PRATEEK: Integration of Multimodal Neuroimaging Data to Facilitate Advanced Brain Research

Principal Investigator - Dr.Pravat K. Mandal

USER MANUAL

MAY, 2021

NEUROIMAGING AND NEUROSPECTROSCOPY LABORATORIES
NATIONAL BRAIN RESEARCH CENTRE, INDIA

Funded by the Ministry of Electronics and Information Technology (MeitY), Government of India

This toolbox is being developed under the supervision of Dr. Pravat Mandal, at the Neuroimaging and Neurosprctroscopy lab, National brain Research Center, Manesar.

For any further clarifications and bug reporting please report at ninslab.toolboxes@gmail.com.

First release, May, 2021

Contents

1 OVERVIEW 7

2 INTRODUCTION 9

2.1 Introduction 9

2.2 Description of Neuroimaging Modalities 10

3 Pre-Requisites 13

3.1 Software Prerequisites 13

3.2 Folder Structure 13

4 Execution Scheme 15

5 Steps to run PRATEEK 17

List of Figures

2.1 F/home/bigdata/Desktop/title.pngunctional MRI Activation Maps 10
2.2 MRS Voxel Position 11
2.3 QSM Image 12
2.4 MEG Multiple Dipoles 12

3.1 Core Folder Structure 14

4.1 A. Execution scheme of PRATEEK toolbox. B. Processing pipeline for fMRI-MRS multimodal data 16

5.1 Primary Window 17
5.2 Initialized interfaces for single-modalities 19
5.3 Initialized interfaces for multi-modal combinations 20
5.4 Error Window 21
5.5 Initialized interfaces for single-modal combinations 21
5.6 Initialized interfaces for multi-modal combinations 22
5.7 fMRI initialized interface 23
5.8 MRS initialized interface 23
5.9 QSM initialized interface 24
5.10 MEG initialized interface 24
5.11 fMRI-MRS initialized interface 25
5.12 MEG-MRS initialized interface 25
5.13 fMRI-QSM initialized interface 26
5.14 MEG-fMRI initialized interface 26
5.15 Initial GUI Interface 27
5.16 Atlas Selection 27
5.17 Atlas Selection: Neuromorphometrics.nii 28

5.18 Region of interest selection 28
5.19 Mask generation : fully initialised 29
5.20 Result Folder in the main Subject Directory 29
5.21 Overlap Percentage 30

1. OVERVIEW

PRATEEK provides a user friendly MATLAB based Graphical User Interface platform to coregister and integrate multiple neuroimaging modalities. The toolbox features data organization, single-modality processing pipelines, and their spatial integration. The principle advantage of the proposed toolbox is its applicability to any of the neuroimaging modalities (fMRI, MRS, MEG and QSM) over any anatomical region of the brain. This toolbox minimizes the need to have expertise in handling different neuroimaging tools or processing and analyzing multimodal data ensuring user's convenience for further advanced brain research.

2. INTRODUCTION

2.1 Introduction

Neuroimaging modalities such as Magnetic Resonance Imaging (MRI), functional MRI (fMRI), Magnetic Resonance Spectroscopy (MRS), Quantitative Susceptibility Mapping (QSM) and Magnetoencephalography (MEG) are important in non-invasively studying the structural, functional and biochemical properties along with critical processing of the data from different regions of the brain.

These neuroimaging techniques are utilized to study various aspects of ageing, brain developmental, neurological and psychiatric disorders. Various studies have used a unimodal imaging approach which provides limited information to evaluate the changes in the particular region of brain during AD progression. However, a wealth of complementary information can be gathered from a multimodal approach and will lead us to a better understanding of the complexity of the disease processes. Integrating different neuroimaging modalities will further help to provide a detailed understanding of the underlying physiological processes from a specific Region Of Interest (ROI).

In this work, a unique approach is developed to generalize spatial integration of the outcomes from multiple neuroimaging techniques. The data acquired from four different neuroimaging techniques namely, fMRI, MEG, MRS, and QSM has been integrated. The common region extracted from this integration is further quantified by a metric termed as “overlap percentage”. PRATEEK toolbox can work for any of the aforementioned neuroimaging modalities over any anatomical region of the brain. A graphical user interface “PRATEEK” toolbox has been developed featuring data organization, individual processing pipelines, and their integration. This toolbox minimizes the need to have expertise in handling different neuroimaging tools or processing and analyzing multimodal data ensuring user’s convenience for further advanced brain research.

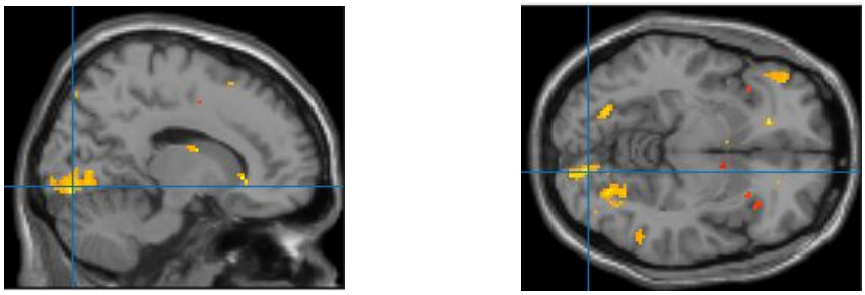
2.2 Description of Neuroimaging Modalities

Before getting to the technical details let's dive into a brief descriprion of all the modalities available and understand the need for multimodal integration.

1. Functional Magnetic Resonance Imaging

   The brain is constantly active, be it while performing a task like reaching out to pick up a cup of coffee, like understanding language in a conversation, or when a person is at rest an not performing any task. Brain activity at rest and while performing different tasks is distributed in different networks connecting specialized regions of the brain.Functional magnetic resonance imaging is a technique to non-invasively measure and map brain activity. It is being used in many studies to better understand how the healthy brain works, and in a growing number of studies it is being applied to understand how that normal function is disrupted in diesease.

   When neuronal activity in an area increase their activity in response to a stimulus, the physiological demand for oxygen in that area increases and is delivered to neurons by haemoglobin in capillary red blood cells. The result of this phenomenon is a change in the relative levels of oxy- and deoxyhaemoglobin during activity as compared to rest. Haemoglobin is diamagnetic when oxygenated but paramagnetic when deoxygenated. This difference in magnetic properties leads to small differences in the MR signal of blood depending on the degree of oxygenation. Since blood oxygenation varies according to the levels of neural activity these differences can be used to detect brain activity. This form of MRI is known as blood oxygenation level dependent (BOLD) imaging. Brightly coloured blobs on fMRI maps represent the active regions in the brain.



(a) Sagittal View (b) Axial View

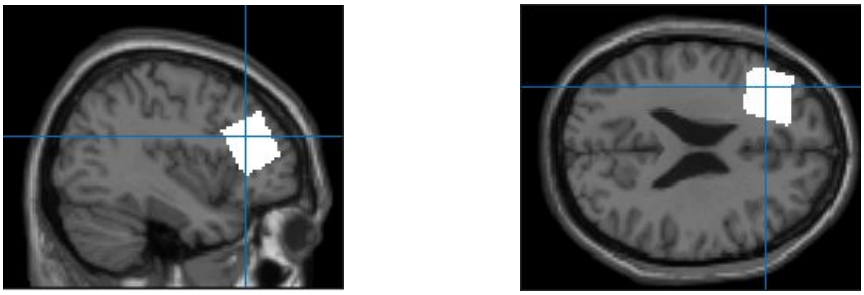
Figure 2.1: F/home/bigdata/Desktop/title.pngunctional MRI Activation Maps

2. Magnetic Resonance Spectroscopy

   Magnetic Resonance Spectroscopy (MRS) is a noninvasive test for measuring levels of various neurochemicals in the brain. These chemicals can include N-Acetyl Aspertate (neuronal marker), Creatine (energgy maker), Choline (cell membrane marker), myo-inositol (glial marker), etc. antioxidants like Glutathione and neurotransmitters like GABA and Glutamate.

