FCLAB: An EEGLAB module for performing functional connectivity analysis on single-subject EEG data

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***Abstract*— Functional connectivity (FC) analysis constitutes a fundamental neuroscientific approach that has been extensively used for the investigation of brain's connectivity and activation patterns. To that end, several software tools have been developed. This paper presents FCLAB, the only EEGLAB-based plugin, which is able to work with EEG signals in order to estimate and visualize brain functional connectivity networks based on a variety of similarity measures as well as run a complete graph analysis procedure followed by a detailed visualization of the ensuing local and global measures distribution. FCLAB entails optimization procedures for the implementation of the connectivity structures and is the result of long-term research in EEG functional connectivity. The computed functional connectivity measures have been carefully selected to reflect the state-of-art in the field. Future work focuses on extending the platform for multi-subject analysis in order to enable the implementation of statistical analysis tools.**

Keywords— EEG; functional connectivity analysis; graph analysis

I. Introduction

The neural activity of the human brain constitutes an exceedingly complex, nonlinear and dynamic biological system [1]. Commonly, it has been attempted to investigate this dynamic system through electroencephalographic (EEG) studies, both in physiological [2] and pathological situations as well [3, 4]. It has been long established that univariate neuroimaging investigations may fail to depict the complexity that underlies different brain areas communicating with each other during a neurophysiological process [5]. The neuronal representations of such process and the multivariate nature of brain activity can be approached employing functional connectivity (FC) [6, 7].

Connectivity analysis has been established as a useful tool to study the organized behavior of brain activity, and it can be performed either at the source or the sensor level. While the former is considered more interpretable regarding to neuroanatomy [8], the solution of the "inverse problem" induces a degree of uncertainty [9], as well as methodological issues. FC analysis at the sensor level, on the other hand, may be more methodologically robust but it has serious limitations in the interpretation of its results and, as such, requires caution [8, 9]. Through careful analysis, sensor level FC can provide intuitive results and has been applied so far to study a number of pathological conditions including Alzheimer's Disease [10], autism spectrum disorder [11], drug addiction [12], and generalized social anxiety disorder [13] among others.

As FC has been steadily becoming more popular, a number of neuroimaging software tools have integrated or have been developed with FC analysis as their primary aim. Through the use of toolboxes such as Brainstorm [14], eConnectome [15], EEGNET [16], or FieldTrip [17], to name but a few, the computation of connectivity has become more problem-free, less code-heavy and far more accessible to researchers and clinicians. EEGLAB [18] is currently one of the most widely distributed Matlab toolboxes, for EEG analysis, featuring an extensive user base and live community, dedicated workshops and support network. A great number of plugins have been developed to offer EEGLAB users with new tools and options. So far we have identified a lack of a plugin to allow functional connectivity analysis integrated within EEGLAB's interface.

In this work, we present FCLAB, an EEGLAB plugin that aims to implement all necessary steps of functional brain connectivity analysis of EEG data at the sensor space by investigators who are not comfortably familiar with other specialized software tools. FCLAB incorporates an adequate analysis infrastructure that reflects the state of the art in the field and is the result of long-term research in EEG FC. Using this plugin, FC analysis on single-subject EEG data is now an option for the user base of EEGLAB. Through EEGLAB's user-friendly interface, the user is able to (a) compute functional connectivity networks for different brain rhythms based on a variety of widely used (as well as user-defined) similarity measures, (b) visualize the connectivity networks using three different representation methods, (c) run complete graph analysis (including an option for Minimum Spanning Trees construction), and (d) depict the distribution of each graph-related local and global measures, in three ways (e.g., the topological distribution).

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II. FCLAB'S WORKFLOW

FCLAB's flowchart is schematically depicted in Fig. 1. The EEG structure is first loaded into the FCLAB's environment through the EEGLAB's interface. Then the user can select a similarity measure as well as define the brain rhythms. Through the visualization interface the user can project the connectivity graphs onto head models. Finally, the user can compute and visualize several local and global metrics on different versions of the original functional connectivity network (e.g., thresholded, binarized, etc.).

III. GRAPH THEORY

Graph theory forms a conventional graphical approach for the mathematical modeling of complex networks. A graph $\boldsymbol{G}$ can be defined as a pair $(\boldsymbol{V}, \boldsymbol{E})$ where is $\boldsymbol{V}$ a set of vertices and $\boldsymbol{E}$ is a set of edges. Graphs can be categorized according to the edge's direction as directed or undirected, and according to edge's weight as weighted or unweighted (binary). Weighted graphs are more accurate models of real networks, unlike unweighted graphs, where much of the information is lost due to arbitrary thresholding [19]. Moreover, the lack of connections in unweighted graphs often leads to the well-known disconnection syndrome [20] with negative implications on the computation of useful graph-theory metrics and the overall cohesion of the network [21].

