Final Degree Project

Biomedical Engineering Degree

"Reconstruction of EEG alpha band sources during a working memory task"

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Acknowledgments

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Abstract

Working memory denotes the temporary retention of a small amount of information in a readily accessible form for subsequent action. It facilitates planning, comprehension, reasoning, and problem-solving. Although there is still some debate, working memory has been specifically associated with the prefrontal cortex based on animal intracranial recordings. On the other hand, recent scientific evidence indicates that the alpha frequency range of the electroencephalogram (EEG) is related with working memory storage, but the anatomical sources of these signals are still unknown. The goal of this project is to determine the brain regions involved in generating stimulus-selective alpha-band EEG signals during a working memory task, using a source reconstruction approach. To this end, I compared activity currents estimated in three regions of interest (ROIs), the prefrontal cortex, the posterior parietal, and the visual cortex, during a visuospatial working memory task in 5 subjects. Structural Magnetic Resonance Imaging (MRI) was obtained for each subject and EEG was acquired during the performance of the task. I applied previously defined source reconstruction algorithms to the EEG filtered signal – in alpha waves – to data extracted during the task for each of these 5 subjects. The method used to perform the source reconstruction – to solve the inverse problem - was LORETA. To assess stimulus selectivity, I compared sources in the two brain hemispheres in two different conditions during the task, when memorized stimuli were presented either in the left or the right hemifields and considering the three ROIs of interest. We found that prefrontal cortex and posterior parietal regions showed more selectivity for the stimulus and had more activity during the delay of the working memory task than the visual cortex. This result validates my approach to estimate the anatomical sources of stimulus-selective alpha-band EEG signals in cognitive tasks.

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1. Introduction

Since the discovery of electroencephalography (1929), researchers and clinicians have attempted to localize the neuronal activity in the brain that generates the scalp potentials measured noninvasively with EEG. The poor temporal resolution of techniques like positron emission tomography, single-photon emission computed tomography, and functional magnetic resonance imaging, caused the fact that EEG was used in this field..[1]

The particular advantage that the EEG has over other imaging methods is its high temporal resolution, which allows the origin of activity to be distinguished from its propagation and information flow in large-scale brain networks to be examined.

Source reconstruction methods used EEG and MRI information to study which and where are the sources that produce these voltages in the scalp electrodes. Current source reconstruction is defined as an ill-posed inverse problem, since the number of electrodes is less than the number of current sources. [2,3] The process is divided in two phases: solving the forward problem and the inverse problem. The first one tries to define the model that generates the scalp potentials corresponding to a specific current distribution inside the brain and the inverse problem used this model to work back and estimate the brain current sources that best fit the scalp EEG measurements.[4]

There are some methods able to solve this ill-posed problem such as minimum norm estimation (MNE), weighted resolution optimization (WROP), low resolution brain electromagnetic tomography (LORETA), etc. LORETA is the one that best does the estimation and the correct localization in 3D space.[5]

Usually, the aim of source reconstruction is to relate functional human tasks to brain regions. This is done by having a sample of subjects performing a determined task while an EEG is recording their brain activity. This way, when the source reconstruction is done, the current brain source can be associated with the specific task. Since different frequency bands in EEG are related to different brain functionalities and actions, sometimes, the EEG signal is filtered to obtain a specific frequency band and compute then the source reconstruction.

In this study, LORETA is a method used to compute the source reconstruction of some subjects who performed a working memory task. Some studies reveal the relation between working memory (WM) and alpha frequency band in EEG source activity. Thus, to study that, it is proposed to obtain only the EEG activity from the alpha frequency band and compute the source reconstruction, also using the MRI information of the subject. The next step is distinguish the current brain sources (Loreta current values) with an atlas, which can define the label of each area and then analyse and compare the specific ones with interest.

This review is organized as follows: firstly, a brief explanation about the project, its methodology, its objectives, scope, etc., is presented. In the background section, there is a comprehension of some key concepts and the state of the art of the project. Then, a review of the potentials groups that have or are doing similar things is explained in market analysis. Later, the project is described explicitly, and the results are presented and discussed. Next sections – execution plan, technical and economic feasibilities, and legal aspects – consider other important parts of the project such as the planning and the legal laws. Finally, conclusions are settled.

1.1 Motivation and description of the project

The project takes place in the Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), a Biomedical Research Institute associated to Hospital Clinic, in Barcelona. Specifically in the neurosciences branch of the institute, Albert Compte leads a group focused on the area of theoretical neurobiology of cortical circuits. One of the lines of investigation of this group is "Network mechanisms of working memory in the prefrontal cortex". [6]

There, the researchers combine computational model simulations with data analysis of electrophysiological single-neuron recordings from collaborating laboratories in order to define the mechanistic basis of working memory in the prefrontal cortex.

Of specific interest for the host laboratory at IDIBAPS is the period of memory trace reactivations immediately preceding stimulus presentation. These periods of reactivation are presumably related to differences in working memory in schizophrenia patients related to controls, but a specific localization of the brain areas related to this dysfunction in neuropsychiatric disorders is still missing. [7,8]
This research project aims to identify the brain sources of these reactivation signals.

Indeed, the project – which takes part in this line to help achieving these objectives - consists of performing a source reconstruction with EEG and MRI data from a control group. They performed a working memory task for 500 trials approximately, while an EEG with 43 electrodes attached to the scalp recorded their electrical activity. During the trials of the task there are several periods of time related with a brain function. For example, if the task consists of a visual stimulus, the visual cortex of the participant would increase its electrical activity. The project, thus, tries to find which brain areas are related with the working memory. Since the researchers in this line found some evidence that the working memory could be related with the alpha frequency band of EEG, a filtering process of this data is applied in order to find these responsible areas solving the inverse problem. [9]

The source reconstruction pipeline is already done by Ana Cordon, a last year student who undertook the Final Degree Project in this line. This way, most of the source reconstruction pipeline used in this project is from her project. It contains some EEG and MRI processing data, the solution of the forward and inverse problem and finally the visualization of the source reconstruction with mne environment. Mne is the python package used in this case. It is an open-source Python package for exploring, visualizing, and analyzing human neurophysiological data like MEG, EEG, and more.

The project will have a structure like a Final Degree Project. Consequently, the following aspects are required: the project has an assigned tutor, a memory of the project has to be written and it will be exposed in front of a jury.

The conclusions that IDIBAPS will be able to take with the help of the project information and results will be important all over the neurology research to the aim of understanding brain behaviour and, specifically, memory-task related topics.

1.2 Overview of the methodology

Before starting the project, previous research of the student is needed. This research is done within bibliography on the topic and the work done in this research line of IDIBAPS. As said, last year, a student named Ana Cordón did her Final Degree Project in this line. Thus, this project follows Ana's one and needs data, techniques and methods that Ana processed and created, respectively. This way, it is important to understand Ana's project, pipeline and results.

Once having enough knowledge and considering the objectives of the project, an approximated planning is constructed with its timeline. Some decisions will be done during the assessment such as which technique use, which data take, how to obtain the results, etc. Some of them will be decided during the work, but other ones are needed before. Usually, the decision is made only by trial-error procedures, which made you lose a lot of time. Is for this reason that planning the project by a timing is helpful. Following a Work Breakdown Structure (WBS), a Gantt diagram, then, is created.

Later, when the pipeline of the project is set, the project can start. It is important to consider a lot of things before deciding which pipeline follow, which data take, etc. Some research is also done in this moment.

The application of the pipeline in the project is done by performing it within one subject. Then, it can be applied to other participants. Since this is done by programming, it can lead to a lot of errors and wasting of time.

The obtaining of the results and the discussion of them is almost the final part of the project and needs the help of the tutor and research to conclude accurately the project.

During the execution of the project, the report can be written but mostly, it will be the last part. And finally, it is presented in the middle of June in front of a tribunal.

To see the execution plan, see section 6.

1.3 Objectives

The objective of the project is to study the activity of three determined brain sources by performing a source reconstruction with EEG signal filtered in alpha. Related to this objective, here there are some subobjectives and tasks to achieve:

- To implement, test, and improve the precursor technique: an mne-python pipeline capable of visualize and analyse the neurological information using source reconstruction and localization.
- To solve the inverse problem in a specific frequency range of EEG: alpha.
- To perform source reconstruction in two different conditions – from left and right stimuli – and to compare them.
- To extract a set of brain regions from an atlas, extract the desired brain regions areas to understand their activity during a working memory task.

1.4 Limitations and restrictions of the project.

The project is limited temporary because of the structure of a Final Degree Project. In this case, 10 months is the length of it. Also, there is not much available data for the project so some process could not be done, furthermore, the statistical analysis is not very rigorous as the experimental sample was not large enough. Finally, the programmes used have their own limitations. These obstacles cause difficulties while performing the product and project.

1.5 Scope

The project consists of a system capable of solving the inverse problem using LORETA method and diversify which activity is related to each brain region. It is able to determine the differences between brain activity coming from stimulus on the right and on the left and filter the EEG data in a desired frequency band. With the help of an available brain atlas, it is possible to select the desired regions and study the activity on them. All these information can be shown in graphs. For example, using an activity – time plot it is possible to see results in a clear way.

However, the method is not capable of directly relate brain regions with brain functionalities. It is not a diagnostic technique but sure it could to be used in diagnosis fields with human help.[9]

1.6 Location of the Project.

The present study has been conducted in collaboration with the Brain Cognition and Behaviour Laboratory at the IDIBAPS research centre. All the work and some meetings have been performed remotely. However, most of the meetings were carried out with Albert Compte's group at the IDIBAPS centre.

2. Background

In this section, I provide a theoretical background to have a better understanding of concepts and ideas related to the project followed by the state of the art.