MRS measures the levels of these neurochemicals based on the relative precession states of their organic hydrogen ions and coupling between neighbouring protons. In most conventional methods, slice selective RF pulses are applied to excite protons in only a small volume of the brain called a Voxel. Readout is for relaxation of the protons from this voxel is collected as their precession relaxes back to align with the magnetic field of the scanner. The frequency of these metabolites is measured relative to a reference signal and is expressed in parts per million (ppm) and plotted on a graph with peaks height and area representing signal intensity.

MRS has applications in various diseases such as stroke, epilepsy, tumor, dementia and movement disorders to name a few. It is used to measure the levels of metabollites in the affected brain areas as compared to controls to determine the changes is metabolism of the diseased brain tissue as compared to healthy brain areas.



(a) Sagittal View (b) Axial View

Figure 2.2: MRS Voxel Position

3. Quantitative Susceptibility Mapping

Quantitative Susceptibility Mapping (QSM) provides a novel contrast mechanism in Magnetic Resonance Imaging (MRI) different from traditional Susceptibility Weighted Imaging.The voxel intensity in QSM is linearly proportional to the underlying tissue apparent magnetic susceptibility, which is useful for chemical identification and quantification of specific biomarkers including iron, calcium, gadolinium, and super paramagnetic iron oxide (SPIO) nano-particles.

QSM utilizes phase images, solves the magnetic field to susceptibility source inverse problem, and generates a three-dimensional susceptibility distribution. Due to its quantitative nature and sensitivity to certain kinds of material, potential QSM applications include standardized quantitative stratification of cerebral microbleeds and neurodegenerative disease, accurate gadolinium quantification in contrast enhanced MRI, and direct monitoring of targeted theranostic drug biodistribution in nanomedicine.

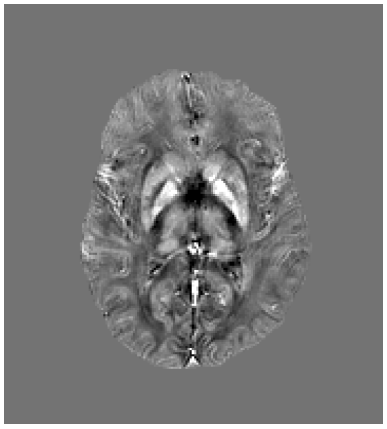


Figure 2.3: QSM Image

4. Magnetoencephalography (MEG)

   Magnetoencephalography (MEG) is the measurement of the magnetic field generated by the electrical activity of neurons. The oscillatory signals obtained from MEG provides insight into the neuronal mechanism underlying cognitive process. It is usually combined with a magnetic resonance imaging to get what is called magnetic source imaging. The technology that has helped record these minute magnetic fields is super-conducting quantum interference detector which is like a highly sensitive magnetic field meter. To attenuate the external magnetic noise the MEG scanner is housed inside a magnetically shielded room. The actual sensors recording magnetic fields are magnetometers and/or gradiometers. MEG fields pass through the head without any distortion. This is a significant advantage of MEG over electroencephalography. MEG provides a high spatial and temporal resolution.

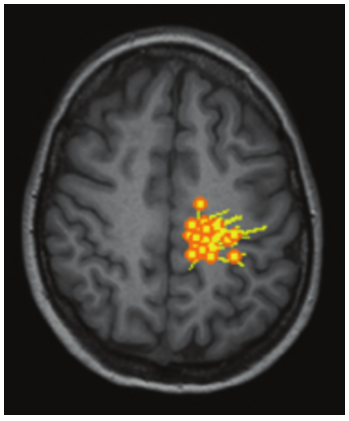


Figure 2.4: MEG Multiple Dipoles

3. Pre-Requisites

3.1 Software Prerequisites

1. 4 GB RAM minimum.
2. LINUX Operating System (Ubuntu 18.04 and above)
3. Matlab Version (R2017b and above)
4. Freesurfer Version 6

3.2 Folder Structure

The processing pipeline in the toolbox requires data to be organized in a format inspired by BIDS (Brain Imaging Data Structure). Primary motive for maintaining this folder structure is to give a organization structure to the entire processing procedure and at the same time provide an easy way to navigate amongst multiple folders and files. The PRATEEK toolbox provides a feature to generate modality combination-specific folder structure, and verify its file organization in case of manual data organization.
The unprocessed files need to be saved in the Raw folder of modality specific root folders.

