Software tool using different methods for analysis and comparing fMRI signals in Biomedical and Medicine studies

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Abstract *— Within the bunch of analysis which can be done using neuroimaging derived from fMRI, brain connectivity is one of the most outstanding one. These studies can be split in functional connectivity or statistical relations between regions of the brain and effective connectivity, which looks for causal dependencies. "DeustoTech Brain Connectivity Methods" consist of a MATLAB based toolbox which provides a whole framework for exploring a set of mathematical methods imported from other fields for being applied in brain connectivity. This software integrates functions and atlas regions for extracting BOLD signals from fMRI images and band-pass filtering options for removing artifacts. The methods for connectivity analysis this toolbox works with, are basically divided into two groups: phase synchronization and effective connectivity methods. Along with the visualization options it offers, this toolbox is a great starting point for those who want to learn more about the newest applications of signal processing in neuroscience.*

Index Terms — BOLD signals, fMRI, Granger causality, signal processing, phase synchronization.

INTRODUCTION

The use of technology is a vital element for the education on 21st century students regardless their field of study. Hence, this article presents a formative proposal for students both of engineering and medicine, using a tool which is ad hoc designed for educational purpose.

The software described in this paper, offers a straight forward way of learning more about brain connectivity issues as it is associated with signals obtained from fMRI studies.

Many recently published studies are including anatomical connectivity measures obtained by Diffusion Tensor Imaging (DTI), as well as functional connectivity and effective connectivity measures either working on block designs, event-related or resting-state paradigms.

It is well known that the brain uses large-scale mechanisms and distributed organization not only in resting-state performance, but also when solving complex cognitive tasks. The aim of applying this kind of analysis to our data is to achieve a better understanding on how the brain networks are built [1]. The software tool introduced in this article, gives the essential structure for learning how to carry out functional and effective connectivity studies in fMRI, with a different approach for each of those.

Computer science and engineering are providing solutions to the problem of going throw these complex calculations. Indeed, the fact of working with BOLD (Blood Oxygen Level Dependent) signals as time-series, gives the chance for dealing with this fMRI data as signals. Those signals will describe the behavior of the subject inside the scanner and other methods derived from more signal-focused technics can be imported to this research area.

Even though brain connectivity is one of the biggest challenge neuroscience has to face, it is believed that some mathematical methods provide interesting information about how the coupling of brain regions occurs. Some phase synchronization and effective connectivity methods, have been considered to help the typical correlation based connectivity analysis.

In this article, we briefly introduce, a toolbox created for the study of algorithms for processing of BOLD time-series. It is also focused on teaching how sophisticated methods can be accessible for students with little background of digital signal processing and even less knowledge of neuroimaging.

METHODS

The bunch of methods which have been integrated, have been widely used with other biological signals as EEG, but also in extremely distinct scopes as econometrics.

The implemented algorithms can be split into two groups: the first one would deal with phase synchronization methods for functional connectivity and the second one with Granger causality and its variations for effective connectivity.

Phase Synchronization for Functional Connectivity

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Phase synchronization approach is believed to explain some relations between long distance separated brain regions that other methods could not explain properly. The phase synchronization methods integrated on the toolbox had been borrowed from EEG technics and implemented in fMRI environment, using MATLAB. These are:

- Mean Phase Coherence [2].
- Phase Lag Index [3].
- Imaginary part of Coherence [4].

This kind of approaches have been ignored for many years in fMRI as the time resolution of this technology was not appropriate for using such phase-oriented philosophy.

This fact is rapidly changing as scanner´s performance is getting better and more acquisition speed can be reached. The advances, are reducing needed TR (repetition time) on the acquisitions, and this leads to new possibilities.

Granger Causality for Effective Connectivity

According to the effective connectivity, our general strategy is based on Granger causality [5]. Hence, this method has been integrated together with some modifications of it, oriented to the frequency spectra:

- Bivariate Granger causality Index [6].
- Multivariate Granger causality Index.
- Partial Directed Coherence [7].
- Directed Transfer Function [8].

As Granger causality is a method based on signal prediction or modeling, it needs a first step of solving a Multivariate Autoregressive (MVAR) model with the obtained data. There have also been integrated different algorithms to perform this prediction, such as:

- Ordinary Least Squares.
- Recursive Maximum Likelihood.
- Kalman Filter.

Therefore, it becomes relatively easy to combine different approaches for the same data and compare the results with each of those, or combine datasets with the same methods for between-subjects simple studies.

SYSTEM DESIGN

The software tool described in this paper, has its core on the mathematical methods which can be applied to the signals. However, working with those signals implies several steps to acquire the time-series from the fMRI volumes, to remove artifacts and to prepare signals in the right way for connectivity analysis.