2.1 Theoretical background

2.1.1 Brain source reconstruction of scalp EEG signals.

The activity of the brain cells communicating via electrical impulses as we engage in behavioural tasks can be detected by a technique called electroencephalography. This detection is possible with electrodes attached to the scalp. Then, the EEG signal obtained shows the average electrical activity from the scalp surface area corresponding to the specific brain states that occur at a specific time of the task[10]. In a typical human adult EEG signal has a voltage range between 10 microvolts to 100 microvolts amplitude when measured in the scalp.[11]

EEG activity reflects the temporal summation of the synchronous activity of millions of cortical neurons that are spatially aligned. This activity conforms EEG normal waveforms, which can be classified into five different frequency bands. Each frequency band has been related to specific brain functionalities. [11,12]

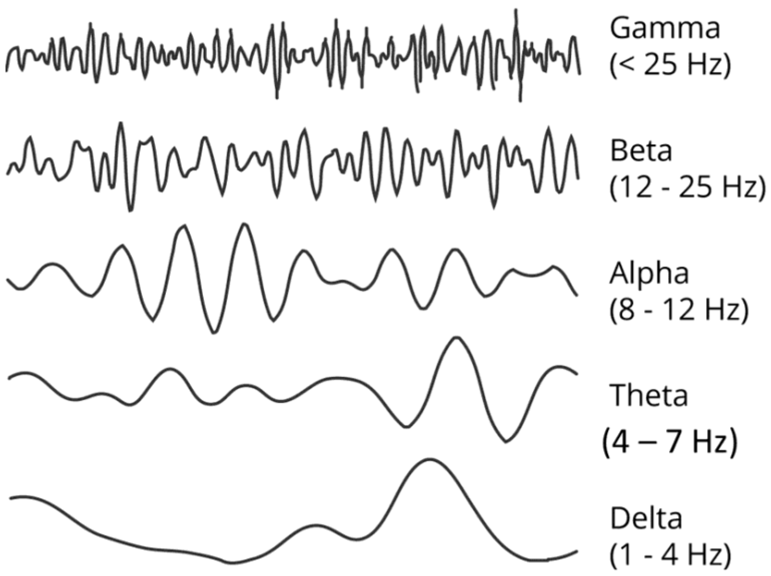

Figure 1 Decomposition of the EEG signal into different frequency bands [1].

- Delta (1-4 Hz): Slowest EEG waves, which are normally detected during the deep and unconscious sleep.
- Theta (4-7 Hz): They are observed during states of quiet focus.
- Alpha (8-12 Hz): They are the most dominant rhythms in normal subjects.
- Beta (12-25 Hz): Characteristic for the states of alertness, anxious thinking, and focused attention.
- Gamma (over 25 Hz): Observed during active information processing.

EEG is a widely used technique as it shows an excellent temporal resolution but lacks in spatial resolution. To overcome this deficiency EEG can be fused with MRI data, to provide great spatial resolution. This approach consists in using computational modelling of dipoles located at different positions inside the brain to infer the specific anatomical location of active dipoles that contribute to the measured scalp EEG signal.

MRI is a non-invasive imaging technology that produces three dimensional detailed anatomical images. It is based on powerful magnets which produce a strong magnetic field that force protons in the body to align with that field. It detects the change in the direction of the rotational axis of these protons found in the water that makes up living tissues. [13]

Using the available temporal and spatial information, the source reconstruction can be implemented. This process is typically divided into two phases: the forward and the inverse problem. The first one consists of defining the model that generates the scalp potentials corresponding to a specific current distribution inside the brain. After this, the inverse problem uses this model to work back and estimate which brain current source best fits the scalp EEG measurements. [4]

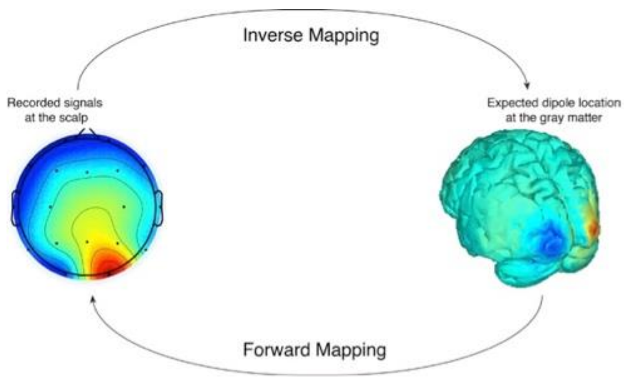

Figure 2 Schematics of source reconstruction approaches for brain source analysis[14]

When performing the source reconstruction and solving the inverse problem, it is possible to do the source localization using atlases. These describe one or more aspects of brain structure and/or function dividing it in several areas. Atlases have important applications in research and potentially in future in clinical practice, e.g., as templates for identifying brain structural or functional changes, and increasingly for use in surgical planning. [15,16]

2.1.2 Inverse solution

Solving the inverse problem is fundamental in all neurosciences branches as it gives insight about spatial and temporal activity inside the brain for different tasks given a set of measures from outside. The EEG inverse problem is an ill-posed problem; there isn't a unique solution. This can be explained by the fact that the measurements do not contain enough information about the generators. [4]
To reconstruct an approximate solution, regulation techniques and methods are needed. The usual methods are MNE and (LORETA). [17]

MNE looks for a distribution of sources with the minimum current that can give the best account of the measured data. The regularization procedure sets the balance between fitting the measured data (minimizing the residual) and minimizing the contributions of noise. [18,19]

LORETA solves the EEG inverse problem via a mathematical solution. Then, it provides an estimate of current density in the 3D brain volume, thus providing an estimate of where in the brain the scalp-recorded EEG is being generated. [20]

2.1.3 Alpha power and working memory.

EEG frequencies are very subtle indicators of cognitive processes, and different processes are reflected by different EEG frequencies within a narrow frequency window.

In this project, alpha frequency band is the focus of interest. It is known that alpha power is related to the encoding of human working memory (WM) content [21]. To obtain the band-specific frequency power for a giver period of time, a spectral analysis of the EEG is needed. [22]

WM is defined as the ability to maintain and manipulate information in memory over a short period of time. It is essential for a wide range of cognitive function such as language, learning, and general intelligence [23].

Into the WM, operational stages of encoding, retention, and retrieval are associated with neural oscillations in various frequency bands. Research studies that have been performed in this field have concluded that EEG signal in the alpha band is related with the WM. In this sense, increases in alpha oscillations have been observed during retention of information and the distribution of alpha oscillations over scalp electrodes reflects the spatial content stored in memory in the retention interval. [24]

2.2 State of the art

When source localization preliminaries, the low spatial resolution of EEG was complemented by the application of head models. They started having a spherical geometry but clearly a realistic head shape improves the accuracy of the source localization algorithms. Now, the best source localization has been done by fusing the MRI information, which provides a great spatial resolution, with the EEG one. [25,26]

There are applications of EEG source localization such as the Brain-Computer Interfaces (BCI). A BCI is a communication system which enables the brain to send messages to the external world without using traditional pathways as nerve or muscle. EEG-based BCI is a technique used to measure brain activity and by the way that different brain signals are translated into commands that control an effector. This has been applied in neurological pathologies like Epilepsy, schizophrenia, and some neurodegenerative diseases. [27,28]

Indeed, in 2020 a research line in Athens appeared to be working on assessing differences in EEG source localization during a visual working-memory tasks in three different groups of epileptic type subjects. Also, they compared three inverse solution methods: low resolution brain electromagnetic tomography (sLORETA), the weighted minimum norm estimation (wMNE) and the dynamic statistical parametric mapping (dSPM). The study showed that all the three methods yield essentially the same results. [29]

Currently, there are lots of studies are investigating abnormalities of the brain function due to epilepsy with the use of anatomical MRI, fMRI and EEG recordings.

A study in Amsterdam [30] consists of a source reconstruction in theta, alpha, beta and gamma frequency range. Despite is relation with our study, it do not analyse the sources current during a working memory task but a Simon task, which is a behavioural measure of interference/conflict resolution. [31]

Source reconstruction and some imaging techniques have been used to localize the brain areas active in working memory tasks. The first studies are found in the 1930s and they showed that the frontal lobe was important for learning and memory. The studies were done with monkeys, which have a larger frontal love in comparison to other mammals. The results imply that the prefrontal cortex may normally be involved in retaining information in working memory.

Further, human brain imaging experiments suggested that numerous brain areas in the prefrontal cortex are involved in working memory.

In one study by Courtney et al., brain activity was recorded by positron emission tomography (PET). The main results of it explained that different areas of the frontal lobe were related to different working memory tasks. For example, in visual working memory tasks, the area LIP (lateral intraparietal cortex) seemed to be engaged[32,33.]

Other researchers used fMRI to investigate brain areas responsible of working memory [34]

Reviewing information, the actual evidence says that the areas which appear to retain working memory information are fronto-parietal brain regions, including the prefrontal, cingulate, and parietal cortices. [35,36]

However, there are several studies that defend the fact that working memory responsible areas are continuously changing. Also, it is known that, as there are some regions, for each type of working memory task, different regions are activated. [37]

For this reason, specialists address future challenges to find alternative methods that can, either corroborate the ones already done or start new investigations. Another solution is, in case working with EEG data, filter it so it is easier to focus on the interests. Indeed, alpha power is positively related to WM performance; participants who had higher alpha power during WM encoding achieved better memory performance. Thus, some research has been done in this field and there is confidence that working memory areas may be carefully known following this line. [38]

2.3 State of the situation

Since source reconstruction emerged, several research groups have used it to specify and relate brain areas with specific human actions. This type of research can be done by recording EEG data from subjects performing a specific task. Then, the source reconstruction can be later applied to the data to find the active brain regions.

This process has been widely applied in working memory tasks to assess their brain related areas. These studies have concluded that fronto-parietal brain regions, including the prefrontal, cingulate, and parietal cortices are the referred ones. [35]
Expressly, in this project, subjects performed a working memory task while an EEG system recorded their brain activity with the electrodes. Moreover, MRI is done to every subject. With this data, a source reconstruction using LORETA method is applied. Then with the use of an atlas it is possible to associate each area with its correspondent activity. Hence, knowing at what specific time the working memory task is done, the responsible regions can be assessed.

In line with this view, previous work has demonstrated that oscillatory activity in the alpha band (8–12 Hz) plays a role in WM maintenance, but the exact contributions of this activity have remained unclear.

3. Market analysis

The role of source localization algorithms has been accelerated in the recent years mainly in the areas of diagnosis and treatment of various diseases. The poor temporal resolution of techniques like positron emission tomography, single-photon emission computed tomography, and functional magnetic resonance imaging, caused the fact that EEG was highlighted in this field.

Not only for that, recently there is being an important resurgence of the EEG technique: the use of machine learning makes possible the obtaining of much more information. It has been seen that the EEG has the ability of decoding very detailed aspects, such as the contents of memory. This is caused by its high temporal resolution and simultaneous registration in many electrodes. Moreover, compared to other technologies, it is much cheaper. These cause that it can be used in domestic contexts and, looking at the future, there is a possibility of telemedicine.