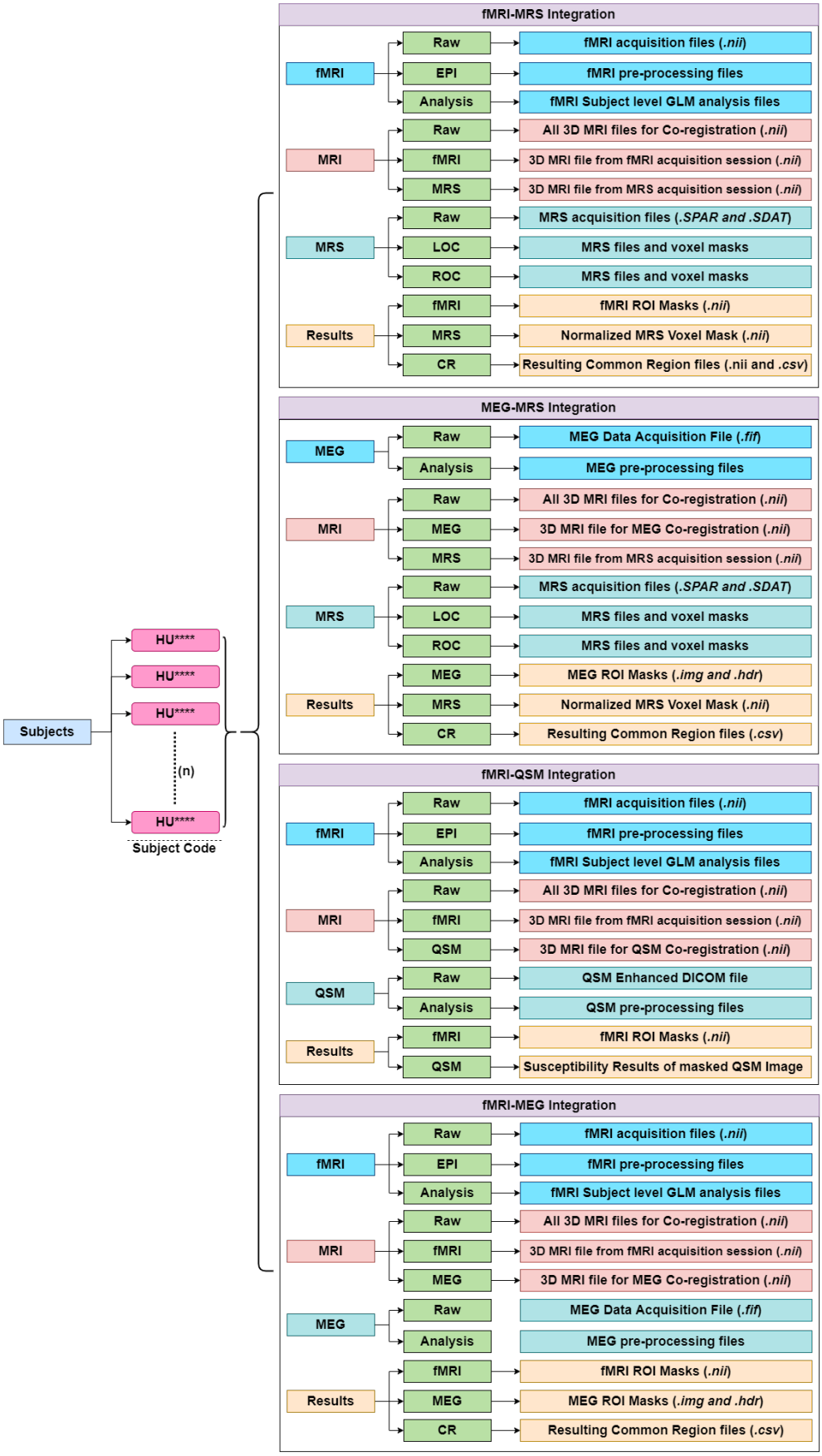


Figure 3.1: Core Folder Structure

4. Execution Scheme

The execution process for the data processing and integration pipelines implemented in the PRATEEK toolbox has been presented in Figure 4.1. The pipeline begins with the input of data files and a choice between single and multimodal data processing. It is followed by the execution of respective processing steps and visualization of the resulting common region. Data processing and integration pipeline for the fMRI-MRS combination has been shown inset. This pipeline involves pre-processing of the fMRI data followed by single level analysis and the creation of an ROI activation mass and their normalization. These masks are spatially integrated to get an isolated common region.

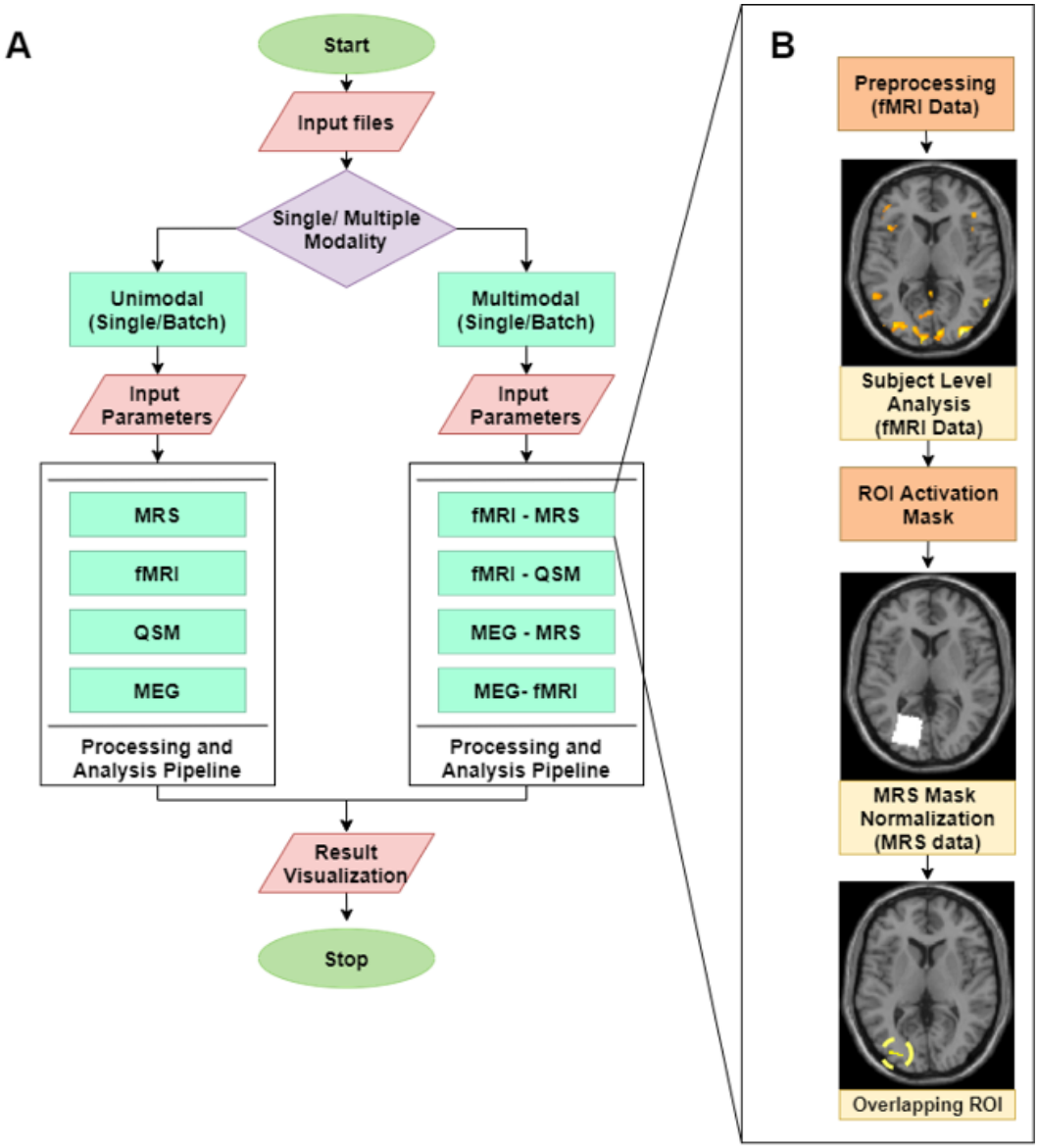


Figure 4.1: A. Execution scheme of PRATEEK toolbox. B. Processing pipeline for fMRI-MRS multimodal data

5. Steps to run PRATEEK

PRATEEK can be run as a standalone program or by manually running the scripts using MATLAB. The following sub sections demonstrate the step by step procedure for operating the interface.

1. Type main() in MATLAB command window. PRATEEK GUI main window opens as show in Figure 5.1.

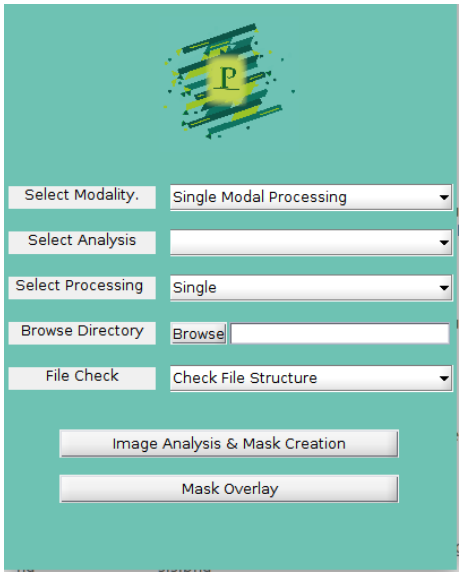


Figure 5.1: Primary Window

A description of the features or options present are provided below.

(a) Select Modality - This feature allows the user to opt for processing and analysis of single modality data or multimodal data.
(b) Select Analysis - This feature allows the user to choose the analysis module pertinent to the

previous step. The options provided to the user are as follows:

i. Single Modal Processing
   - MRS (Mask) Analysis
   - fMRI Analysis
   - MEG Analysis
   - QSM Analysis

ii. Multi Modal Processing
   - fMRI - MRS Analysis
   - MEG - MRS Analysis
   - fMRI - QSM Analysis
   - MEG - fMRI Analysis

> R It should be noted here that MRS processing here does not refer to the acual concentration mapping but only refers to the creation of the voxel mask using the coordinate system from the . SPAR and .SDAT files.

