ALICE: Automatic Localization of Intra-Cranial Electrodes

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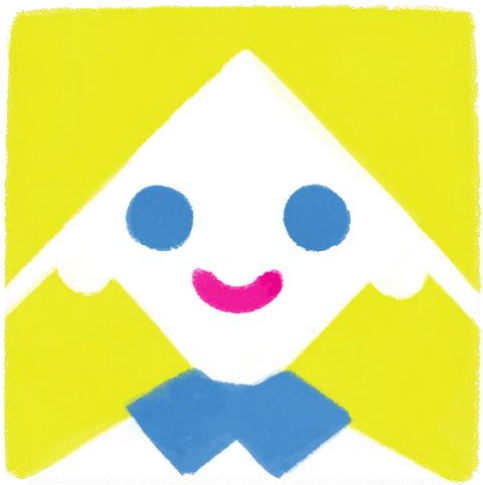


"An article about computational results is advertising, not scholarship.
The actual scholarship is the full software environment,
code and data, that produced the result."
Buckheit and Donoho (1995)

1. How to install ALICE?

1.1 Download and install AFNI and SUMA as described in afni.nihm.nih.gov.

1.2 The ALICE was primarily developed in a Linux platform. If you are also using a Linux platform be sure to had the following path to your *.bashrc*.

Open your *.bashrc* in the terminal and add the following lines (in blue) after the last **export/source** lines inside the **if ["$P1"]** branch:

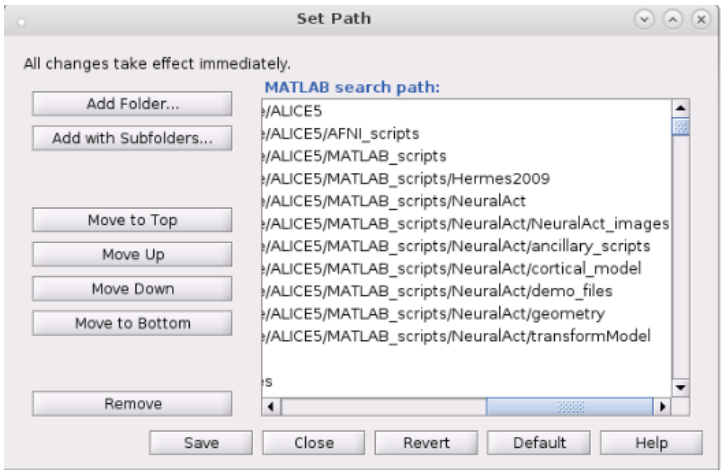
```
if [ "$PS1" ]; then
…
    #New AFNI path december 2016

    #where AFNI is installed, e.g.:
AFNI_INSTALLDIR=/Scratch/AFNI/afni_2016-12-02/linux_fedora_21_64

    # add the AFNI binary path to the search path
    PATH=${AFNI_INSTALLDIR}:${PATH}

    # Location of the plugins
    AFNI_PLUGINPATH=${AFNI_INSTALLDIR}

    # Location of the timseries models (also plugins)
    AFNI_MODELPATH=${AFNI_INSTALLDIR}

    # Location of the talairach daemon database
    AFNI_TTATLAS_DATASET=/usr/share/afni/atlases

    # Suppress warning for missing mpeg output
    AFNI_IMSAVE_WARNINGS=NO
    export   PATH   AFNI_PLUGINPATH   AFNI_MODELPATH   AFNI_IMSAVE_WARNINGS
    AFNI_TTATLAS_DATASET

    # set PATH so it includes user's private bin if it exists
    if [ -d ~/bin ] ; then
       PATH=~/bin:"${PATH}"
    fi

fi
```

Save the *.bashrc* file. **Close** the editor program and the terminal window. In a **new** terminal do `suma -update_env .`

Note: AFNI uses python **2**. So, make sure the command 'python' in the terminal uses python2.

1.2 Open MATLAB (version > 2015a).

1.3 Add the source-code folder to your path using `addpath` or using the *Set Path* icon. And verify that SPM12 is in your MATLAB path too.



2. Prepare input files

Before starting running the program be sure to have the necessary input files. For that you have to run the FreeSurfer segmentation on the patient's MRI anatomical scan. The ALICE procedure requires 3 input files: the **CT** (in *nii format), the Freesurfer **T1** scan (T1.mgz or T1.nii) and the Freesurfer **cortical ribbon mask** (ribbon.mgz or ribbon.mgz).