Therefore, the toolbox functions can be divided in big groups of functions attending to the objective they fulfill on a connectivity analysis workflow. This way, we can divide the toolbox in four main blocks as can be seen in Figure 1.

- Signal obtention.
- Filter.
- Methods execution.
- Results viewer.

Signal Obtention

There are some different ways for importing the signals, as it is programmed on MATLAB, it can load any dataset saved with a readable extension.

To enhance the usability, it has also been integrated a whole ROI extraction set of functions. Regions of interest can be loaded from old studies or taken from provided Brodmann atlas.

The signal extraction feature has been integrated from the MarsBAR 0.43 toolbox, based on SPM functions and it requires both programs to be installed.

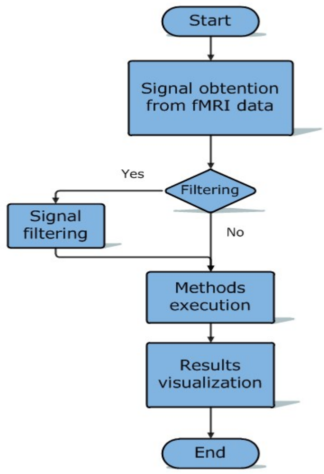

FIGURE. 1
MODULES FORMING THE TOOLBOX SYSTEM DESIGN AS WORKFLOW CHART

Filtering

Filtering is an optional feature which this toolbox includes. This will be very useful in case you are operating on raw data.

If the signals have been imported from other program or cleaned with other software, this step can be skipped.

The band-pass filter is often set to very low values (0.01 - 0.1 Hz) [9] [10], as a way of extracting the most interesting frequency components of the signal.

Methods execution

Once the data is introduced, and every signal is cleaned so each signal, explains the behavior or performance of a given area of the brain for a subject, the user has to select the analysis he wants to carry out on this data.

The graphical user interface, gives the student the chance of choosing which method is going to be executed on the data, some methods may ask the user to introduce few parameters or to select a specific operation mode, see Figure

2. Then the desired function will be called. It is going to work with imported functional images and selected ROI.

For executing the desired method, the user will choose one or some of the tests available on the toolbox, as can be seen in Figure 3. The methods the user choose will depend on what the researcher is looking for as there are two opposite studies which can be applied: functional connectivity and effective connectivity.

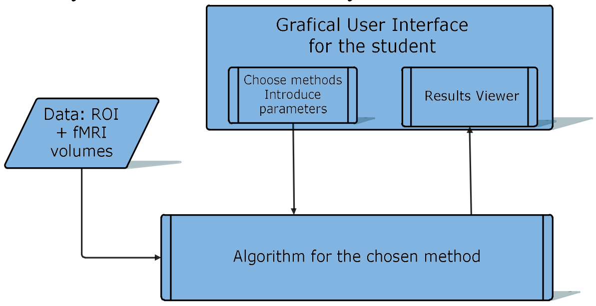

FIGURE. 2
MODULES EXPLAINING THE METHODS EXECUTION

For executing the desired method, the user will choose one or some of the tests available on the toolbox, as can be seen in Figure 3. The methods the user choose will depend on what the researcher is looking for as there are two opposite studies that can be applied: functional connectivity and effective connectivity.

Once the method has been run, it will give back the results as 3D or 4D matrixes that the result viewer will appropriately interpret and print out.

Results Viewer

Once any of the above mentioned mathematical methods have been applied the interactions between the signals which represent brain areas can be easily visualized with results viewer.

This will be the necessary feedback, perfect for a reasonable understanding of the performance of the methods.

Yet it is not implemented a visualization on the brain space, but it shows tables and graphics for assessing the obtained results

Graphical User Interface

All the above mentioned blocks are grouped together inside a GUI. This way, it becomes really easy to access all the features of the tool, and efficient because the feedback it provides will be enough for a satisfactory experience for the user since the first time they try it.

As it does not include all the functions that big software packages (SPM, AFNI, FSL...) are used to add for image processing and statistical evaluation, it is just focused on the signal processing itself.

The software will be opened with a simple command on MATLAB command window. Once this is done, the user is able to use all the facilities of the software using the buttons in any of the screens, see Figure 4.

It also includes many options to plot the signals both in time and frequency, which it makes it easier to understand the data we are working with.

RESULTS

As neuroscience is a very wide field where many professional profiles are required, it is often common to find multidisciplinary teams. This software tool is also oriented to students not related with engineering whose mathematical and computer science background is poor.

For this reason, the toolbox has an attractive and robust interface to prevent from the many usability issues the script based software usually have. It has visualization and plot options in almost every step.

The functions are written in MATLAB, even if complex methods are implemented is quite easy to study the algorithms. Taking advantage of the standard functions and manuals MathWorks offers, the student will soon be able to write and add scripts himself. The tool has been made to make the user feel free to change and adapt parameters.