(c) Select Processsing - It allows the user to perform either single subject processing or multiple/ batch processsing.

(d) Browse Directory - The user has to select the directory that contains the subject data. The data in those folder have to be arranged in the prescribed format as aforementioned in the Section 3.2.

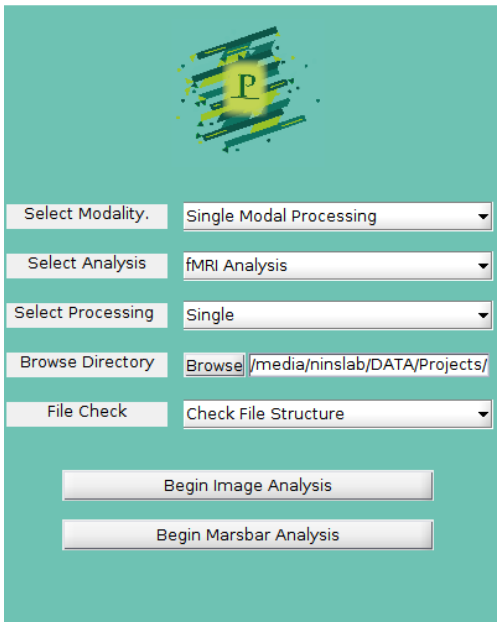
(e) File Check - This consists of two modes of operations:
   - Check file structure - It checks whether the folder structure of all the subjects present in the directory wherein the analysis and the processing has to be performed is in accordance to the prescribed norms. This reduces the manual efforts of the user in a way that the user does not have to go and check all the structure individually.
   - Generate file structure - It generates a new subject folder within an existing directory or create a completely new one.

> R It should be noted here that both the file structure options are heavily dependent on the modality and the analysis that has been selected. Special care should be taken since the folder structure for each modality is different.

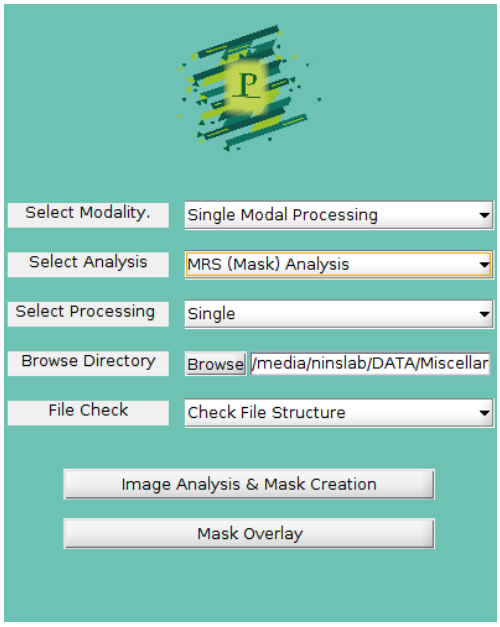
2. Initialize all paramaters.

All the parameters as mentioned for below subject to important user inputs such as modality and analysis are compulsory and have to be filled

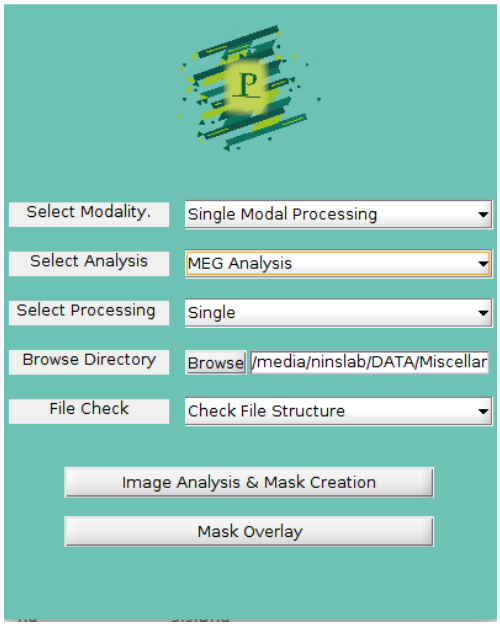
(a) Single Modality Processing
User can select between fMRI, MRS, QSM and MEG for single modal processing. Screenshots for the initialized interfaces are displayed below.



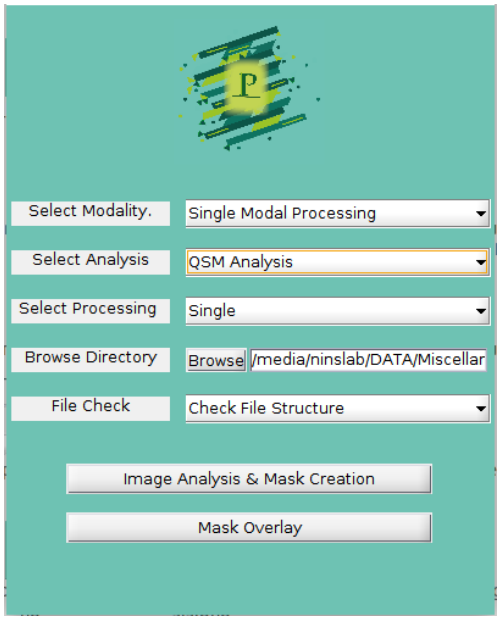
(a) fMRI initialized interface



(b) MRS initialized interface



(c) MEG initialized interface

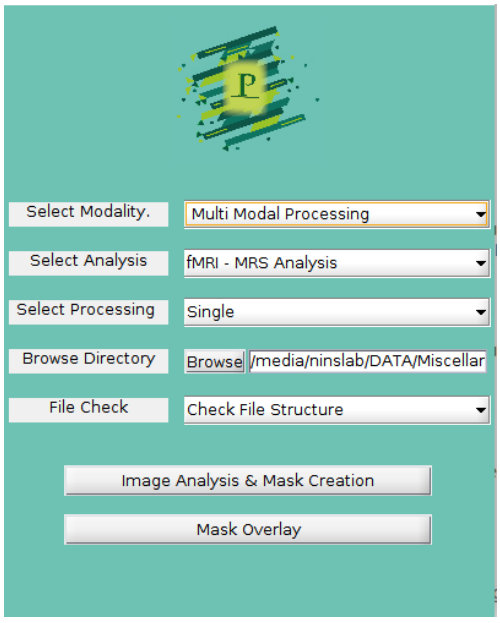


(d) QSM initialized interface

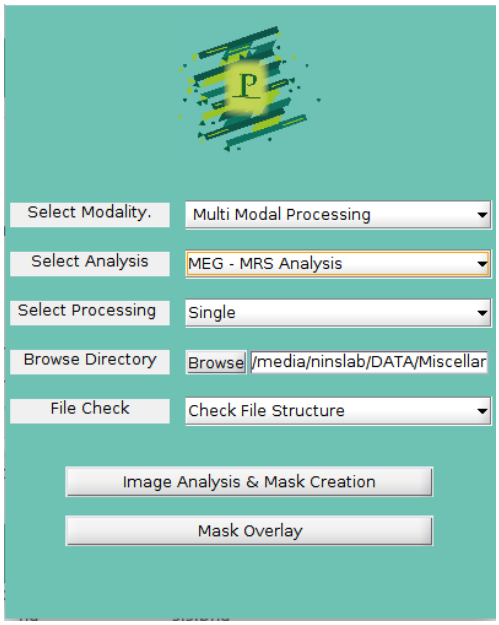
Figure 5.2: Initialized interfaces for single-modalities

(b) Multi Modality Processing

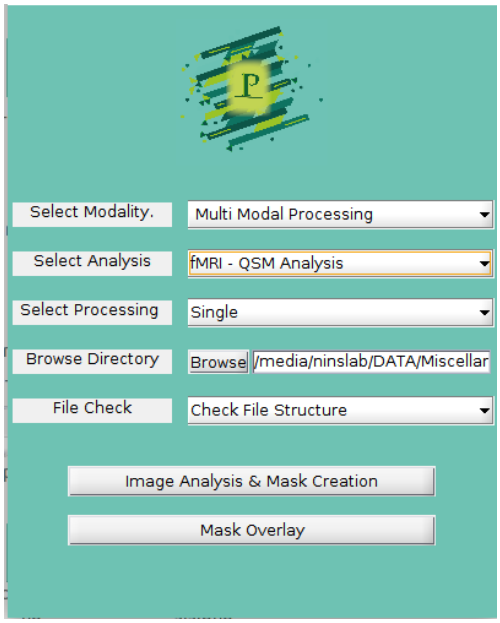
User can select between combinations of fMRI-MRS, MEG-MRS, fMRI-QSM and MEG-fMRI for multi modal processing. Screenshots for the initialized interfaces are displayed below.