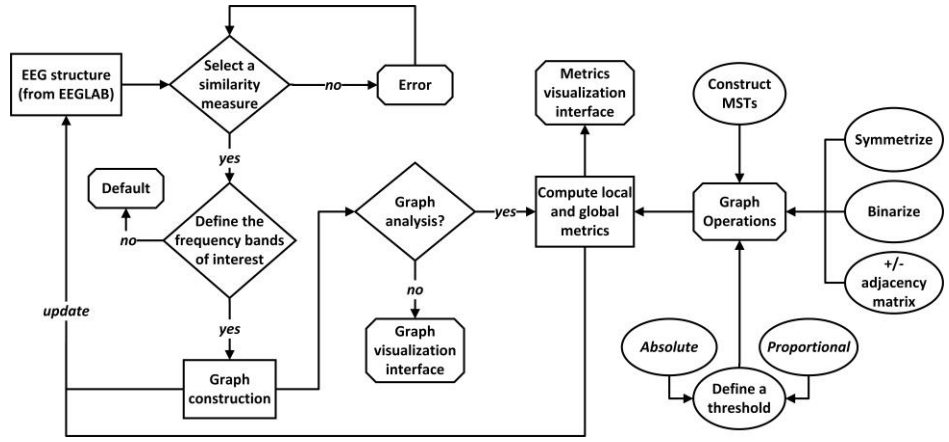

Figure 1. Flowchart of the FCLAB's workflow.

IV. FUNCTIONAL CONNECTIVITY METRICS

Until now, FCLAB includes five different metrics for the computation of similarity matrices: (i) Pearson's Correlation, (ii) Magnitude Square Coherence, (iii) Mutual Information, (iv) Phase Lag Index, (v) Imaginary Part of Coherence. The first three are explicitly described in [22]. Herein, only the last two are described as those that are more robust to artifacts introduced by volume conduction (i.e., linear mixing of uncorrelated sources) [23, 24].

A. Phase Lag Index

The Phase Lag Index (PLI) is a measure of the asymmetry of the distribution of the phase difference between two signals. It is defined as [23]:

$$PLI = |sign(\sin(\Delta\varphi(t_k)))|, \quad (1)$$

where $k = 1,2, \dots, N$, N is the number of samples and $\Delta\varphi$ is the phase difference or relative difference between the two signals and is computed based on Hilbert transform. PLI ranges from 0 – 1, where 1 indicates perfect phase locking for $\Delta\varphi \neq 0 \; mod \; \pi$ since the latter value corresponds to the phase difference of signals with common source.

B. Imaginary Part of Coherence

The imaginary part of coherency (iCOH) is insensitive to artefactual 'self-interaction' caused by volume conduction, because a signal is not time-lagged to itself and thus manages to identify the synchronizations of two signals that are time-lagged [24]. It is defined as:

$$iCOH = imagin(R_{x,y}(f)), \quad (2)$$

where $R_{x,y}(f)$ is the coherence, of signals x, y, at f. Coherence is defined as the absolute value of coherency. The latter measures the linear relationship of the two signals at f. In fact, coherence acts as a generalization of correlation to the frequency domain with its values varying on the interval [0, 1], where 1 indicates a perfect linear prediction of y from x.

V. MINIMUM SPANNING TREES

An alternative way of modeling a weighted graph is based on the notion of the Minimum Spanning Tree (MSTs). A spanning tree is an acyclic subgraph connecting all nodes of the initial graph, with n nodes and $n - 1$ edges and, therefore, achieves a form of dimensionality reduction with a sparse graph connectivity structure. An MST is a spanning tree that minimizes the total cost of the graph. The main advantage of the MST representation of a graph is its ability to overcome biases introduced by comparing networks themselves preserving only the most important edges [25].

VI. GRAPH ANALYSIS DESCRIPTORS

A. Local descriptors

A variety of local descriptors has been included in FCLAB and all of them are based on the Brain Connectivity Toolbox [26]. *Degree* is the number of neighboring nodes connected to the node of interest. *Betweenness centrality* is the fraction of all shortest paths in the network that contain a given node.