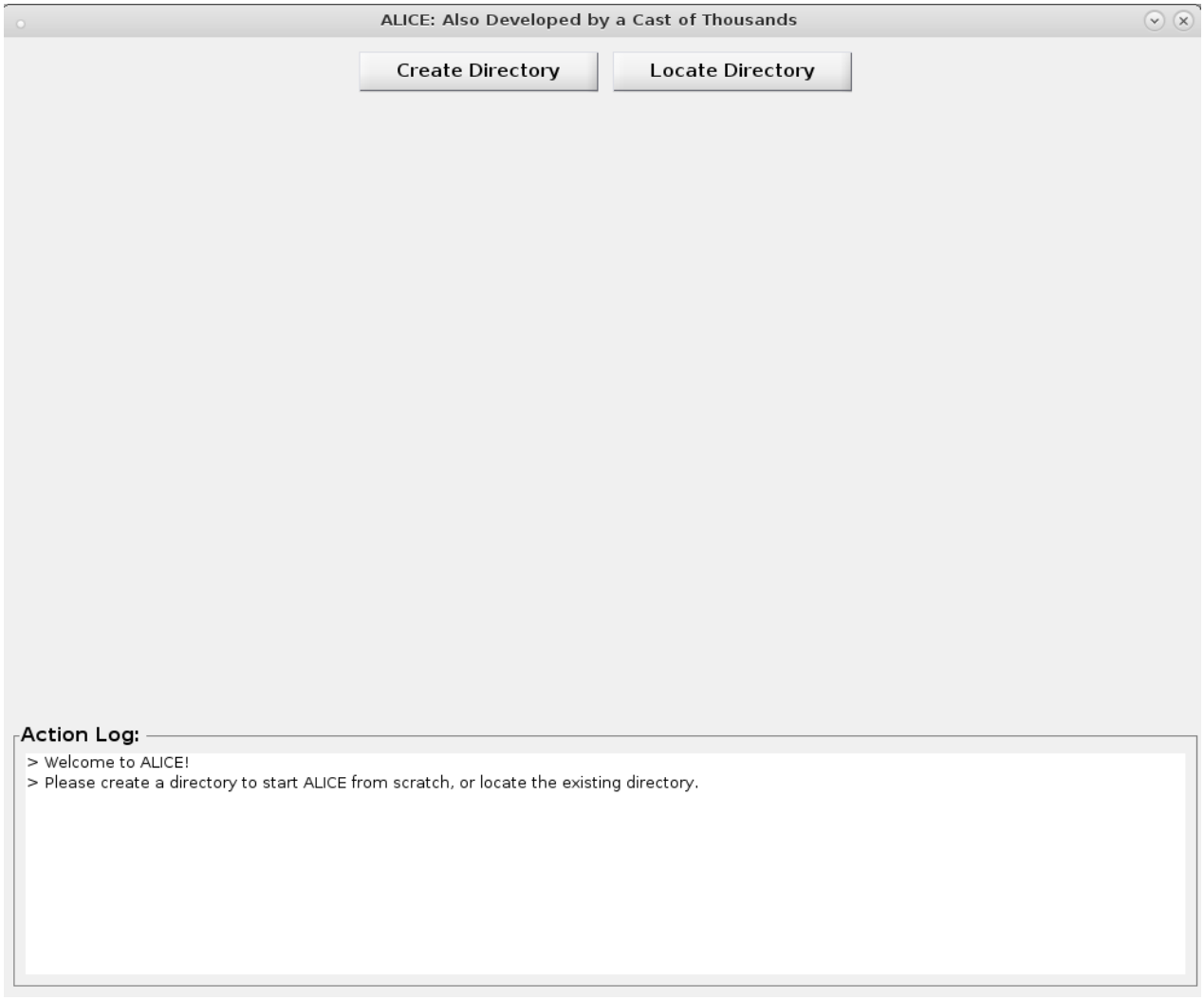
3. Overview of the user interface

Locate MATLAB current directory to the folder where you wish the program to save the output files. Be sure to have writing permissions in that folder.

Start the ALICE program by typing 'alice' in the MATLAB command window:

```
>> alice
```

The following window with open:



Now you are ready to start the electrode localization procedure. All actions and instructions are provided in the **ACTION LOG**. For more details follow the steps described in the next sections.