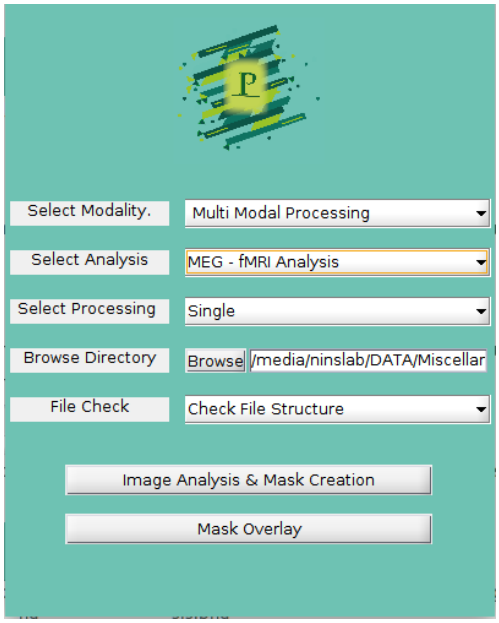
(a) fMRI-MRS initialized interface



(b) MEG-MRS initialized interface



(c) fMRI-QSM initialized interface



(d) MEG-fMRI initialized interface

Figure 5.3: Initialized interfaces for multi-modal combinations

3. File check.

This function consists of two processes that have been integrated to ensure that the folder structure required for the analysis pipeline is being followed. They have been described in detail below -

(a) Check File Structure This functions runs a check on all the subject folders consisting of data to ensure if the folder structure is correct. It will produce error or output warning messages

if the folder structure is not being followed. If the folder structure is correct, “OK” will be displayed on the console. If the structure has some file or folder missing then the results would subsequently throw an error message on the screen as shown in the below figure.

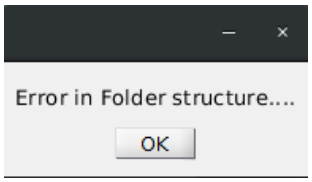
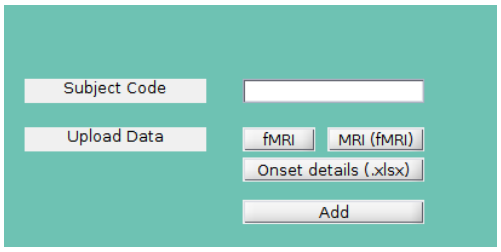


Figure 5.4: Error Window

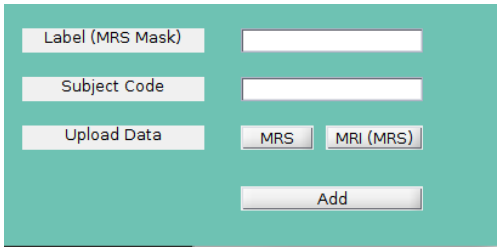
(b) Generate File Structure

This function generates a complete folder structure for the provided modality combinations. The user need not create it themselves, they can operate this functionality and just select the files required for their analysis. The structure will be generated automatically. Screenshots have been given below for both single and multi-modal analysis modules.

