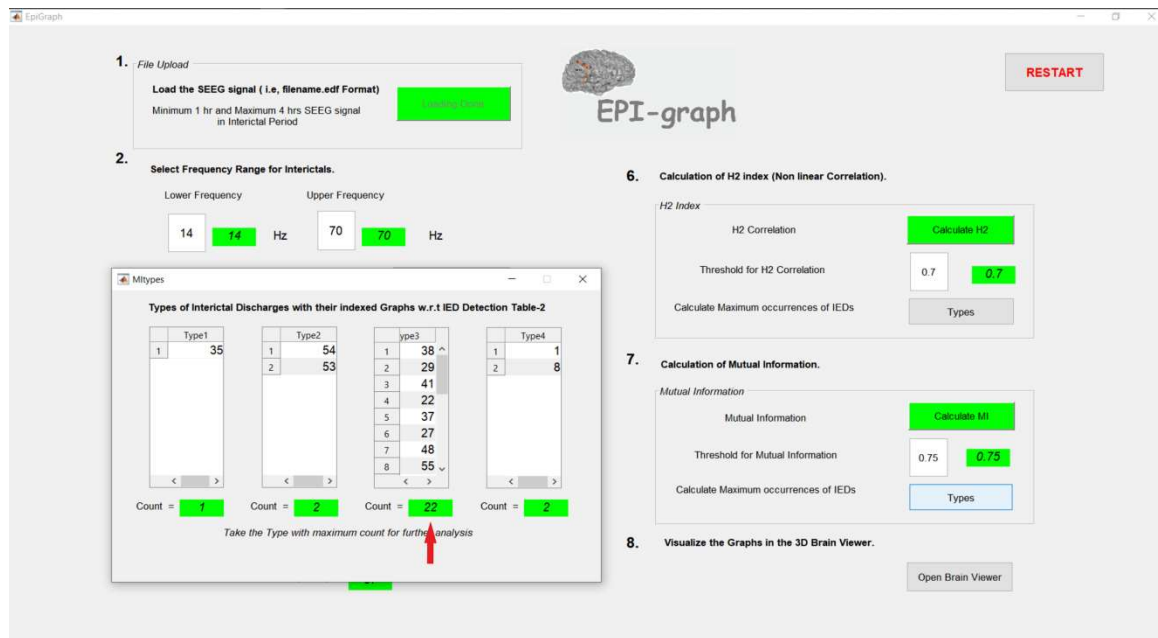
7.1. On clicking the button “Calculate MI” and mutual information will be computed for all the detected IEDs. Graphs for all the detected IEDs will be saved in this path *Patient\_Name/Normal\_Graphs/Graphs\_MI*.



7.2. Set the correlation threshold for the graphs. The threshold and clustered graphs will be saved in separate folders.

7.3. Click on the “Types” button and it will group all interictal discharges into different types. A table will pop up having respective IED numbers under each type.