Because of these, EEG signal analysis techniques have a promising future for medical biomarkers that can distinguish or detect diseases.

Although there is little research focused on the source reconstruction frequency band specific (usually it is done with voltage), rhythms in EEG are the ones most often related to specific processes. This knowledge could be applied in a lot of neuroscience fields such in diagnosis. As said about EEG, working as a biomarker, source reconstruction would have a great impact in this field.

3.1 Sectors to which it is directed

EEG can provide reliable information about the neuronal activity in the brain, with the temporal dynamics of this activity in the millisecond range. Also, source reconstruction - knowing which and where are the responsible sources for each task at a specific moment - can be applied in many branches of the field. In short, the project is a method able to filter EEG data to obtain alpha power and, solving the forward and inverse problem, it allows obtaining valuable data from each area of the brain. This, just changing some parameters, it can be dedicated to the study of pathological, physiological, mental, and functional abnormalities of the brain to increase our knowledge about them, among other possible applications. [9]

For example, the ability of the pipeline to filter EEG data can be useful considering that EEG signals are usually contaminated by various noise or artifacts. Using filtering strategies, they can be removed in order to obtain and correctly understand the desired output. Moreover, it is known that each EEG frequency band has its own significance in various mental processes. Using the filtering process it is possible to keep the desired band to analyse the correspondent processes. [39]

Specifically, the product directs to the research line built in IDIBAPS by Albert Compte "Network mechanisms of working memory in the prefrontal cortex" and this project will have a very important outcome for the conclusions of the line. [40]

4. Conception design

In this section a brief explanation of the pipeline of the project will be explained, like can be seen in the next figure. The ones marked with an asterisk are the steps where there were presented more than one methodology. Here, it is discussed which would be the suitable one for each task or step. To make these decisions a lot of factors should be considered. Sometimes, it ends to be a "try and error" methodology to know which technique is better for the pipeline.

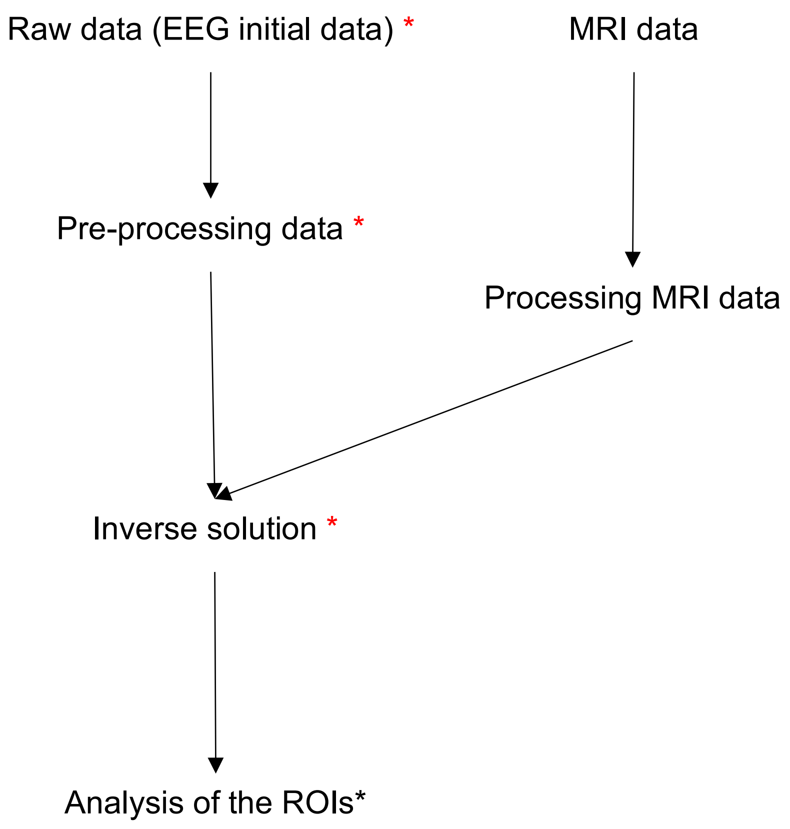

Figure 3 Workflow of the project. The asterisks highlight the steps where more than one methodology could be done.

Relating with the code language, the project comes after a previous work done with mne-python, where the inverse problem and source reconstruction were solved. Thus, the same software and environment were used in this work and following a similar pipeline.

The first decision came from choosing which initial data use. There were two possibilities bearing in mind that the project was supposed to work on alpha power. Firstly, if the initial data was EEG in voltage, the following steps will go for filtering this data to alpha frequencies and then come back to the time domain and start the source reconstruction process. On the other hand, there was a data available already converted into alpha power. This would remove the steps explained before.
However, in the EEG voltage-based data, there were much more information needed for the process and in the pre-processed one, there was just electrode information. For the project, some extra data was needed, such as where the stimulus appeared. Considering this, the initial data was the EEG voltage-based one.

About this extra data, the location of the stimulus that appear during the task was thought to be a good marker to study the selectivity of some ROIs during it. This way, the activity recorded when the stimulus appeared on the left side of the subject should be higher on the right brain, and vice versa. This took part in the pre-processing data step.

Then the filtering process was needed. The alpha frequency band is between 8 and 12 Hz. For this reason, considering a low-pass, high-pass and band-pass filter, the most suitable one was the band-pass filtering, specifically a Butterworth filter.

The following process was yet created in previous projects, the source reconstruction. As it was a validated technique, this project used the mostly the same pipeline.

However, some things were changed from this previous code: the source space generated for the source reconstruction and the method used to solve the inverse problem.

Firstly, the source space needed to achieve the objectives of the project was a mixed source space. Ana's project had a surface one. The basic difference is that it considers more brain areas than the surface source space.

About the inverse problem, Ana used the method "dSPM". On the contrary, in this pipeline Loreta was used. Loreta provides smooth and better localization for deep sources with less localization errors. Some research say that Loreta is the useful technique for source reconstruction. Specifically, the python method was the Standard Loreta (sLoreta). [41]

Finally, to assess the regions of the brain, an atlas was required. After considering many of them, the one that fits better in the objectives of the project was the Desikan-Killiany-Tourville (DKT) atlas. The reason of this choice was that the brain regions the project was focused on were more clearly separated in this atlas.

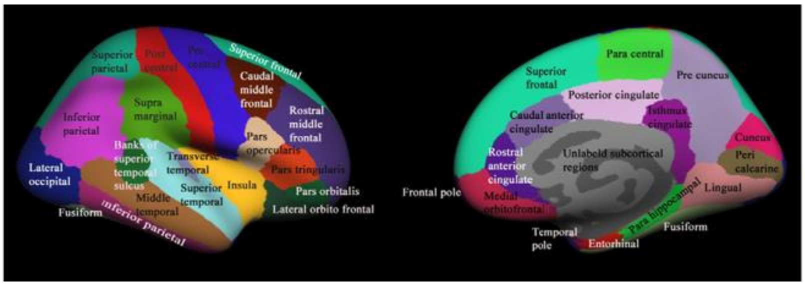

Figure 4 DKT classifier atlas [42]

5. Detailed engineering

The aim of the project is to do an EEG source localization of the brain alpha sources during a working memory task. Indeed, there are three brain areas that, in the last step, their activity and data is extracted and studied to compare them and extract great conclusions. Considering this final objective, an atlas is applied to the inverse solution output to study these brain areas.

This project is done using python language. Some python libraries are used, like numpy, matplotlib, scipy, pandas, among others, but the one that is able to perform the source reconstruction is *mne*.

If we have another look in the next figure, we can see an overview of the process did. The obtaining of the raw and initial data isn't part of the project but required for it. After the processing of this data, the forward and the inverse problem are solved to finally have the source reconstruction information. Then, the atlas can be applied to this data and extract the three ROIs.

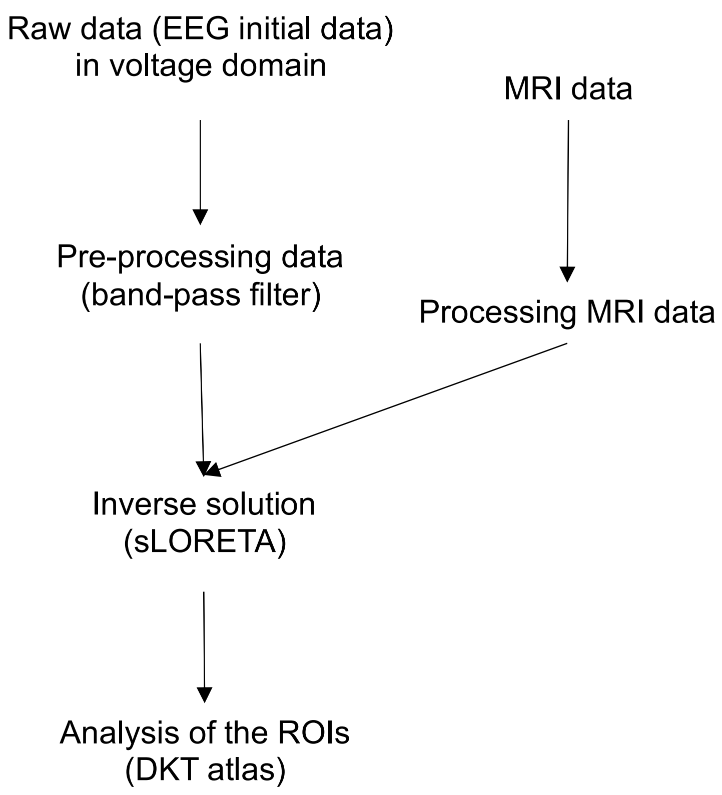

Figure 5 Final workflow of the project

All this process is done for each participant who took part in the study. Mostly, for the obtaining of the results (see section 5.3), the final information is averaged.

The following sections introduce the initial data, a pipeline presenting the steps undertaken to solve the source localization problem, and a discussion of the results obtained.

5.1 Initial data and processing

A source reconstruction process requires not only EEG but anatomical information which can came from the MRI data. Also, this EEG data, not only needs to be processed that sometimes it needs to be in the shape that the *mne* functions demand.

This section introduces the initial data that was facilitated to the developer of this project. It is described the trial description, the experimental sample, and the EEG and MRI data processing.