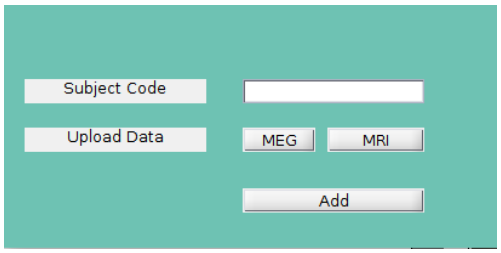
i. Single Modality Processing



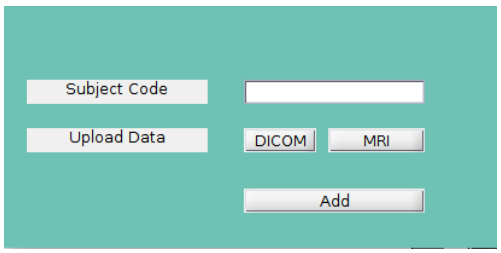
(a) fMRI Generation interface



(b) MRS Generation interface



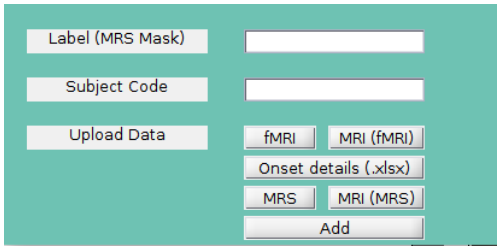
(c) MEG Generation interface



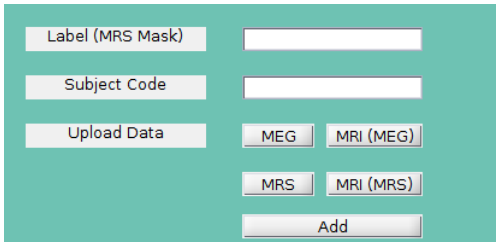
(d) QSM Generation interface

Figure 5.5: Initialized interfaces for single-modal combinations

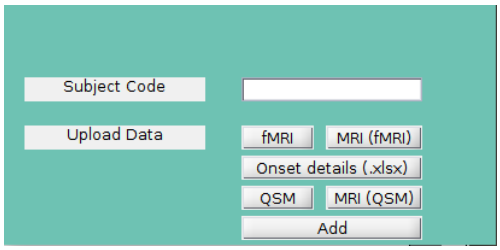
ii. Multiple Modality Processing



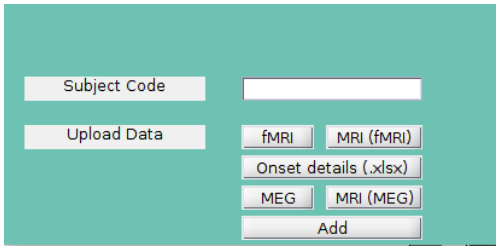
(a) fMRI-MRS Generation interface



(b) MEG-MRS Generation interface



(c) fMRI-QSM Generation interface



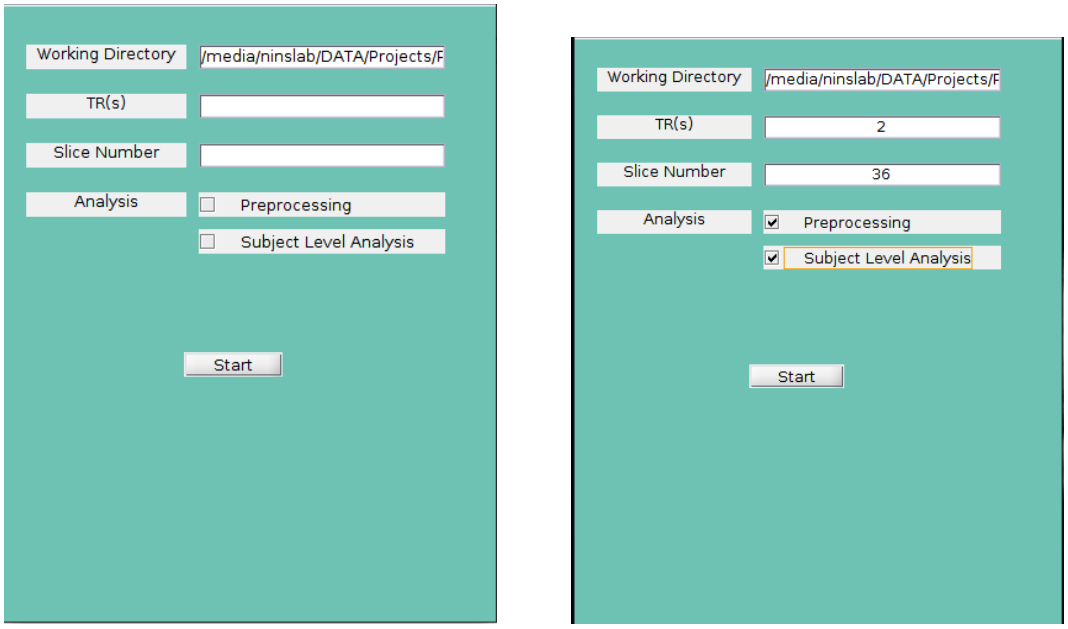
(d) MEG-fMRI Generation interface

Figure 5.6: Initialized interfaces for multi-modal combinations

4. Begin image analysis
   Clicking this button launches another interlinked interface. This interface also consists of multiple user inputs. The inputs are modality specific,hence the user has to be careful during the initializing phases.

   Please note that the image given below as sample images are purely representative in nature and paramteres can be changed according to need and as per the user's requirements.

   (a) Single Modal Processing
   fMRI Analysis- User need to input an excel sheet containing onset and duration details (in sec) of the paradigm's condition which to be examined.The user can directly paste the excel sheet in the subject folder or can input while generating the folder structure. Working Directory will be automatically filled from the Primary window. Data acquistion parameters - repection time (TR) and slice number need to be entered according to the data. User can check the Analysis according to his need.



(a) Initial Interface (b) Sample Interface

Figure 5.7: fMRI initialized interface

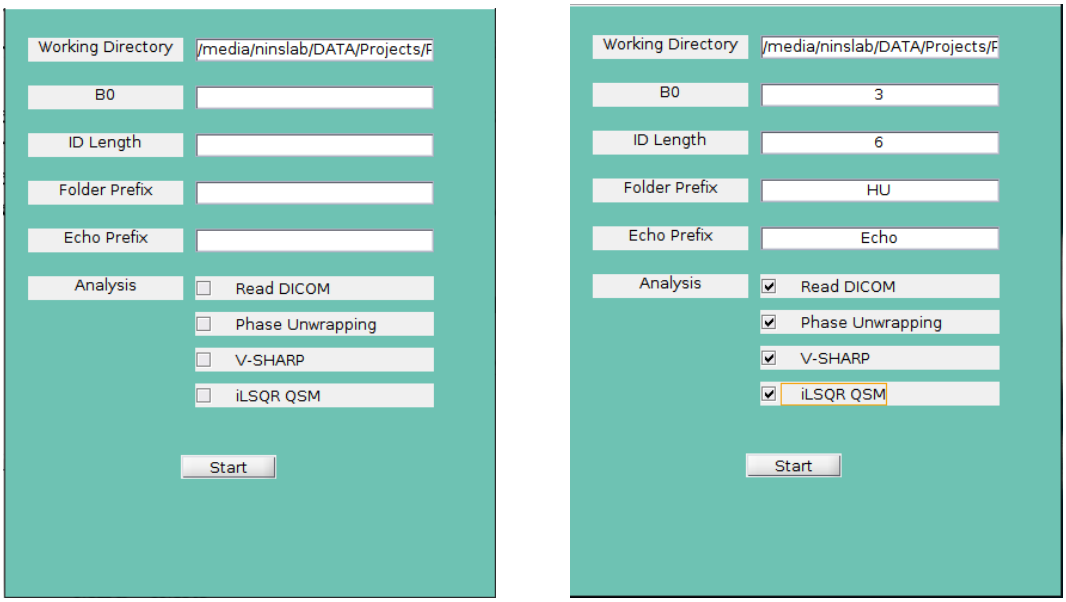
MRS Analysis- User have to input the label name indicating the region where the voxel is placed. The label should also be present in the MRS input file name. The user can select one or more options in the Analysis section according to the need.

(a) Initial Interface (b) Sample Interface

Figure 5.8: MRS initialized interface

QSM Analysis- User have to input magnetic field strength (B0) depending on the scaneer.

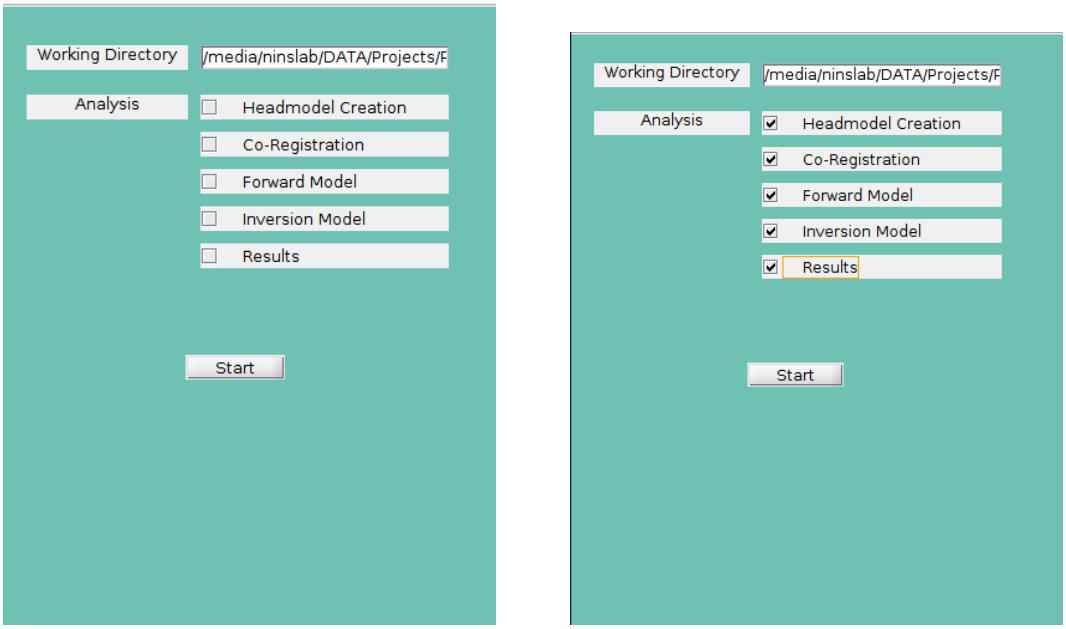
Further, user need to input ID Length, Folder prefix and Echo Prefix which depends on the folder and input filename. One or more options can be selected in Analysis section as required.



(a) Initial Interface (b) Sample Interface

Figure 5.9: QSM initialized interface

MEG Analysis- Working Directory is automatically updated from the primary window. Analysis section has options of processing steps which is to entered according to requirement.