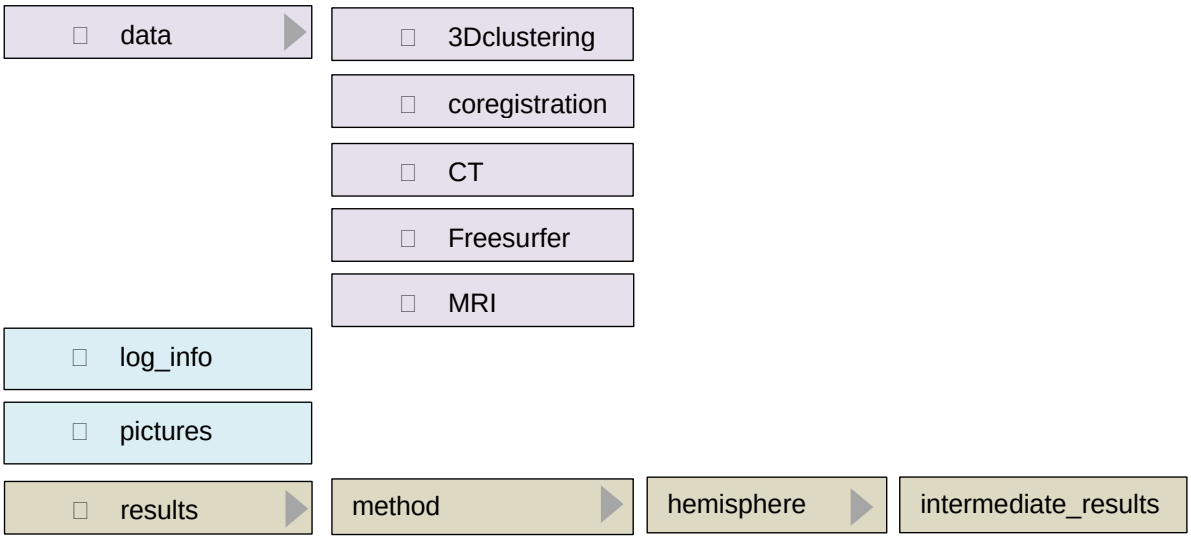
4. Start the electrode localization procedure:

The first step in the pipeline is to create a folder were all the input and output files will be stored, labeled and logged.

When you start the program two buttons appear on the top (see figure above). Choose to:

1. **Create a folder:** If you are starting the program for the first time for a given subject, choose **'Create Directory'**. The program will create a new directory where the important files are stored. When necessary the program will also copy functions to the respective folders.
2. **Or Locate an existing one:** If you have previously created a folder *using this pipeline*, interrupted the pipeline and now wish to proceed with the program, choose **'Locate Directory'**. When loading a directory, the program will automatically recognize the source files and display the path on the interface. No need to load the files again.