5.1.1 Working-memory task description

The analysis of the evolution of all the trials in the working memory tasks needs the understanding of this task.

Participants performed a visuospatial working memory task for 1 hour and a half. This amount of time makes possible the performance of many trials, approximately 500.

The description of the trial is shown in figure 6. It consists of a grey square screen which, initially, shows a black fixation point on the centre during 1.1s. Participants are asked to maintain their eye gazed fixated on this fixation point while it it black. Then, a coloured circle is added in a random position on a fixed-radius circle around the fixation point. It lasts 0.25s and then disappears. This is the stimulus of the trial. The aim then is, during the delay time (0, 1 or 3s depending on the trial type) after the stimulus, to memorize the position of the coloured circle and when it appears again on the centre, replacing the fixation point, to move it with the mouse and take it to the stimulus memorized position. This is known as response and should occur within 3 seconds for the trial to be correct. After that, the mouse needs to be dragged back to the centre and another trial starts. Each trial lasts 8 seconds approximately.

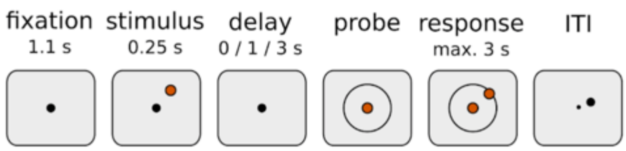

Figure 6 Description of the trial [43]

5.1.2 Experimental sample

A total of 22 subjects participates in the IDIBAPS study. All of them, recruited from the Barcelona area, are neurologically and psychiatrically healthy control participants (ctrl; age 24.9 ± 10.4 years, mean ± s.d.).

Unfortunately, since not all the subjects had the minimum amount of data to undergo the whole process of the project, they were removed from the study. Therefore the sample used in this project only had 5 subjects (n=5).

5.1.3 EEG data information

During the performance of the task scalp EEG was recorded from the participants. The EEG used 43 electrodes on the scalp to record it.

EEG data was pre-processed and stored in a *matlab* file, containing other information like the frequency sample, electrodes position labels, information of the position where the stimulus appeared and obviously, the electrical activity, among others. Each trial was divided by segments from t=-0.5s until t=1.25s and centred (t=0s) when the stimulus appeared.

The exact location of each electrode was determined with a neuronavigation apparatus and stored for each participant and session in a separate text file.

To see the *python* code implemented for the next sections, see ANNEX 12.1. For the EEG data, ANNEX 12.1.1 and 12.1.4 show how it was read and imported in *python.*

5.1.4 Processing EEG data file

To achieve the objectives of the project, the EEG data requires some processing. Since we are particularly interested in source reconstruction in the alpha band, the EEG data needs to be filtered. Also, a differentiation between two types of task trials – stimulus presented on the left or on the right visual hemifield– is done. This way, two similar datasets are obtained and these two had been filtered in alpha band.

5.1.4.1 Separation between right and left stimulus

In the section "trial info" in the *matlab* EEG file has the information about where the stimulus appeared. It was assessed with the angle in degrees with respect the horizontal positive axis. Also, this information was processed dividing the circumference of 360 degrees in 8 parts, as shown in the figure 7.

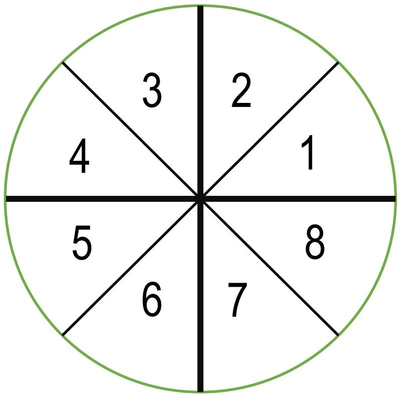

Figure 7 Graph to determine where the stimulus appeared

With this information, one can divide the EEG dataset in two, EEG with stimulus on the right of the centre and EEG with stimulus on the left. Thus, the 500 trials approximately were divided in two groups. If the stimulus appeared in the region 1, 2, 7 or 8, the trial goes with the right dataset. In contrast, if it appeared in the 3,4,5 or 6 regions, with the left one. Applying this differentiation, all the following steps of the process were done twice, one for each dataset. (See ANNEX 12.1.2)

5.1.4.2 Filtering process to obtain alpha frequency band

To obtain a specific frequency band of the EEG signal it is needed to filter it. Since the interested frequency band is between 8 and 12 Hz (alpha band) the best option was to apply a band-pass filter. Specifically, a Butterworth filter with the function *signal.butter()* from the library *scipy* was used. (see ANNEX 12.1.3)

After that, the final data was one filtered EEG signal for the trials with a right stimulus and the other one filtered EEG data for the left stimulus ones.

In the following figure we can see the filtered EEG data for one electrode with and without the filtering process.

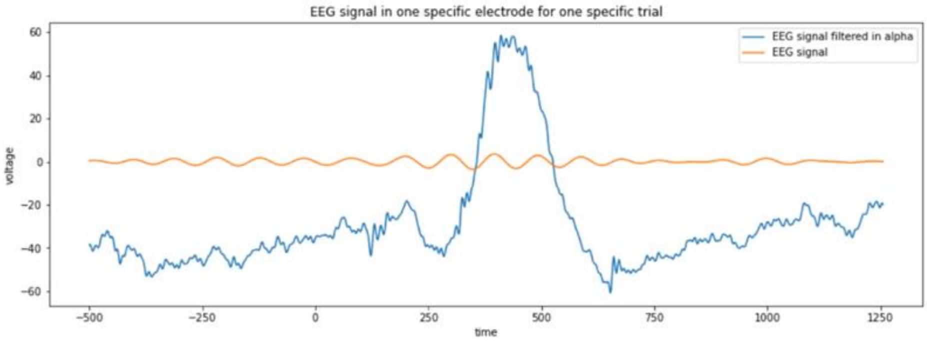

Figure 8 Plot of the EEG signal and the alpha band extracted from the signal. From Control number 7

5.1.5 MRI data

The anatomical information needed for the source reconstruction was contributed by Magnetic Resonance Imaging technique done to each participant in the Hospital Clinic. The MRI was acquired in a Prisma 3 Tesla magnet and included several MRI sequences (3D T1-weighted (T1W) image, diffusion MRI, and 1 H-MRS to detect glutamate) that, in total, last 85 minutes[44]. Here I used the 3D T1W structural image, stored in a DICOM dataset.

5.1.6 Processing MRI data

A processing of the MRI data of each subject was done with a FreeSurfer command on the terminal. FreeSurfer is an open-source neuroimaging toolkit for processing, analysing, and visualizing human brain MR images[45]. Once this was finalised, a folder named "SUB" and the number of the participant is created with some useful files to implement the following pipeline.

5.2 Source reconstruction

The pipeline implemented with python for the source reconstruction used a package named *mne*. The source reconstruction was performed with the Loreta method and the pipeline was taken from Ana Cordon's Final Degree Project who create a python code for each subject participating in the study. To finally apply the LORETA method, some data needs to be processed to be the exact input that the *mne* function which solves the inverse problem requires. In the following sections a brief explanation of these necessary inputs is done and, following, the implementation of the inverse solution.

5.2.1 EEG data required

The data structure used in the pipeline in reference to the EEG data were Raw, Epochs, Evoked objects, and information of the EEG recording. The information attributed needed for the mne functions that created the epochs and the evoked data contained the sampling frequency, the channel types and positions, the positions of the head digitation points used for coregistration, and a list of bad channels. The information provided to compute it was from the neuronavigation file from each subject, which had data related to the electrode's position, labels, etc.

The raw data was already processed and transformed into the trials format by the IDIBAPS research group so then, the epochs can be directly created with the *mne* function *EpochsArray()*. As said, the information attribute was used to compute the epochs. EEG epoching is a procedure in which specific time-windows are extracted from the continuous EEG signal. [46]

The average of these segments forms the final evoked data. As known, this procedure was done for both right and left stimulus data. These will be inputs for solving the respective inverse solution. [47] (see ANNEX 12.1.5)

Furthermore, to solve the inverse problem, covariance estimations from the recordings are required. Thus, a noise covariance is computed using the mne function *mne.compute_covariance()*. It has information about field and potential patterns. [48]

5.2.2 Forward solution

Solving the forward problem means calculating the potentials at the determined electrodes given an electrical source. This procedure is necessary to later solve the inverse problem. [1]

The function that computes the forward solution is *mne.make_forward_solution()* and has the following inputs: information, trans file, bem model and source space.

First, the information attribute provided by neuronavigation and EEG data it was already created before to compute the epochs and evoked EEG data.

Then, the function needs information about the positions of the electrodes over the scalp of the subject. This process is called co-registration and it is done within a window opened when writing "mne co-reg" on the terminal. There, the MRI coordinate system, and the real head coordinate system are aligned. The final output is a file called "trans" with a ".fif" extension. [49]

Another input the forward solution needs are the BEM surfaces and model, which describes head's geometry and conductivities of its tissues. In the case of EEG, three layers are used: the inner skull, the outer skull, and the skin. The standard electrical conductivities estimated by the MNE model are 0.3S/m for the brain and the scalp, and 0.006S/m for the skull.[50]

The BEM surfaces are the triangulations of the interfaces between different tissues needed for forward computation. This can be done through the computer terminal with the following command specifying the subject mne *watershed_bem SUB00*. For this function FreeSurfer is also required. [51,52]

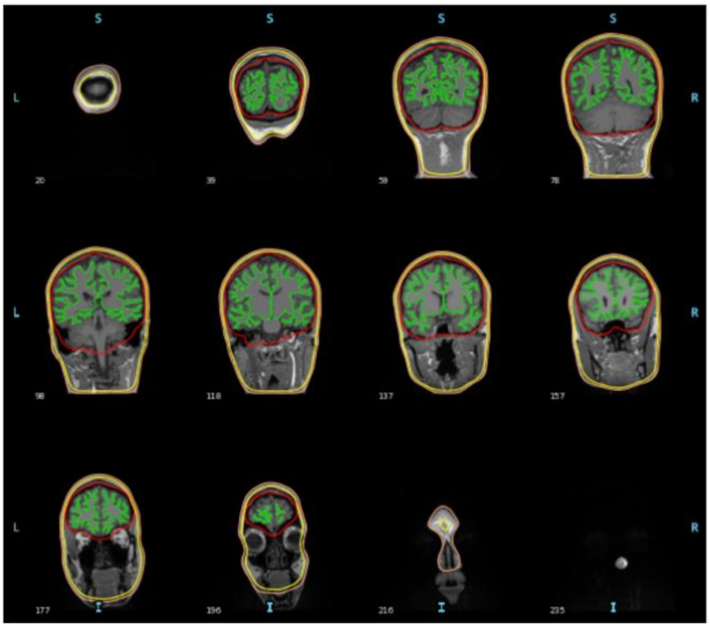

Figure 9 Surfaces segmented by FreeSurfer. From Control 7

The last input required is the source space. There are three types of source space: the surface, the volume, and the mixed source space. Since the idea is to apply an atlas and separate some brain regions to observe its own activity, a source mixed model is computed. The source space has the information about the location of the dipolar sources[53].