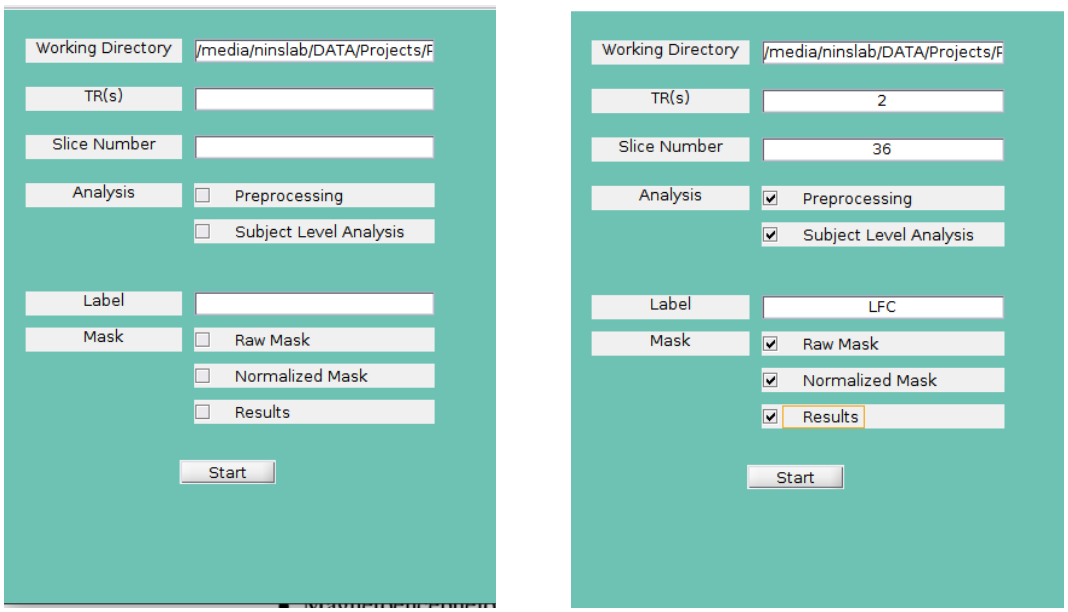


(a) Initial Interface (b) Sample Interface

Figure 5.10: MEG initialized interface

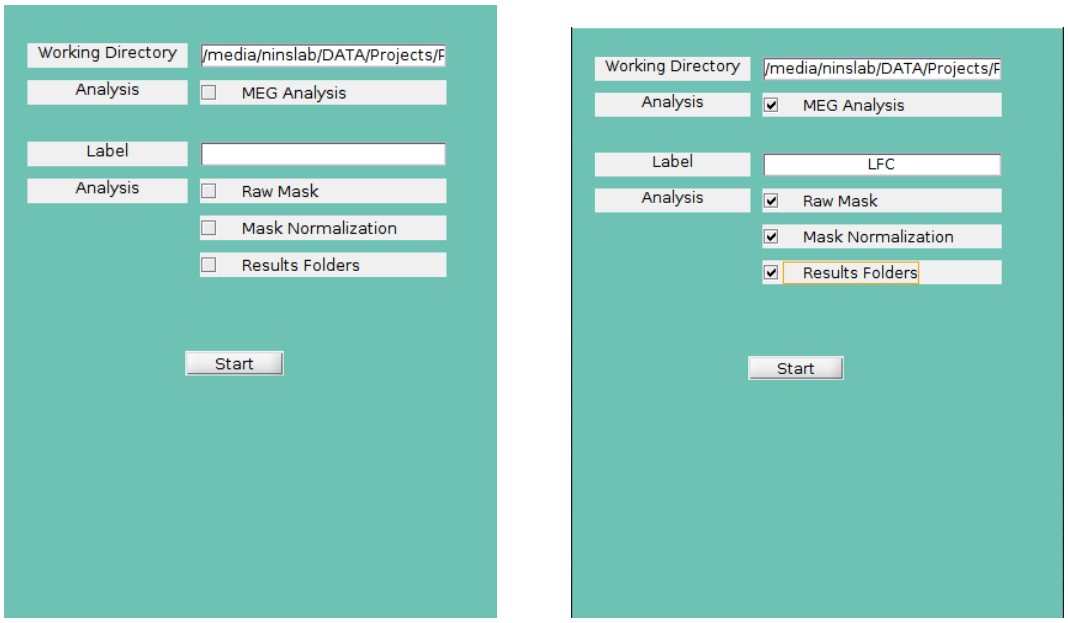
(b) Multi Modal Processing

After the selection of specific combination of neuroimaging data, corresponding interface opens up. User has to input the parameters as discussed in single modal processing. Screenshots for all the modalities combinations are displayed below.



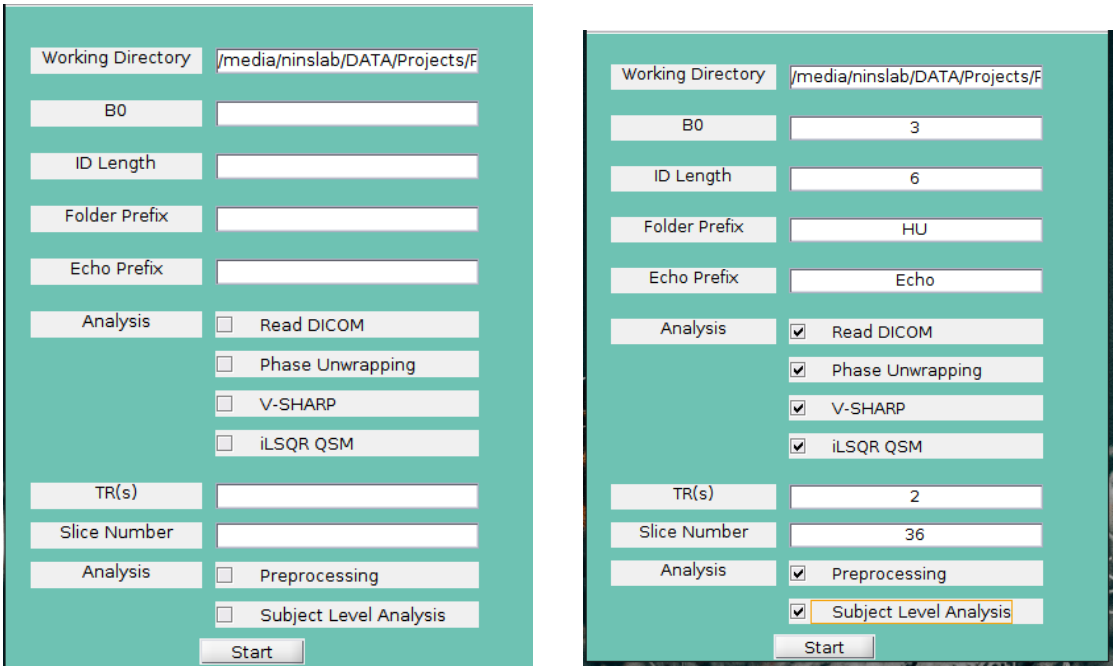
(a) Initial Interface (b) Sample Interface