Local assortativity measures the extent to which nodes are connected to nodes of similar strength. *Clustering coefficient* is the average geometric mean of all triangles associated with each node. *Eigenvector centrality* is a self-referential measure of centrality. *Local efficiency* is the global efficiency computed in the neighborhood of the node, and it is related to the clustering coefficient. *Eccentricity* is the longest shortest path from the node of interest to any other node and thus quantifies the central topological organization of a network.

B. Global descriptors

Global descriptors have been also incorporated. MST related descriptors are described in the sequel. *Leaf number* is the number of nodes with degree equal to one. *Diameter* is the maximum eccentricity (longest shortest path) of the nodes whereas radius is the node with the smallest eccentricity of the tree. *Kappa or degree divergence* is a measure of the broadness of the degree distribution and it is related to resilience against attacks, and the information flow of tree nodes. *Tree-hierarchy* (T_h) is a measure that quantifies the balance between diameter reduction and overload prevention and denotes whether a tree configuration is optimal or not. Moreover, other global descriptors, related to general graphs and not just MSTs, are also included in FCLAB. Those include: (a) the *characteristic path length* which is the average shortest path length between all pairs of nodes in the network, (b) the *global efficiency* which is defined as the average of inverse shortest path length, and (c) the *strength* which is the sum of the weights of the edges.

VII. Graph Visualization Models

A. Adjacency matrix

A functional connectivity graph with n nodes can be visualized as an nxn symmetric matrix, where the element (i, j) contains the similarity between the channels i and j. The similarity measure can be any of those described in *Section III* or provided by the user. In addition, a variety of colormaps to visualize the weight values is provided along with an option for thresholding the graph to assist the user to visualize a sparser structure containing the edges of interest.

B. Head model

A more representative and qualitative way for visualizing a functional connectivity graph is based on head models. The head model can be seen as the projection of the functional connectivity graph onto a 2D space model. The location of the nodes is based on the provided channel location file which contains the coordinates of the EEG channels. This introduces a more realistic connectivity illustration than the adjacency matrix. The head model is the most common visualization technique of functional connectivity graphs.

C. Head-in-head model

The head-in-head model is a more detailed and modern brain connectivity visualization approach, firstly introduced by [24]. More specifically, the model plots a small circle at each electrode position representing the scalp and containing the similarity values of the respective electrode with all other electrodes.

VIII. Application Results

The data used and presented in this study were from a single normal subject with the purpose of demonstrating the usability of the plugin without performing any neuroscientific analysis at all. The single-subject EEG dataset can be loaded into Matlab's workspace using EEGLAB. The user interface of FCLAB is displayed in Fig. 2A. The investigator is able to select the functional connectivity measure of interest, as well as, define the brain rhythms for examination. In addition, an