To compute the mixed source space, first, a surface source space is done using the following function *mne.setup_source_spac*e. One parameter of this function is the spacing, which it is recommended to be an octahedron with six subdivisions. To the surface source space it is added a volume source space computed and, this way, the mixed source space is generated. The final output of the mixed space contains 9 spaces and 9632 vertices. Each vertex is a dipole position from the scalp.

The related code can be seen in the ANNEX 12.1.6.

Finally, computed and created the inputs required, the forward problem can be solved.

5.2.3 Inverse solution

Once computed the forward operator, the evoked data and the noise covariance, an inverse operator can be generated using the following function: *mne.make_inverse_operator*. Since there are two datasets, the right and the left stimulus, this is done twice. Also, there is only one forward operator, as it is independent of the EEG data.

This way, two inverse operators are computed. These will be inputs for the next action, the solution of the inverse problem. In ANNEX 12.1.7 we can see how the inverse problem was solved.

5.2.3.1 Solving the inverse problem with Loreta method

Mne function *mne.minimum_norm.apply_inverse()* estimates the active sources on the mixed source space by receiving information from the inverse operator (evoked info, forward operator, and noise covariance matrix) and the evoked data by using the desired method. The usual methods are: dSPM, MNE, sLORETA, and eLORETA.

Since some research determines Loreta as the best suitable method to compute the source reconstruction in 3D space, in this pipeline, the chosen method was "sLoreta". The standard Loreta (sLoreta) is the advanced version of Loreta. [4]

This technique is based upon computation of current distribution throughout full brain volume. The standardized Loreta assumes the standardization of the current density which implies that not only the variance of the noise in the EEG measurements is considered but also the biological variance. [54]

5.3 Results

The separation procedure between trials was done to obtain two different datasets. The first one was for the trials that had the stimulus on the left visual hemifield and the second one, on the right visual hemifield. The aim of the project was to implement a source reconstruction pipeline to determine the sources of alpha-band EEG signals during a cognitive task. To this end, we set to validate our method by determining the brain regions that contain stimulus-selective activity during a working memory task. In this task, it is known that occipital sources contain stimulus selective signals mostly during the stimulus presentation, while prefrontal sources have instead dominant stimulus-selective signals in the mnemonic delay period. Parietal sources are both selective to stimuli during stimulus presentation and during the delay. We validated our methods in several ways: we first study stimulus-selectivity in the two hemispheres before this separation of regions. The idea is to ensure that the data obtained in the inverse solution is related with the memory task trials. When confirmed that, one can start applying the atlas in the data to study the regions of interest (ROIs).

5.3.1 Contra and ipsilateral influence in visual stimulus

Scientific evidence supports the idea that visual stimuli produce neural activation in cortical sources located in the opposite hemisphere from the visual hemifield where the stimulus is presented. This way, contralateral (opposite site to the stimulus location) hemisphere activity is higher than ipsilateral (same site). This is because visual information is processed first in the contralateral visual cortex, then gradually it crosses the vertical meridian as receptive fields become larger in higher order areas and information is processed also in ipsilateral cortical areas. In figure 10 we can see how visual information projects from the retina to the primary visual cortex, so that visual information on the right visual hemifield, in red colour, is processed on the left cortical hemisphere. Similar, the left visual information in colour blue, goes to the right hemisphere.

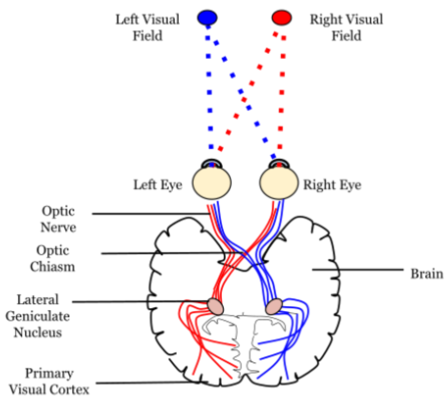

Figure 10 The processing visual stimulus information inside the brain.[55]

In this project, we use this evidence to validate our alpha source reconstruction; for each dataset from each subject, activity of each hemisphere is summed up. This way, for right stimulus dataset we have activity on the whole right hemisphere (ipsilateral) and on the left one (contralateral) during the trial length and same path for the left stimulus dataset. A mean between the two contralateral is done and between the two ipsilateral from both datasets. Finally, for each subject, a data frame is obtained with the contra and ipsilateral activity during the trials.

A smoothing processing is also done to the final data from each subject based on a moving average window by convolution. [56] (See ANNEX 12.2)

When averaging the subjects' datasets, the next plot is obtained, where it is possible to see the differences between contra and ipsilateral MNE current (see Fig 11). Like in all the following plots, the error bar shown indicates that standard error of the mean, which was computed with the standard deviation of the sample divided by the square root of the sample size (n=5).

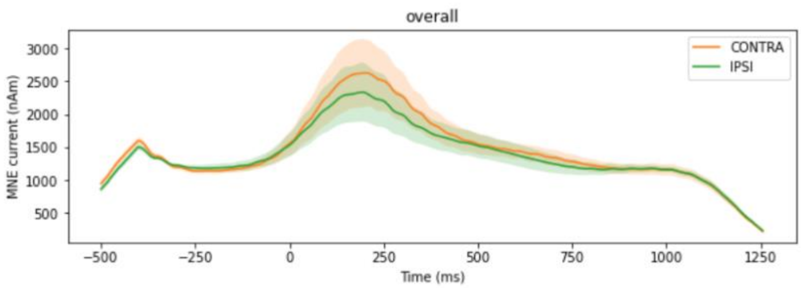

Figure 11 Plot of the contra and ipsilateral average above participants.

In order to assess significant differences between source activations in contralateral and ipsilateral trials, the difference of source currents in contra and ipsilateral trials is computed for each participant. Then, the mean and standard error of the mean of these differences is plotted in figure 12. The asterisks mark where the difference is significant for a 95% confidence level. Figures below have the x axis limited between [0,1250] milliseconds since in this case we want to study the evolution from when the stimulus appears.

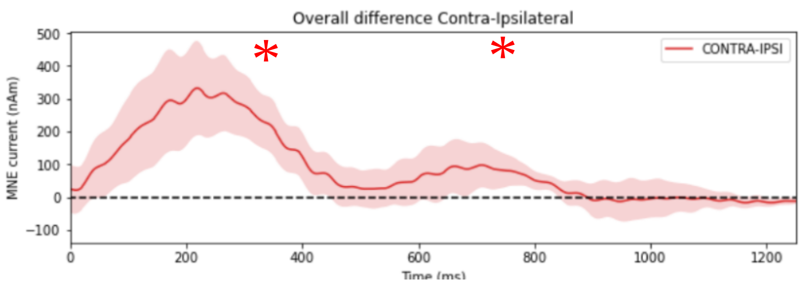

Figure 12. Difference between contra and ipsilateral source activity averaged across all the participants. The shadow indicates one standard error of the mean. * $p<0.05$

In figure 13 we have the difference between contra and ipsilateral MNE current for all the participants who took part in the project. In IDIBAPS data, they are named with a number in order to identify them. We studied control 7, 10, 15, 16 and 23.

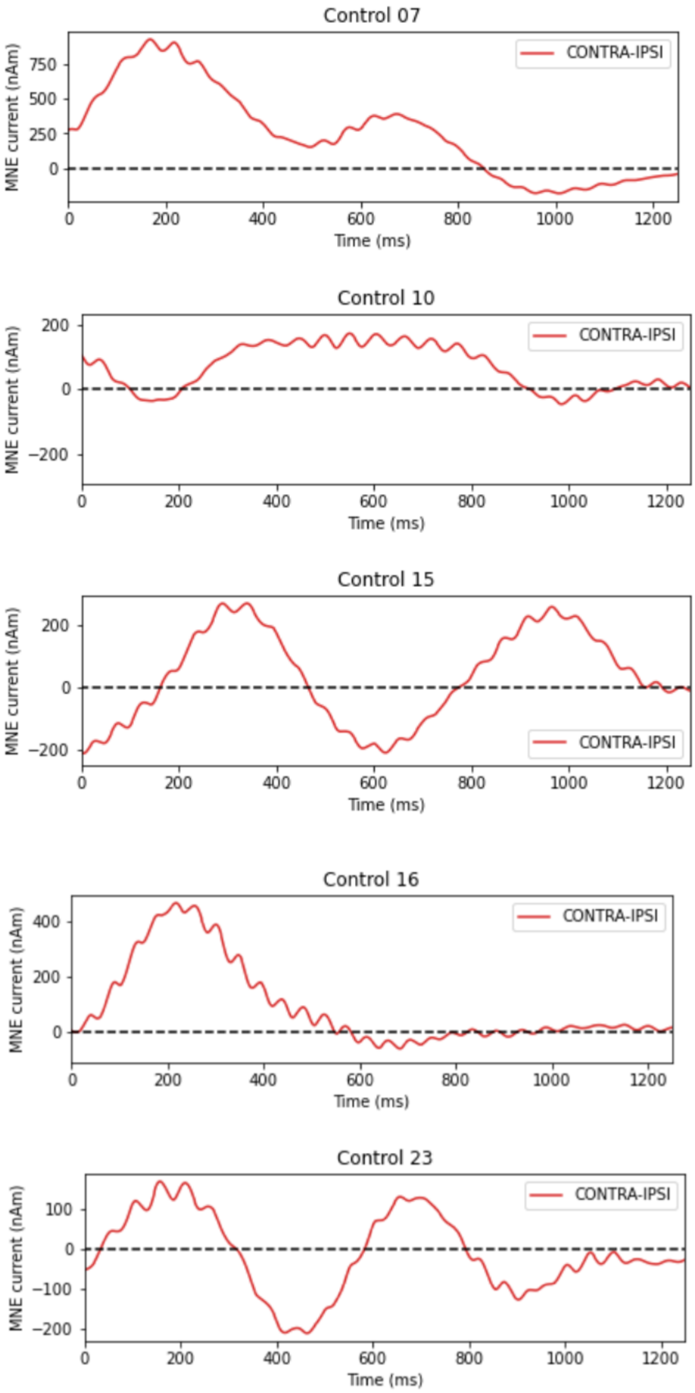

Figure 13 Contra minus ipsilateral current for each subject.