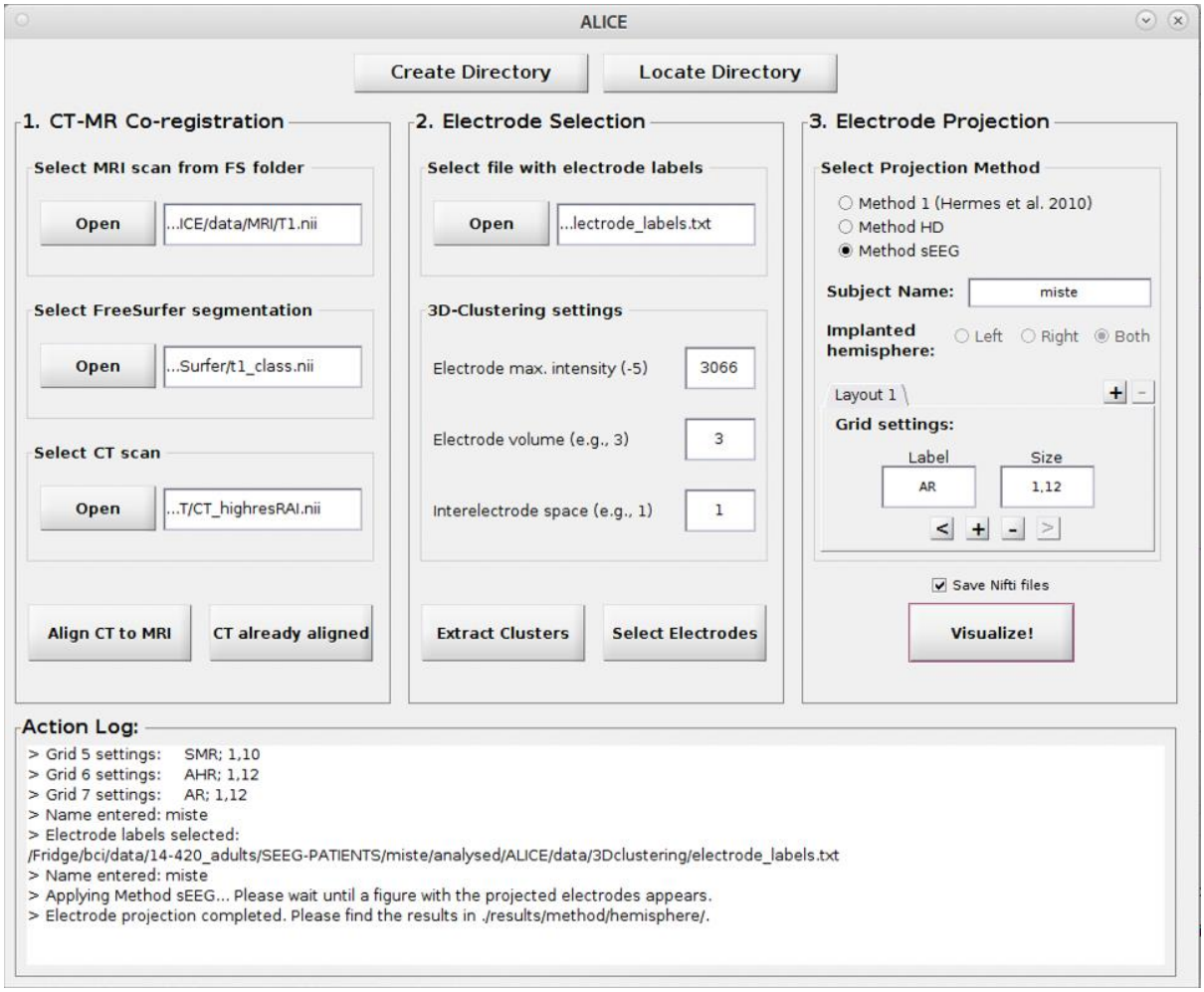
The ALICE folder is organized as follows:



The original files, renamed, will be copied to the corresponding folders. Please do not copy or move the files yourself, strictly use the interface to locate and copy the (source) files.

All steps that you perform will be logged inside `./log_info` in three separate files for the three procedural steps. These files are useful to keep track of the steps performed in case debugging is necessary.

Coordinates and cortex (*.mat and *.txt) files are saved in `./results/method/hemisphere/` and intermediate files are saved in `./results/method/hemisphere/intermediate_results/`. PNG pictures of the projected electrodes displayed on the brain surface are saved in `./pictures`.
Now, follow the three steps indicated in the interface:



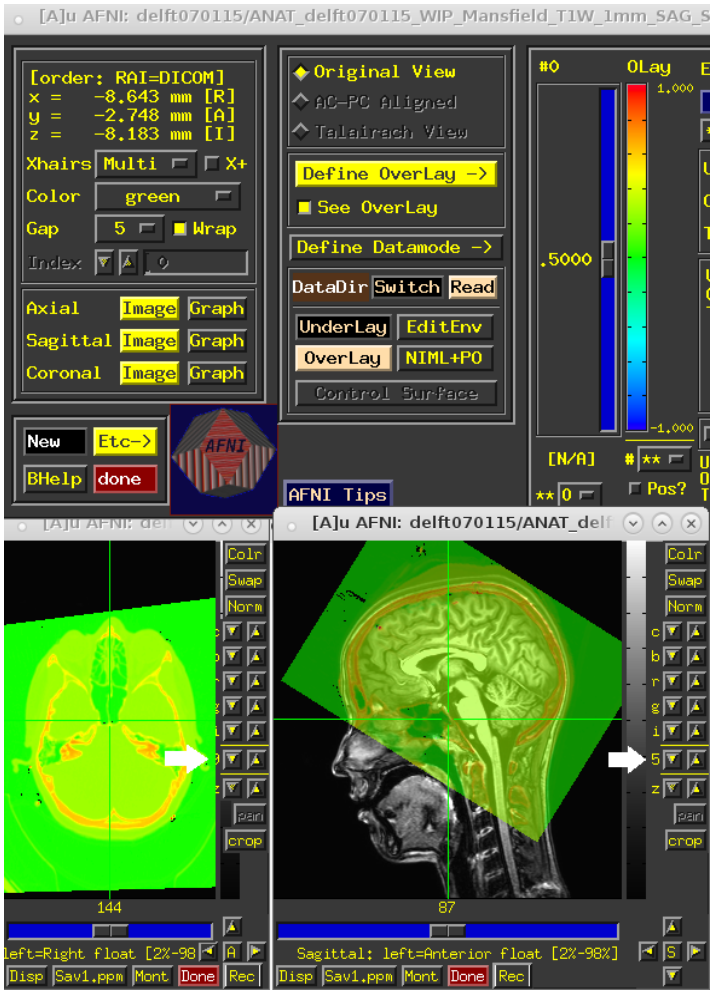
1) STEP 1: Locate the input files (if not yet loaded with LOCATE DIRECTORY).

