CNNP Cortical Folding User Interface (UI)

Unser Manual

This manual explains functionalities and requirement for proper use of *CNNP Cortical Folding UI*.

For further assistance or to report any issues, visit our [official website](https://www.cnnp-lab.com/home).

The current version of the UI requires MATLAB to be executed. Go to the [official website](https://uk.mathworks.com/products/matlab.html) for further information. For optimal performance and appearance, use MATLAB 2023a or later version. The oldest version tested was 2021a, showing complete functionality but having some issues with appearance. Additional software will be required for certain functionalities. System and hardware requirements are:

* *Processor*: Intel® (or MATLAB for Intel® processor)
* *RAM*: 16GB or more recommended.
* *Operative System*: Linux, Mac, and Windows all support main functionalities. **Windows has some restricted functionalities**; further details in “*Processing pial-outer-smoothed files*”.

# Complete Usage Workflow

The UI is designed for easy and fluent use, by dynamically changing appearance to indicate the following step. To start the UI, double click on the file “*Main.mlapp*”. On Linux device follow these steps: open MATLAB, open “*Main.mlapp*” file, press ‘Run’. For a complete workflow the following steps should be taken.

## Dataset/s selection and management

A computer screen shot of a brain

Description automatically generatedThe UI is designed to allow the analysis of several dataset simultaneously. After launching the app, the initial interface should be as shown in Figure 1. Press “*Add Datasets*” and folder selection user interface will be initiated. Select the **root folder of the dataset(s)**. The UI will analyse file structure and content identifying the number of subjects available in the root folder, based on the presence of FreeSurfer folder structures. This information will be internally stored for next steps and presented to the user.

The program requires one of the specific file structures as follows:

* Dataset > *FreeSurfer* > Subject > Session >
* Dataset > *FreeSurfer* > Subject >

*FreeSurfer* output files including the smoothed surfaces should be placed inside the subject/session folder.

Multiple datasets can be introduced to the UI: press “*Add Datasets*”, select the new dataset root folder. The user can then choose which datasets to process by toggle the selection buttons to the left of each dataset name. The red button with a trash bin symbol (to the right of the “*Add Datasets*” button) **resets the UI** removing all stored information relating datasets and configurations.

Figure 1Initial UI appearance

## A computer screen shot of a computer screen Description automatically generatedConfiguring cortical folding feature estimation

When at least one valid dataset is introduced to the UI and selected as shown in Figure 2 several panels will become available. These are configuration options to set up the cortical folding parameters estimation.

**Any change on these configuration parameters will reset the progress on the following steps**.

“*Hemisphere"* Panel: Indicates which hemisphere will be analysed: left, right or both hemispheres. Note that the options average and sum of hemisphere is not yet implemented, thus are not available yet.

“*Mode*” Panel: Indicates the level of parcellation (hemisphere or lobes) and the spatial scale options to estimate cortical folding features.

* ‘*Hemisphere*’: Estimation for entire the hemisphere.
* ‘*Lobe*’: Divides each hemisphere in lobes, based on selected atlas. Currently, only LUT atlas is included: more atlases will be implemented in the future.

Figure 2 UI appearance during configuration mode

* A screenshot of a computer

  Description automatically generated‘*Multi-scale*’: Select the scale for feature estimation: *Higher Scales* and *Lower Scales* are explained below(1) and *No Scales* uses the native scale (i.e., the spatial scale that is normally used in FreeSurfer).

## Validity of available subjects/sessions (Screening)

After configuration, the screening section will appear as shown in Figure 3. Press the ‘*Screening*’ button to start the validation process on subjects/sessions included. The UI will check the presence and validity of:

1. ‘*lh.pial-outer-smoothed’* & ‘*rh.pial-outer-smoothed*’ files in the FreeSurfer folder structure, required to estimate cortical folding features.
2. Intermediate subject-level output files (go to “*Estimating the cortical folding parameters”* for more information) including cortical features matching the defined configuration.

The screening process may take several minutes, depending on the total number of subjects/sessions. Progress bars will indicate the estimated remaining time. The screening report table will show:

Figure 3 Screening step

(1)Scales are generated with an initial scale (s) and the number of iterations (3). The initial scale is increased by a power of two every iteration ([s\*2^0, s\*2^1, s\*2^2, s\*2^3]). *Higher Scales* are generated with initial scales [0.325, 0.35, 0.375] and 4 iterations. *Lower Scales* are generated with initial scales [0.225, 0.25, 0.275, 0.3] and [5, 5, 4, 4] iterations respectively.

* ‘*DataSet*’, the name of the tested dataset.
* ‘*Subjects*’, the number of available subjects.
* ‘*Smoothed*’, the number of subjects including both valid ‘*pial-outer-smoothed*’
* ‘*Processed*’, the number of subjects with extracted cortical parameters matching the set configuration.