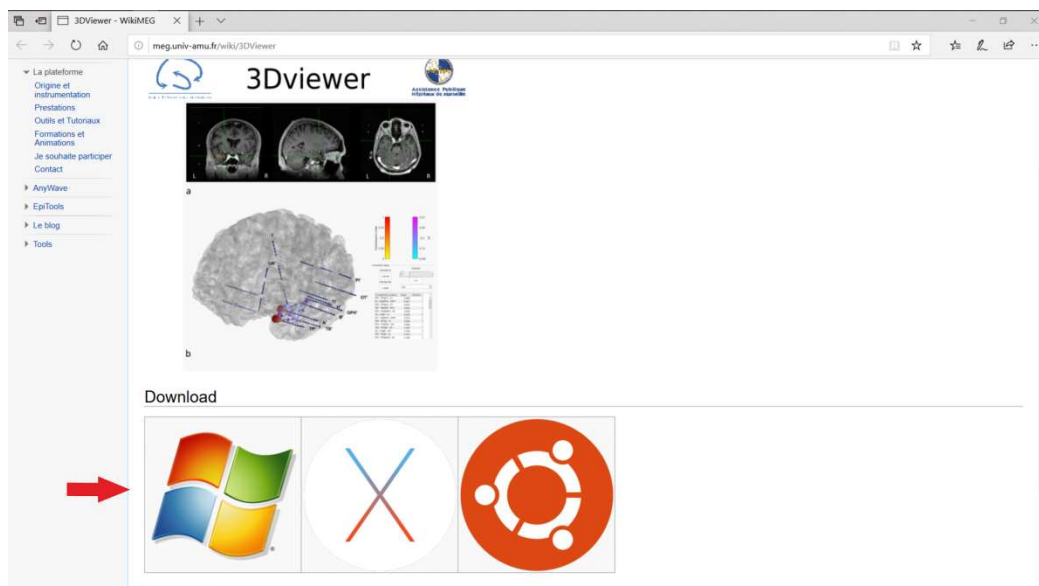




All the necessary files which are required for the 3D Brain Viewer will be saved in this path *Patient\_Name/Types/MI\_0.8*.

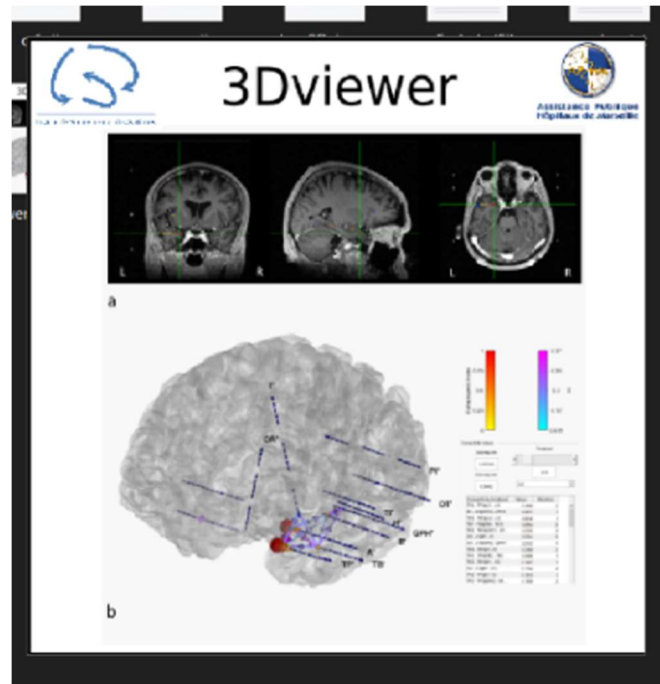
8. For Visualization of the epileptogenic network using graph parameters, we used 3Dviewer developed from MEG laboratory of Marseille, Aix Marseille university.

8.1. Click on the button “Open Brain Viewer” to download the windows version of 3D viewer or visit the website: <https://meg.univ-amu.fr/wiki/3DViewer>





**8.2.** Open the Brain viewer by double click on “Viewer3D\_v1\_01.exe”, if you encounter any execution error then download and install the Windows version of the MATLAB Runtime (version 8.5) for R2015a