Figure 5.11: fMRI-MRS initialized interface



(a) Initial Interface (b) Sample Interface

Figure 5.12: MEG-MRS initialized interface



(a) Initial Interface (b) Sample Interface

Figure 5.13: fMRI-QSM initialized interface

(a) Initial Interface (b) Sample Interface

Figure 5.14: MEG-fMRI initialized interface

5. Begin Common ROI Mask Analysis

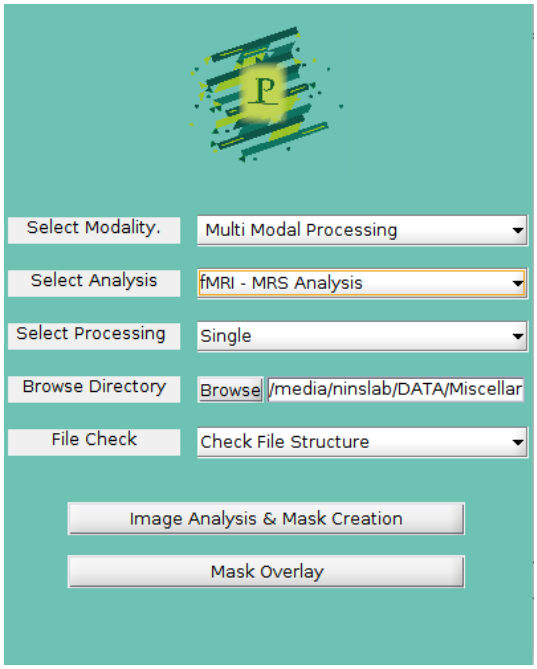


Figure 5.15: Initial GUI Interface

- Click Create and Save Mask.

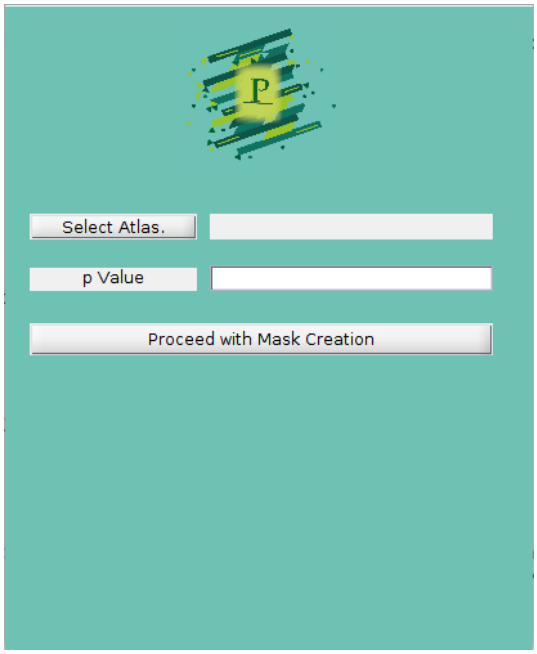


Figure 5.16: Atlas Selection

The masking module is dependent on the directory mentioned, modality and analysis selected. Since procedures implemented are different it is recommended that the user is careful in selection of the initialising parameters before execution.

- Select Neuromorhphometrics.nii from the list and click Done.

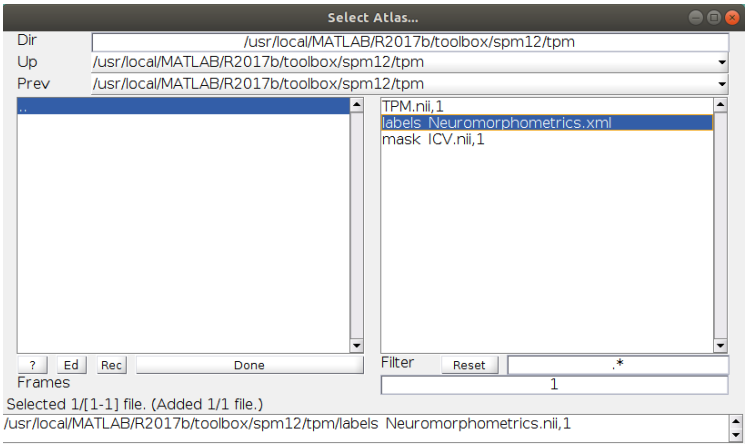


Figure 5.17: Atlas Selection: Neuromorphometrics.nii

- Select region of interet. (Single or multiple (press Ctrl and click)).

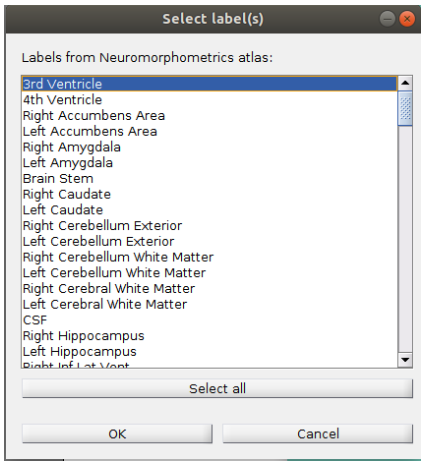


Figure 5.18: Region of interest selection

- Enter p value (Important : No default value set).

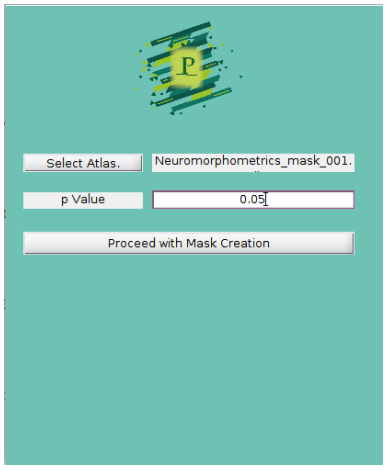


Figure 5.19: Mask generation : fully initialised

- Once initialized, click proceed with mask creation.
- Once process is completed. Go to the subjects' Result folder and observe the calculated results.

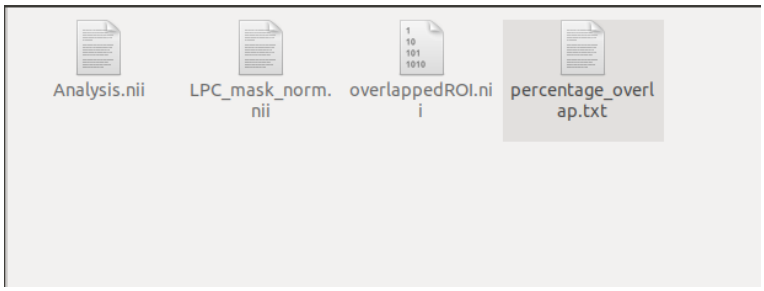


Figure 5.20: Result Folder in the main Subject Directory

Above mentioned example corresponds to fMRI-MRS subject folder. Here the following files corespond to the below mentioned labels:

(a) Analysis.nii : fMRI mask
(b) LPC_ mask_ norm.nii : LPC mask created from the MRS coordinates.
(c) overlappedROI.nii : resultant common ROI mask resulting from the above two modalities.
(d) percentage_ overlap.txt : text file that records the percentage overlap between the two modalities as given below.

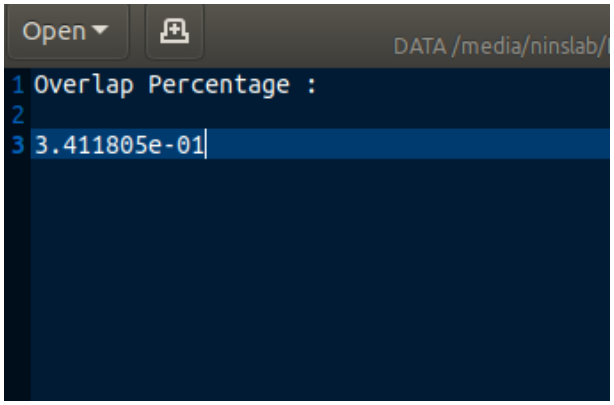


Figure 5.21: Overlap Percentage

ROI here is Left Parietal Cortex or LPC.