Use the 'Open' buttons to locate the source files (FreeSurfer T1, FreeSurfer ribbon and CT). These will be copied, renamed and moved to the ALICE folder.

Align the CT to the MRI by selecting **'Align CT to MRI'**. This function will take some time. Be patient.

Once the alignment finishes, AFNI will open and a help message will be displayed with some instructions. AFNI will automatically set the T1 as underlay and the CT as overlay.

To change the transparency of the CT layer use the up-down buttons on the slices view (see figure below, white arrow). Scroll through the slices using the scrolling bar on the button of each view-window.



If the alignment is good, please close AFNI and proceed to **step 2**. If the alignment does not work, there are couple possibilities why:

(1) Sometimes the *.nii from *.dicom conversion does not work properly. If that is the case, the alignment fails, and you should use the *.nii from *.img/*.hdr instead. If that is not available then another alignment method must be used. Contact us for help.

(2) Sometimes the original T1 anatomy scan has submillimeter dimensions (e.g., 0.6 x 0.6 x 0.6 mm). In those cases Fressurfer segmentation runs but the output T1.mgz file is not proper. In this case use the original anatomy in the alignment step instead. However, in order to ensure correct electrode projection, be sure that the original T1 scan and the Freesurfer T1.mgz/nii are in the same space (i.e., aligned). You can check this in MRIcron or SPM. If these are not aligned, do not proceed and contact us for help.

2) STEP 2: Extract the electrode clusters and centers-of-mass.

Please load an *.txt file with the channel labels as saved inside the intracranial data file of the participant at hand. Make sure each line in the *txt corresponds to one channel label. Once located, the file will be copied to the ALICE folder under '3Dclustering' and will be renamed to **'electrode_labels.txt'.**

Loading of this file is essential to proceed with ALICE. In the following steps you will use channel labels to identify the electrodes on the CT rendering.

Next, there are three parameters that can be specified for the extraction of the clusters from the CT:

- Electrode maximum intensity. This value is used to threshold the CT scan in order to cluster volumes above the value. This value will be automatically predicted from the CT file. Please feel free to change this value if the estimated one is too high.
- Electrode volume. This value is a measure of cluster volume. Typically, 3 works for clinical and high-density electrodes.
- Interelectrode space. This value is a measure of distance between the clusters. The value 1 is used as standard, however in some difficult cases (many overlapping electrodes or small high-density grids) 0 might work better.

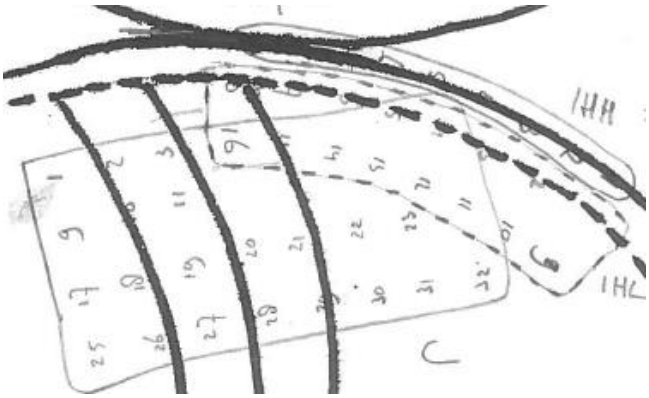
Select the **'Extract Clusters'** button. This function may time some time. Be patient.