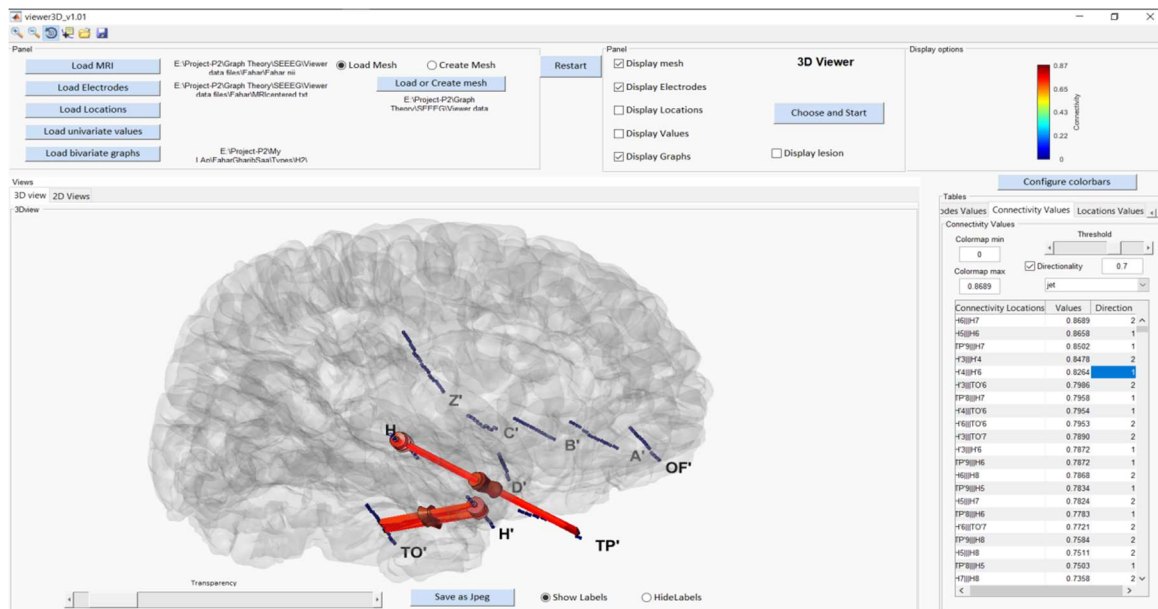


**9.1.** Click on “Load MRI” to load the MRI of the patient which is in “. nii” format.

**9.2.** Click on “Load Electrodes” to load the electrode positions. Load Electrodes were generated from GARDEL using post-implantation of CT and MRI of the patient.

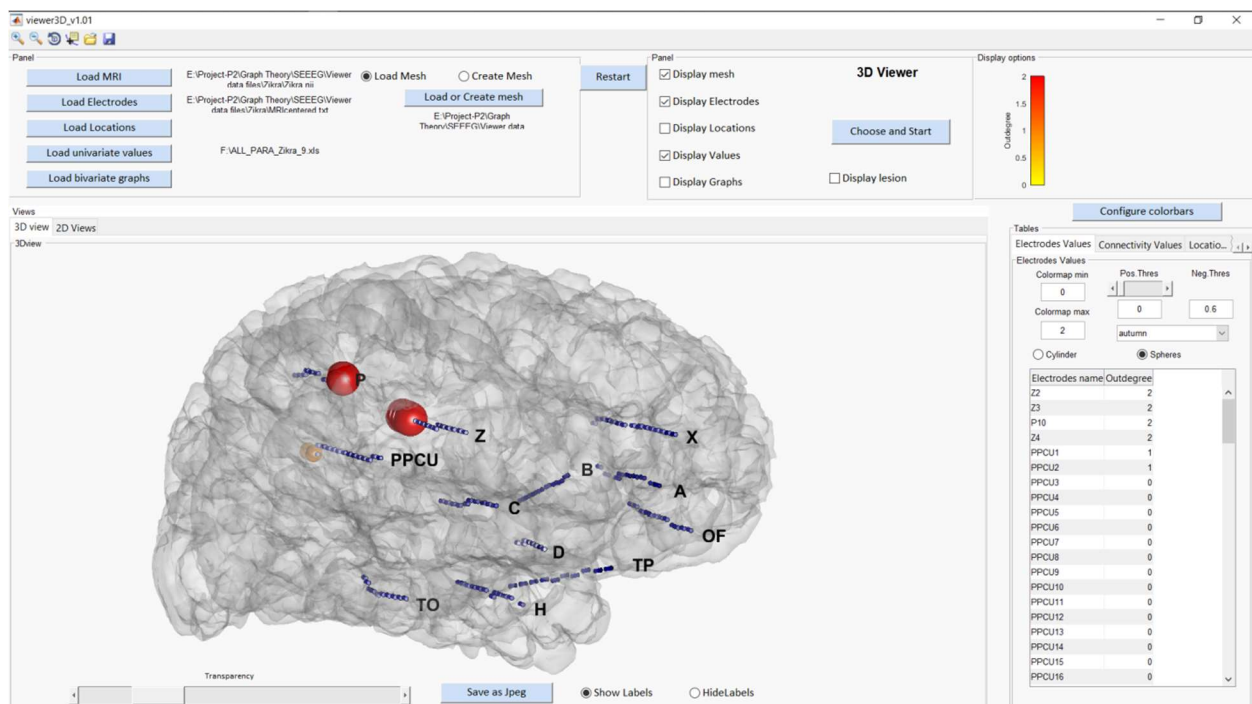
**9.3.** Click on “Load or Create mesh” to plot the 3D brain model. Select display mesh and display Electrodes. Further click on “Choose and Start”.

**9.4.** To load the bivariate data, click on “Load bivariate Graphs”. Select the mat file.



To visualize the network, click on “Display Graphs” and further click on “Choose and Start”.

**9.5.** To load univariate data click on “Load univariate values”. Select the excel sheet with values and corresponding channels.



To visualize click on “Display Values” and further click on “Choose and Start”.