These results show that the contralateral MNE current is higher than the ipsilateral MNE current. When computing the mean (fig. 12), the curve is always above 0; the MNE current is higher in the contrary side where the stimulus appears. As expected, these differences are significant early in the trial, at the time of stimulus presentation. This is consistent with the known lateralization of visual sensory information in the cortex and validates our alpha source reconstruction approach.

5.3.2 Study of different ROIs related with the working memory task

I then turned to validate further the proposed approach by testing the anatomical origin of alpha signals corresponding to sensory processing and to memory storage. Regarding the objectives of the project, there are three brain regions of interest (ROIs): the prefrontal cortex and the parietal cortex - research supports that prefrontal cortex is an area where working memory is processed - and the visual cortex, related with the visual stimulus.

I used DKT classifier atlas database which consists of 40 T1-weighted images from healthy adult subjects with 62 cortical surface labels (31 regions per hemisphere).[57]

Although DKT atlas has different labelling, it is possible to relate them by similarity of the zones. In this case, the ROIs are (see fig. 14):

- "Caudal middle frontal" in DKT for the prefrontal cortex.
- "Superior parietal" in DKT for the posterior parietal.
- "Lateral occipital" in DKT for the visual cortex.

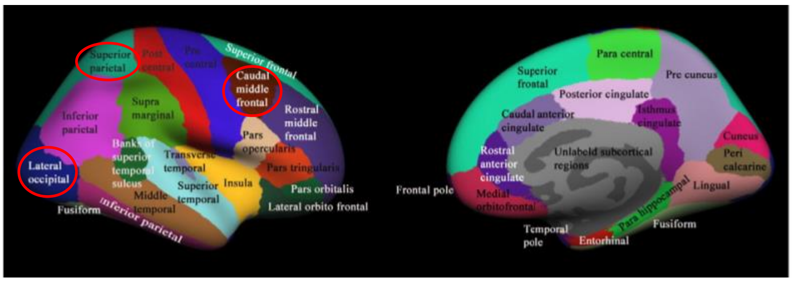

Figure 14 DKT atlas used and the three areas of interest circled [42]

The atlas was applied to each subject and these three labels were extracted. Since in the atlas there is one label region for each hemisphere, following the results in the previous section, we extracted these ROIs from the two hemispheres separately to be able to consider contralateral and ipsilateral conditions.

Firstly, for each subject, we have two datasets. In one, there is data obtained from the right stimulus dataset, the contralateral and ipsilateral activity of the three ROIs. The other one contains analogous information for the trials that had a stimulus on the left hemifield. These two datasets are averaged to obtain just one data frame for each subject, containing average contralateral and ipsilateral source currents in each of the three ROIs. I first sought to obtain the time course of alpha source currents in each ROI, averaging together the ipsilateral and contralateral conditions for each participant and then taking mean and standard errors across participants (see fig. 15). The figure shows stronger stimulus-related current increases in lateral occipital and superior parietal regions, consistent with their more prominent role in visual processing, compared to caudal middle frontal cortex. The time course of the average currents, instead, did not show a clear dynamic specific of the memory period.

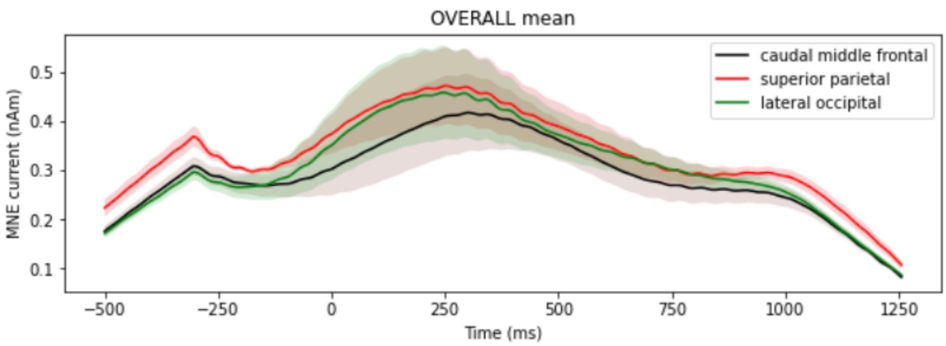

Figure 15 MNE current in the ROIs during the trial.

Then, I quantified the stimulus-selectivity of sources located in each of the ROIs by computing the difference between contra and ipsilateral average currents for each ROI. First, I take the difference of currents for each participant and then I compute the average and standard error of the mean across participants to finally obtain the following plot.

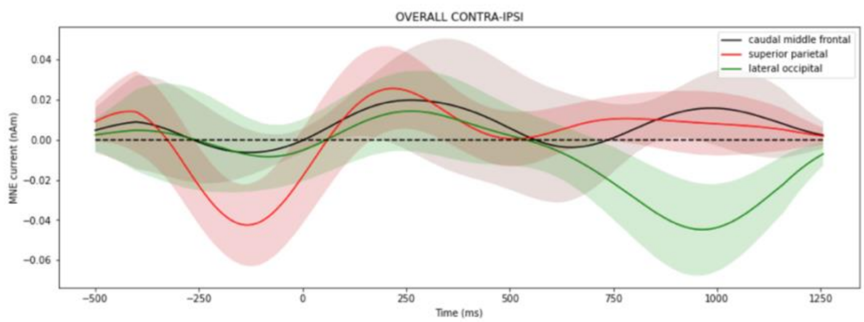

Figure 16 Difference between contra and ipsilateral MNE current for each ROI during the trial performance

Fig 16 shows that selectivity to the location of the stimulus is apparent in all areas upon stimulus presentation but remains positive (meaning stronger currents for contralateral than ipsilateral stimuli) during the delay period only for superior parietal and caudal middle frontal cortices. This is the expected result based on existing literature.

I specifically tested differences in selectivity between ROIs by computing differences of this selectivity measures across ROIs pairs. I compared selectivity in lateral occipital to selectivity in caudal middle frontal and to selectivity in superior parietal cortex, with a focus on the delay period.

This way, in the first plot in figure 17, the difference between selective activity in the lateral occipital area and in the parietal superior cortex across the subjects is shown. Similarly, in the plot below, I plot the difference between the lateral occipital and the caudal middle frontal cortex.

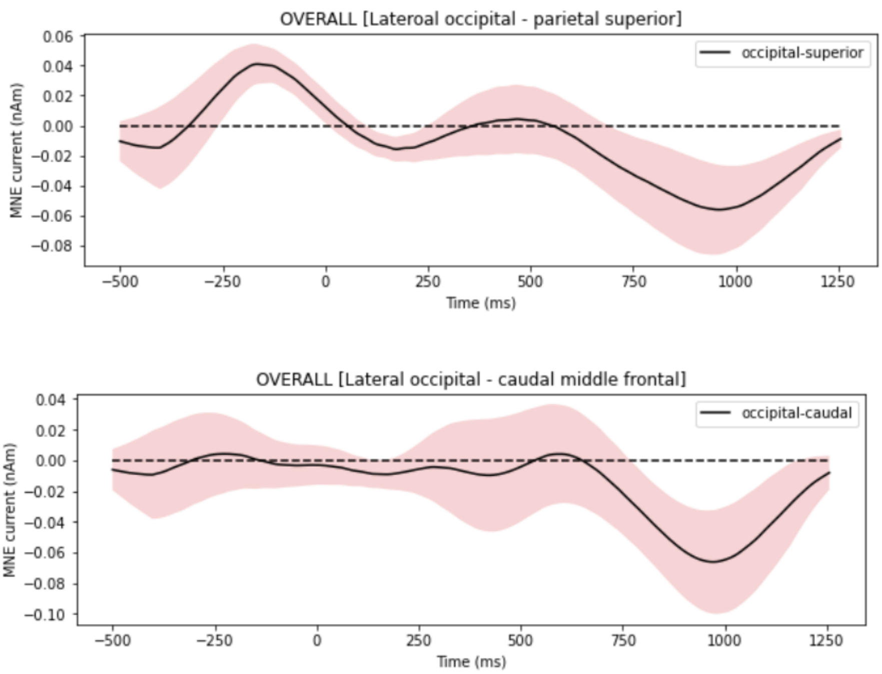

Figure 17 From previous data, the difference between mne current of Lateral Occipital and (above) parietal superior and (below) caudal middle frontal

The results in Fig 17 show that stimulus selectivity is similar for all ROIs during the stimulus period. This is not what we had expected. We anticipated larger selectivity of source currents in response to the stimulus in the visual cortex (i.e. lateral occipital ROI) and weaker signals in the other cortices, especially prefrontal areas. We did not observe this and we think that this could be related to the larger area that is included in the lateral occipital ROI, so that involved sources are largely smeared by averaging with other non-selective sources. During the memory period, however, the results in Fig. 17 are in line with our expectations: selectivity is larger in superior parietal and in caudal middle frontal cortices than in lateral occipital cortex. This is apparent in both comparisons in Fig. 17, although statistically they do not reach significance, possibly because of limitations in the sample size.

5.4 Discussion

We have created a python pipeline capable of performing an EEG in alpha frequency range source reconstruction and extract DKT atlas areas to analyse its current during a task.