Once extracted, SUMA will open. Please check the result in the SUMA interface by using the left-mouse click to rotate, mouse-scroll to zoom in and out, and scroll-lock to pan.

If you see all electrodes well defined by clusters, close SUMA and proceed to the next step. Otherwise, repeat procedure with other parameters.

3) STEP 2: Select the electrodes.

It is time to select the electrodes using the leads layout (electrode layout). Knowing the electrode order and the grid relative position, as described intraoperatively, locate each electrode in SUMA and select the electrodes one-by-one. Please identify the electrode by their 'label' (e.g. C01) instead of their index (e.g., 33).



Electrode grid relative position and label.

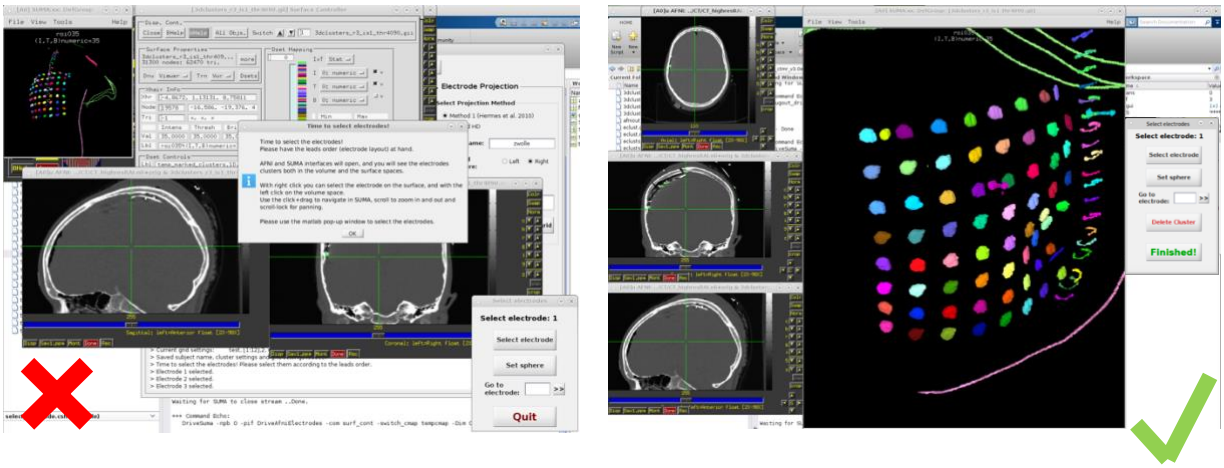
1	2	3	4	5	6	7	8	channels
IHL01	IHL02	IHL03	IHL04	IHL05	IHL06	IHL07	IHL08	1..8
IHL09	IHL10	IHL11	IHL12	IHL13	IHL14	IHL15	IHL16	9..16
IHH1	IHH2	IHH3	IHH4	IHH5	IHH6	IHH7	IHH8	17..24
AH	ECG	orb	emg					25..32
C01	C02	C03	C04	C05	C06	C07	C08	33..40
C09	C10	C11	C12	C13	C14	C15	C16	41..48
C17	C18	C19	C20	C21	C22	C23	C24	49..56
C25	C26	C27	C28	C29	C30	C31	C32	57..64

Leads order per electrode indicated in the 'channels' column.

!! Having this information at hand can be useful

Select the button '**Select Electrodes'**. At this point, three programs will be displayed: AFNI, SUMA and a small Matlab interface (see right panel below). If you do not see one of the interfaces please check AFNI and SUMA are in the *bash* and if you are using the latest version of all the software, or contact us. A message dialog will also be prompt to help guide you through the selection process. Read the instructions in the **message dialog** for more information about the interfaces. When read, please press '**OK'**. Use this step to select **ALL** electrodes on CT that you wish to project later (e.g., clinical grid and/or HD grid and/or depth electrodes).

!! Note: We recommend organizing the windows as follow: AFNI main interface and SUMA object controller can be minimized, SUMA maximized and Matlab electrode selection interface on the side (see below an example).



Use SUMA to select the clusters, using the right mouse click. AFNI jumps to the correct volume position. Navigate in AFNI using the left mouse click.

Use the **'Select Electrodes'** window or specific keys to select the electrodes. Here you can see the current electrode label to be selected.