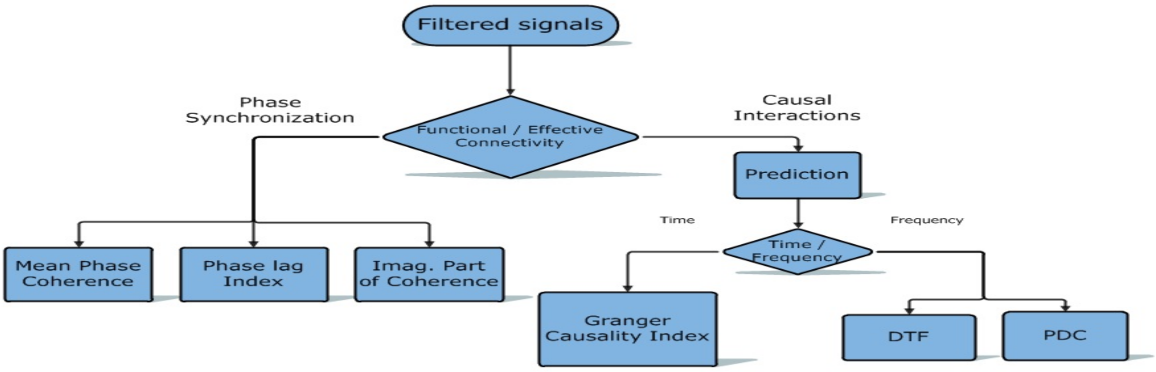

FIGURE. 3

SCHEME OF THE AVAILABLE METHODS ACCORDING TO THEIR CLASSIFICATION

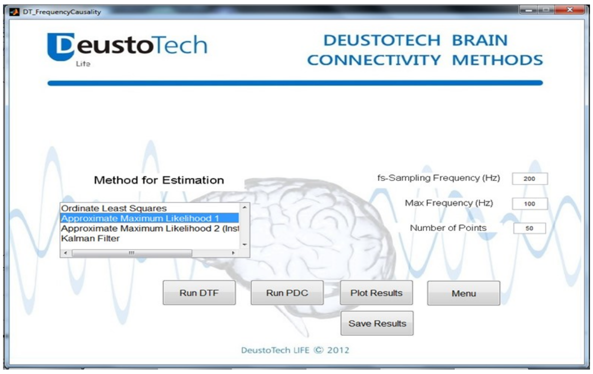

FIGURE. 4
SCREENSHOT OF ONE OF THE INTERFACE PARAMETERS SELECTION MENUS

Not only this, for beginners, it provides a set of different practices, where the student can apply the above mentioned methods which are already prepared for their execution using default parameters as can be seen in Figure 5.

Carrying out these practices the user will achieve the required experience on the use of this analysis.

CONCLUSIONS

Finally, we can conclude that connectivity and brain networks construction is a leading area of neuroscience. This is a yet unexplored field of knowledge where a lot of work needs to be done.

This is a huge challenge that will lead to many years of investigations. Our contribution is this very useful toolbox, directed for those who want to learn how the signal processing most advanced technics can be applied in some fMRI analysis.

This software tool is ideal for seed-based analysis and comparisons between regions. It can also be applied when the aim is to check the effectiveness of some of these methods or which of those approaches can have potential advantages over the others.

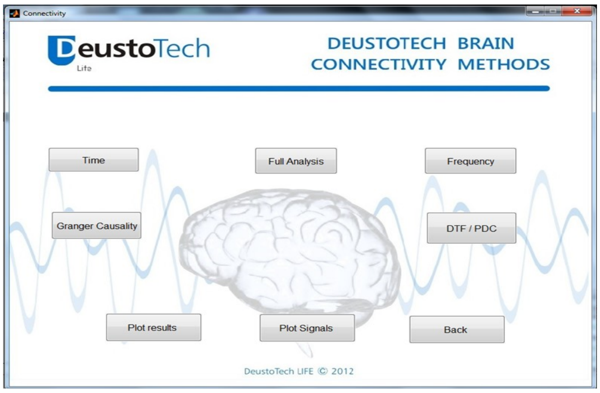

FIGURE. 5
SCREENSHOT OF ONE OF THE TOOL MENUS

Though researchers have used these methods for years, it is often common to see that every department has their own scripts written. It is not so straight-forward as one could think finding these scripts, including different modes, along with other useful tools such as signal extraction, filtering and viewer features.

The toolbox is designed based on a modular system, in order to incorporate new facilities that makes it excellent either in research and educational areas.

Thanks to this, those students about to implement new methods or variations for assessing connectivity of the brain regions through BOLD signals, they may also find this toolbox really useful as it provides the entire framework for this kind of analysis.

These improvements enhance the students to make their own proofs on the algorithms and data.

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