The results that presented in the first part of the project validate the technique, since there is a demonstration that the contralateral activity is more related with the stimulus than the ipsilateral. However, during the trial, only two periods of time show a 95% of significance evidence. Conclusions in some studies defend that the contralateral activity is, at least with visual stimulus, higher than the ipsilateral. [30]

Research on this field defend that, in this type of task, the lateral occipital dominates the stimulus period, but then the other areas – caudal middle frontal and superior parietal – get importance and control the delay period. The reason why this happens is that these areas are related with the working memory. In this task, the delay period is, as said, between the stimulus information and the motor answer of the subject, so it is the type to memorize the stimulus. Also, these latter areas usually show more selectivity with the stimulus, thus, the contrary side hemisphere process more information.

In our results, the lateral occipital area is not the most active during the stimulus, as it was expected. This might happen because this area is big, and it could have some important sources and other ones with less activity. Then, averaging the sources could not be significant as the strong sources become irrelevant.

Also, it is important to say that the study has a small sample (n=5) and averaging and determining standard errors only across 5 subjects is not enough to define conclusions. This is probably why we did not find strong statistical evidence to validate my pipeline, but the consistent trends observed in the direction of the expected effects supports the idea that the pipeline that I propose in this TFG is effectively identifying the electrical sources of alpha-range oscillations inside the brain on the basis of scalp EEG recordings.

Despite there is research that defend all the previous theory, there is not a standardized pipeline available to compute source reconstructions of EEG signals in a specific frequency range. However, there are some research groups which referred to the field. Some of them used LORETA to obtain a 3D brain map with the correspondent sources to achieve their particular objectives. In fact, some of them did the source reconstruction of different EEG frequency bands using Fast Fourier Transform (FFT). They sometimes solve the inverse problem using mathematical calculations which, in our case, were already contained in *mne* functions. The atlas applied for the source reconstruction are also different from our, Talairach [Talairach and Tournoux, 1988] is the most used one. [58–60]

Thanks to these studies, the project used one technique or other one by this research. Methods are studied and the most suitable one implemented. Finally, the overall pipeline contains a source reconstruction using LORETA method of EEG filtered in alpha signal and posterior analysis of the ROIs during a working memory task.

6. Execution plan.

The planning of the project was done by deciding which were the tasks that would take part into it, sorting them and finally set a determined time and deadlines for each task.

6.1 WBS diagram.

In table 1 we can see the project's tasks and the classification of them depending on the course of the project and the precedents of each task.

A WBS is a visual, hierarchical and deliverable-oriented deconstruction of a project. It breaks down the main project objective into smaller and manageable parts, being helpful for project development. [61]

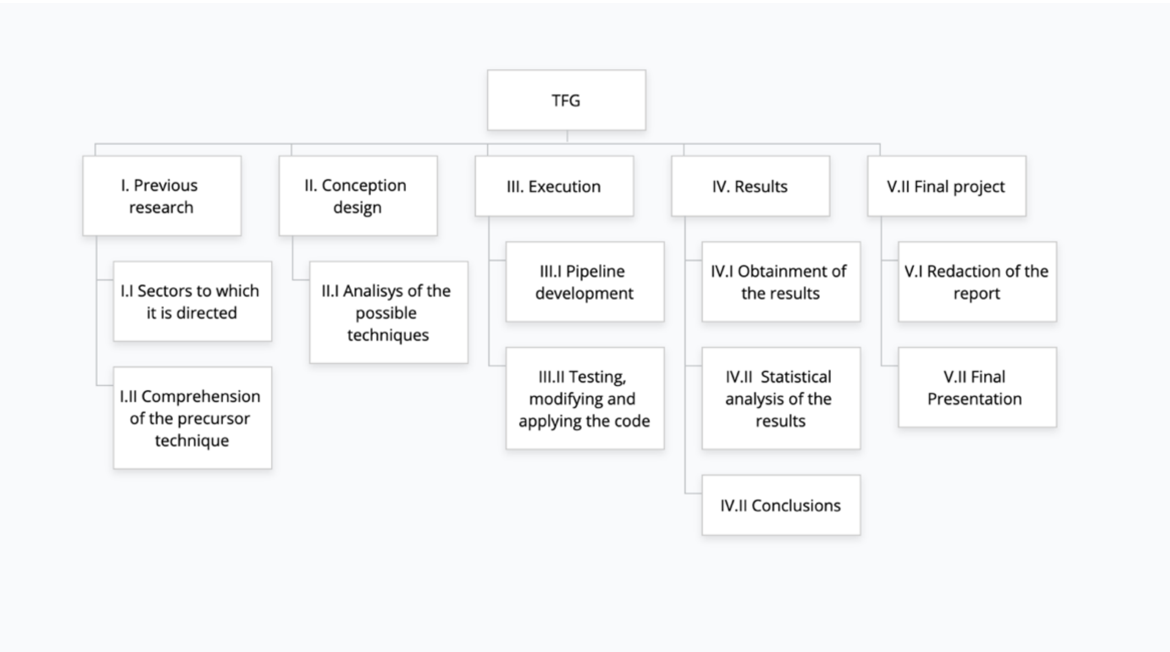

Table 1 WBS diagram

6.2 GANTT diagram.

The Gantt diagram (see table 2) shows the project schedule t from September of 2021 to June of 2022. The total amount of weeks working on the project is 34.

Phase	Task	Weeks
I	**I.I Study and comprehension of the concepts**	3
	I.II Comprehension of the precursor technique	2
II	**II.I Analysys of the possible techniques**	2
III	**III.I Pipeline development**	4
	III.II Testing, modifying and applying the code	2
IV	**IV.I Obtainment of the results**	2
	IV.II Statistical analysis of the results	
	IV.II Conclusions	
V	**V.I Redaction of the report**	
	V.II Preparation of presentation	
	V.III Final presentation	

Phase	Task	Weeks
I	**I.I Study and comprehension of the concepts**	
	I.II Comprehension of the precursor technique	
II	**II.I Analysys of the possible techniques**	
III	**III.I Pipeline development**	
	III.II Testing, modifying and applying the code	4
IV	**IV.I Obtainment of the results**	4
	IV.II Statistical analysis of the results	3
	IV.II Conclusions	1
V	**V.I Redaction of the report**	5
	V.II Preparation of presentation	2
	V.III Final presentation	-
	Total Weeks	**34**

Table 2 Gantt Diagram divided in September 2021-January 2022 and February 2022-June 2022

7. Technical feasibility.

The technical feasibility is presented in a SWOT table 3. A SWOT analysis organizes the strengths, weaknesses, opportunities, and threats of the project.

Strengths	Opportunities
○ The algorithm and the program are from a free software, so its access is easy. ○ Possibility of obtaining more sample as the project is done in IDIBAPS.	○ The algorithm has a huge branch of applications in neuroscience ○ Neuroimaging is important and useful in diagnosis ○ The project takes part in IDIBAPS, a recognised centre of investigation.
Weaknesses	**Threats**
○ Time limitation (10 months) ○ Data-set limitation ○ The EEG signal contains noise ○ The filtering process is not that accurate (order of 2) ○ It is not useful for diagnose	○ Competitors with more dataset, techniques, personal…. ○ The difficulty of obtaining a unique solution.

Table 3 Project's SWOT diagram

8. Economic feasibility

When doing a project, it is important to consider its economic part. This factor will be a determined one as it has to be financed by, in this case, IDIBAPS. Thus, to assess if the project is feasible, a cost has to be computed.

There are several tasks, people or hours inverted in the project that needed to be contemplated in order to approximate this total budget. Firstly, the obtaining of the initial data consisted of a MRI and an EEG to every subject participating. In table 4 it is possible to see the money and the time that these techniques costed.

Technique	€/unit	hour/unit
MRI	248,67 €	1
EEG	100 €	0,5

Table 4 Time and money cost of MRI and EEG techniques

Considering the sample consists of 5 subjects, the table 5 shows the costs above multiplied by all the subjects participating in the study.

subjects	Total cost EEG	Total cost MRI	Sum of the costs
5	500 €	1243,35€	1743,35 €

Table 5 Total cost of the MRI and EEG considering n=5.

In the next table, the hour salary of people who take part in the project is exposed. The technicians had the role of the data acquisition, so they had to be there when the MRI and EEG were performed. Their salary is between 16.000 and 22000 €/year. As the Hospital Clinic is public, we approximated the annual salary to 18000€/year. Considering working 40h par week, this ends to be a hour salary between 8-13€ [62,63]. The cost of the student which can be estimated by considering the annual salary of a junior engineer, and the cost of the tutor, which can be estimated by considering the salary of a senior engineer, are 10-12€/hour and 15€/hour, respectively. [64,65]

Technicians	10€/hour
Tutor	15€/hour
Student	11€/hour

Table 6 Hour salary of the three working collectives in the project

Hence, approximating the hours that they have been involved in the project, the total cost of each can be estimated in tables 7,8 and 9.

weeks	34		
hours/day	3		
Working days/week	5	cost/hour	total cost
total hours	510	11 €	5.610€

Table 7 Total cost of the working hours of the student

technique	total hours	salary of technicians	total cost
MRI	5	10 €	50 €
EEG	2,5	10 €	25 €
			75 €

Table 8 Total cost of the working hours of the technicians

total hours inverted	30
salary/hour	15€
total cost	450€

Table 9 Total cost of the working hours of tutor

Summing these costs up, we obtain the following total cost for the working hours: 6.130€.

Thus, the total cost is computed. Also, in that calculation, the tool that has been used to perform the project, a MacBook Air 2020, had to be summed[66]. The total costs add to 8.229€ as table 10 shows.

MacBook Air	1129€
Workers' salaries	6134€
Techniques costs	1743,35€
FINAL COST	8338€

Table 10 Project's final cost

9. Regulations and legal aspects

The project development considered some legal aspects to ensure the safety and a properly investigation. Since the project needed to extract some data and information of the participants, data and digital rights are protected under the European Parliament and the Council EU regulation UE 2016/679 (April 27, 2016) which regards the protection of natural persons in terms of the processing of personal data and the free circulation of data. The legal basis that justifies the processing of the participants data is the consent you give in this act, in accordance with the provisions of article 9 of EU Regulation 2016/679.

Moreover, the data collected for these studies was collected identified only by a code, so no information was included that allows the participants to be identified. Only the research doctors and his collaborators with specific permission were able to relate the data with the medical record.[67]

Related to the confidentiality and security of the sample, in accordance with Spanish and European Community regulations, the samples are stored in a safe place with restricted access, guaranteeing the right to privacy, in the IDIBAPS-Hospital Clínic of Barcelona Lab.