For each electrode you have the options:

1) '**Select electrode':** Select a cluster in SUMA (right-mouse click) and then push the button 'Select electrode'. 'Select electrode: XX' string on the top of the interface will update accordingly. **The selected electrode will become white**. Please note that usually clinical grids have a marker (smaller) electrode between the first two electrodes of the grid. This makes it easier to identify where to start counting.

2) **'Set sphere':** Sometimes a cluster may be missing or may embody two electrodes. Then use the AFNI volume interface to locate the electrode center-of-mass (left-mouse click to select a voxel) and use the button 'Set Sphere' to create a new cluster around that point.

3) **'Go to electrode':** Sometimes there are channels without ECoG electrodes (see patient example above between channel 25 and 32). In that case, you can choose to go to a specific label (C01) using the 'Go to electrode' field and select enter **'>>'.** You can also choose to redo specific electrodes by using the same field.

4) **'Delete cluster':** This option paints the electrode black.

5) **'Finished!':** When done, select 'Finished!'. Be patient and **wait until the program closes all windows**.

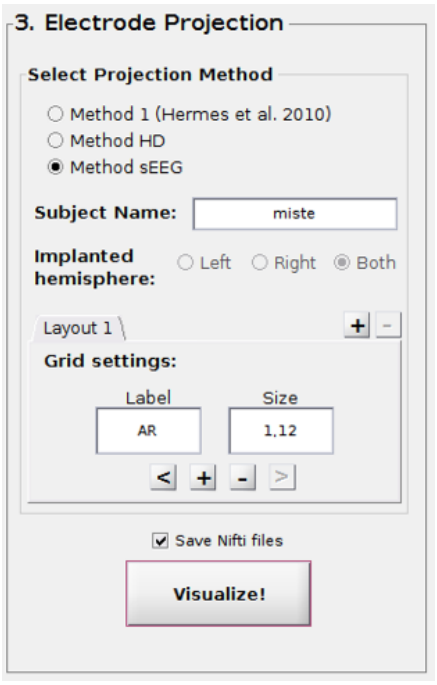
4) STEP 3: Project the electrodes.

Project electrodes using the **Method 1** for clinical grids and **Method HD** for high-density grids or **Method sEEG** for stereo-EEG.

In this step you may enter up to 3 electrode-layouts (i.e., up to 3 tabs with different electrode settings) per subject. A 'Layout' allows to project and visualize different sets of electrodes that require either a different **projection method** or a different **implanted hemisphere**, for example:

- clinical grid (left hemisphere) + HD (left hemisphere);
- clinical grid (right hemisphere) + clinical grid (left hemisphere);
- or clinical grid (left hemisphere) + depth electrodes/sEEG (both hemispheres).

The result of each layout will be saved in a separate folder depending on the method and hemisphere used (see section 4 for details).



Method 1 (Hermes et al. 2010):
Enter the subject **name** and choose the **hemisphere** where the grids were implanted. Add grid information necessary to the orthogonal projection method (Hermes et al. 2010).

Select a layout tab. Add and remove layout tab with '+' and '-' buttons.

Select a layout tab. Per grid insert the grid label as used in the file 'electrode_label.txt' but without the numbering (e.g., '**C**', note that the **label is case-sensitive**) and the grid size (e.g., 4 x 8 can be input as **'4,8'**). Select **'Add Grid'** to add the grid information.

Use the **Action Log** to check which grids were added or deleted.

If you make a mistake you can remove the information add by clicking **'Delete previous grid'.**

Please note that you need to select a 'Method' and 'Hemisphere' every time you change the layout. The 'Method' and 'Hemipshere' is not associated to a specific layout.

Press '**Visualize!'** to project the electrodes and see the result. You will see the projection figures and the final result popping-up.

Method HD (no brain correction, just projection and display on the surface):
Same settings as method 1. This method allows displaying the electrode on the surface assuming the distance from the electrode to the cortical surface to be small (Kubanek and Schalk 2015). Press **'Visualize!'** to project the electrodes and see the result. Two figures show the result before and after being displayed on the surface.

Method sEEG (depth electrodes, no brain correction):
This method will use both hemispheres automatically. No projection performed. Run similarly to Method 1 and Method HD. The output are three brain views saves in png format.

Congratulations!

You have completed the ALICE procedure.

The output files were saved in the folder `/results/method/hemisphere`.