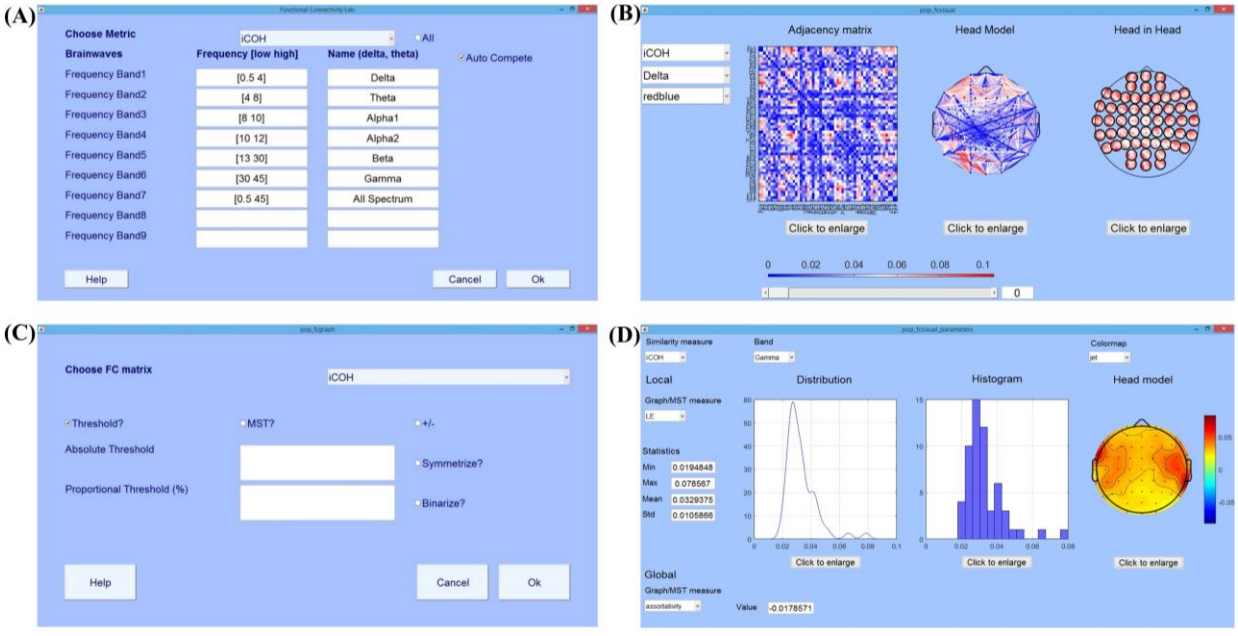

Figure 2. FCLAB's environment. (A) The opening menu for selecting the similarity measure and determining the bands of interest, (B) the functional connectivity visualization interface with a slider for applying various thresholds, (C) the graph analysis panel with options for MST construction, thresholds, etc., and (D) the local and global descriptors visualization panel.

option for auto-filling the frequency bands, according to the most common notation, is provided as well. The user can visualize the functional connectivity graph, per band, using three different representations (Fig. 2B). Additional options are offered for determining: (a) the frequency band of interest, (b) the colormap to be used for weight display, and (c) the threshold value through a slide-bar and an auto updatable box.

Afterwards, the user can run a complete graph analysis (Fig. 2C) by computing the corresponding MSTs along with several local and global MST descriptors (see Section IV for further description). The choice for executing the MST analysis is optional. Additional options are provided for: (a) defining either an absolute or a proportional threshold value, (b) discarding negative weight values, and (c) symmetrizing the adjacency matrix, and (d) taking the absolute matrices of the positive and negative weights separately. Note that the descriptors are computed for each frequency band separately.

The local and global (graph and/or MST) descriptors can be further visualized through an extra interface (Fig. 2D). The latter contains: (a) the probability density, (b) the histogram, and (c) the topological distribution panels for providing an adequate representation of the extracted features.

IX. Discussion and Conclusions

EEGLAB is one of the most widely used open-source, Matlab-based, software tools for EEG analysis. FCLAB's uniqueness lies on the fact that it enables the EEGLAB user (e.g., clinician, researcher, etc.) to perform a complete, user-friendly and adequate functional connectivity analysis followed by appropriate visualization tools. The provided platform is able to construct graphs using a variety of similarity measures on different frequency bands, execute a complete graph (and/or MST) analysis and finally visualize the brain connectivity graphs and descriptors.

FCLAB is an open-source software which can be found in github (https://github.com/ramsys28/FCLAB), where future updates will also be incorporated. FCLAB reflects the state of the art in the field of neuroscience based on the existing research in functional connectivity. Through FCLAB, FC analysis on single-subject EEG data is now an option for the user base of EEGLAB. Future work will mainly focus on extending the platform in order to be able to deal with multi-subject analyses and adding options to enable the user to apply statistical analysis across the samples under examination.

References

[1] X. Wang, J. Meng, G. Tan, and L. Zou, "Research on the relation of EEG signal chaos characteristics with high-level intelligence activity of human brain," *Nonlinear Biomed. Phys.*, vol. 4, no. 1, p. 2, Apr. 2010.

[2] Y. Ma, W. Shi, C. K. Peng, and A. C. Yang, "Nonlinear dynamical analysis of sleep electroencephalography using fractal and entropy approaches," *Sleep Med. Rev.*, pii: S1087-0792(17)30018-7, Jan. 2017.

[3] Y. Bai, X. Xia, and X. Li, "A review of resting-state electroencephalography analysis in disorders of consciousness," *Front. Neurol.*, vol. 8, Sep. 2017.

[4] A. Athanasiou, M. A. Klados, N. Pandria, N. Foroglou, K. R. Kavazidi, K. Polyzoidis, and P. D. Bamidis, "A systematic review of investigations into functional brain connectivity following spinal cord injury," *Front. Hum. Neurosci.*, vol. 11, Oct. 2017.

[5] K. J. Friston, C. D. Frith, and R. S. J. Frackowiak, "Time-dependent changes in effective connectivity measured with PET," *Hum. Brain Mapp.*, vol. 1, no. 1, pp. 69–79, Jan. 1993.