The participants signed all these regulations. Also, they were able decide not to participate in the study or abandon it at any time by telling the doctor, without any prejudice.

The researchers who took part in the project also had regulations. The law 14/2011 (1st of June) presents some key points for the rights and duties of the researches in any scientific investigation. This regulation recognized the rights of the researches by acknowledging their authorship in all the scientific projects that the researcher has taken part in. [67,68]

Finally, related to performing and writing the project, there was the "rules and regulations for the Final Degree Project of the Biomedical Engineering Degree in the University of Barcelona". This was followed during the execution of it. [69]

10. Conclusions and future lines

Reconstructing the generators or sources of EEG signals is an important problem in basic neuroscience as well as clinical research and practice. [70]

Moreover, performing this source reconstruction in a specific frequency range have the potential to be applied in a lot of fields. Each frequency band determines distinct actions and their responsible brain areas, with the source reconstruction, can be localized. This is not only important for control groups, as did in this study, but for neurological diseases, in which it can be applied to either compare between different groups or diagnose. This pipeline has the ability to analyse brain regions activity during tasks, which can be a tool for previous diagnose and biomarkers.

The findings in the study showed that it is possible to perform a filtered EEG source reconstruction using *mne-python*. The results of this pipeline showed that the most lateralize areas of the three of interest were the prefrontal cortex and the posterior parietal. This is highlighted during the delay period, as expected. Specifically in this timeframe, selectivity is larger in superior parietal and in caudal middle frontal cortices than in lateral occipital cortex. However, when the stimulus period, all ROIs show similar selectivity.

Since not enough evidence was found in the results, more data is required to draw better and softer conclusions of the study. With a more extended sample, more analysis would also be possible and techniques would be validated more accurately.

In future lines of the IDIBAPS research group, they aim to apply the technique among different groups, specifically, schizophrenic and encephalitis, to find differences in alpha sources related with the working memory. Also, the distinction between left and right stimulus in the trial is needed for another line where they want to study if there is brain activity in the delay of the current stimulus related to the previous stimulus.

11. References

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12. Annexes

12.1 Source reconstruction code

12.1.1 Reading initial data

```
import numpy as np
import matplotlib.pyplot as plt
import scipy.io as sio
import pandas as pd
import scipy

import mne
from mne.minimum_norm import make_inverse_operator, apply_inverse

# ### Read EEG data - trials
subject = "SUB10"
subjects_dir = "/Users/annaferrerraventos/Desktop/TFG"
subjects_dir
# EEG
mat_am = sio.loadmat("/Users/annaferrerraventos/Desktop/TFG/DATA_C10/EEG/261020180920_single_am_longepoch.mat")
mat_pm = sio.loadmat("/Users/annaferrerraventos/Desktop/TFG/DATA_C10/EEG/251020181707_single_pm_longepoch.mat")

matriu=mat_am
samprate=matriu["fsample"][0,0] #512

trials_num=matriu["trialinfo"][:,1]

bin_current=matriu["trialinfo"][:,11]

trials_am=[]
for element in matriu["trial"][0]:
    trial2 = []
    for trial in element:
        #print(trial)
        electrode_before=[]
        for index, electrode in enumerate(trial):
            electrode_before.append(electrode)
        trial2.append(electrode_before)
    trials_am.append(trial2)

trials_data=np.array(trials_am)

#trial time limit
tmin=-0.5
tmin
tmax=1.25
pretime=-3
posttime=5

pre=int((abs(pretime)+tmin)*512)-2
post=round((abs(pretime)+tmax)*512)+2

trials_dades=trials_data[:,:,pre:post]
```

12.1.2 Separation between right and left stimulus

```
#left visual hemifield data
counter=0
data_left=np.array([])
for i in range (len(bin_current)):
    binn=matriu["trialinfo"][:,11][i]
    if binn==6 or binn==4 or binn==5 or binn==3:
        data_left=np.append(data_left,trials_dades[i])
        counter=counter+1
    else:
        continue
data_left=np.reshape(data_left,(counter,len(trials_dades[0]),len(trials_dades[0][0])))


#left visual hemifield data
data_right=np.array([])
counter1=0

for i in range (len(bin_current)):
    binn=matriu["trialinfo"][:,11][i]
    if binn==1 or binn==2 or binn==7 or binn==8:
        data_right=np.append(data_right,trials_dades[i])
        counter1=counter1+1
data_right=np.reshape(data_right,(counter1,len(trials_dades[0]),len(trials_dades[0][0])))
```

12.1.3 Filtering process

```
import scipy.signal
Wn=np.array([8,12]) #
N=2
b,a=scipy.signal.butter(N, Wn, btype='bandpass', analog=False, output='ba',fs=512)

filt_left=scipy.signal.filtfilt(b, a, data_left,axis=-1)
plt.plot(filt_left[0,0,:])

plt.show()
plt.plot(data_left[0,4,:]), plt.plot(filt_left[0,4,:])

filt_right=scipy.signal.filtfilt(b, a, data_right,axis=-1)
plt.plot(data_right[0,4,:]), plt.plot(filt_right[0,4,:])

plt.show()
```

12.1.4 Reading neuronavigation data

```
neuronav4 = pd.read_csv('/Users/annaferrerraventos/Desktop/TFG/DATA_C10/EEG/C1004_WCOORD.txt',
                         skiprows=6, sep="\t")
x4 = neuronav4.iloc[0:43,3]
y4= neuronav4.iloc[0:43,4]
z4 = neuronav4.iloc[0:43,5]

electrode_position=[]
for index,element in enumerate (x4):
    electrode_position.append([float(element),float(y4[index]),float(z4[index])])
electrode_position=np.asarray(electrode_position)

r4 = neuronav4.iloc[46,2:5]
l4 = neuronav4.iloc[47,2:5]
n4 = neuronav4.iloc[48,2:5]

R4 = []
N4= []
L4 = []


for index, element in enumerate(r4):


    R4.append(float(r4[index]))
    N4.append(float(n4[index]))
    L4.append(float(l4[index]))


anatom4=[R4,N4,L4]

labels=neuronav4.iloc[0:43,0]
labels=labels.tolist()
d = dict() #dictionary keys are labels of channel and arg are position
for index, element in enumerate(electrode_position):
    d[labels[index]]=element
sampling_freq=512

## Creating MNE-Python data structures from scratch
# Create some dummy metadata
ch_types = ['eeg'] * 43
info = mne.create_info(labels,ch_types=ch_types, sfreq=sampling_freq)

# defining anatomical landmarks
naison = np.array([N4[0]/1000,N4[1]/1000,N4[2]/1000])
lpa = np.array([L4[0]/1000,L4[1]/1000,L4[2]/1000])
rpa = np.array([R4[0]/1000,R4[1]/1000,R4[2]/1000])
montage = mne.channels.make_dig_montage(d,naison,lpa,rpa)
info.set_montage(montage)
montage.save("/Users/annaferrerraventos/Desktop/TFG/DATA_C10/EEG/montage_C10.fif")
```

12.1.5 Forward solution

```
src = mne.setup_source_space(subject, spacing='oct6', add_dist='patch',
                             subjects_dir=subjects_dir)

import os.path as op
surface = op.join(subjects_dir, subject, 'bem', 'inner_skull.surf')
vol_src = mne.setup_volume_source_space(subject, volume_label=labels_vol,subjects_dir=subjects_dir,
                                        surface=surface,)
# Generate the mixed source space
src += vol_src
print(f"The source space contains {len(src)} spaces and "
      f"{sum(s['nuse'] for s in src)} vertices")


mne.viz.plot_bem(subject=subject, subjects_dir=subjects_dir,
                 brain_surfaces='white', src=vol_src, orientation='coronal')


conductivity = (0.3, 0.006, 0.3)  # for three layers
model = mne.make_bem_model(subject=subject, ico=4,
                           conductivity=conductivity,
                           subjects_dir=subjects_dir)
bem = mne.make_bem_solution(model)

trans = "/Users/annaferrerraventos/Desktop/TFG/C10-trans.fif"
trans

fwd = mne.make_forward_solution(info, trans=trans, src=src, bem=bem,
                                meg=False, eeg=True, mindist=5.0, n_jobs=1,
                                verbose=True)
```

12.1.6 Creating evoked data

```
#creating epochs
simulated_epochs_left= mne.EpochsArray(filt_left, info, tmin=tmin)
simulated_epochs_right= mne.EpochsArray(filt_right, info, tmin=tmin)

simulated_epochs_left.set_eeg_reference("average",projection=True)
noise_cov_left = mne.compute_covariance(
    simulated_epochs_left, method=['shrunk', 'empirical'], rank=None, verbose=True)
simulated_epochs_right.set_eeg_reference("average",projection=True)
noise_cov_right = mne.compute_covariance(
    simulated_epochs_right, method=['shrunk', 'empirical'], rank=None, verbose=True)

fig_cov_left, fig_spectra_left = mne.viz.plot_cov(noise_cov_left, simulated_epochs_left.info)
fig_cov_right, fig_spectra_right = mne.viz.plot_cov(noise_cov_right, simulated_epochs_right.info)

# CREATING EVOKED DATA
evoked_left = simulated_epochs_left.average()
evoked_left.plot(time_unit='s')
evoked_left.plot_white(noise_cov_left, time_unit='s')

evoked_right = simulated_epochs_right.average()
evoked_right.plot(time_unit='s')
evoked_right.plot_white(noise_cov_right, time_unit='s')
```

12.1.7 Inverse solution

```
inverse_operator_left = make_inverse_operator(
    evoked_left.info, fwd, noise_cov_left, loose=1, depth=0.8)

inverse_operator_right = make_inverse_operator(
    evoked_right.info, fwd, noise_cov_right, loose=1, depth=0.8)


snr = 7.
lambda2 = 1. / snr ** 2
method = "sLORETA"

stc3_left, residual_left = apply_inverse(evoked_left, inverse_operator_left, lambda2,
                              method=method, pick_ori=None,
                              return_residual=True, verbose=True)


stc3_right, residual_right = apply_inverse(evoked_right, inverse_operator_right, lambda2,
                              method=method, pick_ori=None,
                              return_residual=True, verbose=True)
```

12.2 Smooth code

```
def smooth(y, box_pts):
    box = np.ones(box_pts)/box_pts
    y_smooth = np.convolve(y, box, mode='same')
    return y_smooth
```