Several new options will also become available after screening (Figure 4). These can be used to generate smooth surfaces files (*pial-outer-smoothed*), estimate cortical folding parameters, and group outputs into a single file.

## Processing *pial-outer-smoothed* files

**WARNING**

This process is not available for Windows devices as

*FreeSurfer* toolbox is not available for this operative system

**ADVISE**

This process is optional and can be skipped if not needed

A screenshot of a computer

Description automatically generatedIf there are fewer ‘*Smoothed*’ subjects than ‘*Subjects*’ in the screening report table (Figure 4), this indicates missing or corrupted *pial-outer-smoothed* files. We provide the option to generate these missing or corrupt files given some conditions:

1. *FreeSurfer* toolbox is installed on the device at a known location. Visit the [*official webpage*](https://surfer.nmr.mgh.harvard.edu/) to obtain more information about installing FreeSurfer.
2. If using Linux device, [*dos2unix*](https://ioflood.com/blog/install-dos2unix-command-linux/#:~:text=Most%20Linux%20distributions%20come%20with,with%20the%20syntax%2C%20dos2unix%20myfile.) is installed. This will be requested in case of need.
3. MATLAB must have sudo/administrator access (by execution of computer user).

Press “*Extract Smooth Surfaces*” to begin the *pial-outer-smoothed* generation. On Windows devices this command will be blocked. The UI will request the location of *FreeSurfer* toolbox. Please provide **the FreeSurfer version folder** to prevent execution issues.

If all conditions are meet, the process will begin, and a progress bar will indicate the estimated remaining time. Upon completion, a new screening process will be automatically run updating the screening report table.

Figure 4 Latest stages of the UI

**Please note that this is the most time-consuming process of the entire workflow, and large datasets could take several hours to complete.**

## Estimating the cortical folding parameters

The estimation of cortical folding features can be started by pressing “*Process Subjects*”. The initiated workflow estimates cortical folding features for all subjects/sessions following the configuration set by the user. Each subject’s parameters are stored as individual .csv files in *CNNP Format* (go to “*Obtaining grouping outputs for easy usage”* for more details) in the subject directory.

In the presence of pre-existing subject-level csv files (reported as ‘*Processed’* on the screening report table), matching configuration entries are looked for. If new unmatched configurations have been requested (for example, a new parcellation option), features are estimated and included on the same file. If matching configurations are found the settings in the “*Estimation Mode*” panel indicates how to manage them:

* ‘*Append*’:the estimation process is skipped keeping the previously estimated values.
* ‘*Overwrite*’: parameters are estimated, and the **preexisting entries are overwritten**.

A screening process will automatically run at the end to update the screening report table.

## Obtaining grouped outputs

The last step is grouping the estimated cortical folding parameters into a single location. Specify on the output format on “*Output Format*” panel and press “*Group Outputs*”. There are two available formats:

### CNNP Format

Output format also used for subject-level storage of parameters. This consists of a single .csv file including cortical folding parameters, with several additional fields.

* *Dataset*, *Subject* and *Session*: indicate the origin of the data (*\_\*\_* is used in case of no *Session*)
* *Hemisphere*, *Atlas*, *Fines* and *Region*: represent the anatomical location of the brain.
* *Scale*: indicates the scaling factor(1), with 0 representing the native scale.

Data matching the specified configuration is pulled for each subject’s file and stored in a new csv file. The UI will request a file name (the ‘*\_CNNP*’ suffix will be added by the UI) and location to store the grouped outputs.

### FS Format

The FS format is an output format inspired by *FreeSurfer* output file structure. In this case a folder structure is formed as follows: *Output\_Folder > Dataset > Atlas >*. Within the *Atlas* folder, a .csv file for each cortical folding parameter is generated. Each one includes the values for all *Subject*/*Sessions* (rows) and *Regions* (columns). *Scale* is defined on the name of the .csv. *Output\_Folder* will be requested to store the dataset. **It is recommended to generate a new folder** for this step, as it will be overwritten and renamed with the suffix ‘*\_FS*’.

# Further implementations

This cortical folding toolbox has been designed to flow into a further pipeline (Brain MoNoCle) that can provide estimates of brain abnormalities using normative modelling approaches based on a large normative reference sample (n>3,200, aged 5-95 years old). In order to use Brain MoNoCle, please export the grouped outputs in the CNNP format described above.

Brain MoNoCle is available in a web-app here: <https://cnnplab.shinyapps.io/normativemodelshiny/>

For more information about our normative modelling pipeline Brain MoNoCle, please see our latest preprint: <https://arxiv.org/abs/2406.01107>