[6] B. Horwitz, "The elusive concept of brain connectivity," *Neuroimage*, vol. 19, no. 2, pp. 466–470, Jun. 2003.

[7] K. J. Friston, "Functional and effective connectivity in neuroimaging: a synthesis," *Hum. Brain Mapp.*, vol. 2, no. 1–2, pp. 56–78, Sep. 1994.

[8] E. Barzegaran, and M. G. Knyazeva, "Functional connectivity analysis in EEG source space: the choice of method," *PLoS One*, vol. 12, no. 7, p. e0181105, Jul. 2017.

[9] F. Van de Steen, L. Faes, E. Karahan, J. Songsiri, P. A. Valdes-Sosa, and D. Marinazzo, "Critical Comments on EEG Sensor Space Dynamical Connectivity Analysis," *Brain Topogr.*, pp. 1-12, Nov. 2016.

[10] S. Afshari and M. Jalili, "Directed functional networks in Alzheimer's disease: disruption of global and local connectivity measures," *IEEE J. Biomed. Heal. Informatics*, vol. 21, no. 4, pp. 949–955, Jul. 2017.

[11] A. Khadem, G.-A. Hossein-Zadeh, and A. Khorrami, "Long-range reduced predictive information transfers of autistic youths in EEG sensor-space during face processing," *Brain Topogr.*, vol. 29, no. 2, pp. 283–295, Mar. 2016.

[12] N. Pandria, L. Kovatsi, A. B. Vivas, and P. D. Bamidis, "Resting-state abnormalities in heroin-dependent individuals," *Neuroscience*, pii: S0306-4522(16)30639-X, Nov. 2016.

[13] M. Xing, R. Tadayonnejad, A. MacNamara, O. Ajilore, J. DiGangi, K. L. Phan, A. Leow, and H. Klumpp, "Resting-state theta band connectivity and graph analysis in generalized social anxiety disorder," *Neuroimage Clin.*, vol. 13, pp. 24–32, Nov. 2017.

[14] F. Tadel, S. Baillet, J. C. Mosher, D. Pantazis, and R. M. Leahy, "Brainstorm: A user-friendly application for MEG/EEG analysis," *Comput. Intell. Neurosci.*, vol. 2011, pp. 1–13, Jan. 2011.

[15] B. He, Y. Dai, L. Astolfi, F. Babiloni, H. Yuan, and L. Yang, "eConnectome: A MATLAB toolbox for mapping and imaging of brain functional connectivity," *J. Neurosci. Methods*, vol. 195, no. 2, pp. 261-269, Feb. 2011.

[16] M. Hassan, M. Shamas, M. Khalil, W. El Falou, and F. Wendling, "EEGNET: an open Source tool for analyzing and visualizing M/EEG connectome," *PLoS One*, vol. 10, no. 9, p. e0138297, Sep. 2015.

[17] R. Oostenveld, P. Fries, E. Maris, and J. M. Schoffelen, "FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data," *Comput. Intell. Neurosci.*, vol. 2011, no. 9, pp. 1–9, Sep. 2011.

[18] A. Delorme and S. Makeig, "EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis," *J. Neurosci. Methods*, vol. 134, no. 1, pp. 9–21, Mar. 2004.

[19] C. J. Stam, E. C. W. van Straaten, E. van Dellen, P. Tewarie, G. Gong, A. Hillebrand, J. Meier, and P. van Mieghem, "The relation between structural and functional connectivity patterns in complex brain networks," *Int. J. Psychophysiol.* vol. 103, pp. 149-160, May 2016.

[20] C. J. Stam, and E. C. W. van Straaten. "The organization of physiological brain networks," *Clin. Neurophysiol.,* vol. 123, no 6, pp. 1067-1087, Jun. 2012.

[21] A. Goulas, A. Schaefer, and D. S. Margulies. "The strength of weak connections in the macaque cortico-cortical network," *Brain Struct. Funct.,* vol. 220, no 5, pp. 2939-2951, Sep. 2015.

[22] C. Lithari, M. A. Klados, C. Papadelis, C. Pappas, M. Albani, and P. D. Bamidis. "How does the metric choice affect brain functional connectivity networks?," *Biomedical Signal Processing and Control*, vol. 7, no. 3, pp. 228–236, May 2012.

[23] C. J. Stam, G. Nolte, and A. Daffertshofer, "Phase lag index: assessment of functional connectivity from multi channel EEG and MEG with diminished bias from common sources," *Hum. Brain Mapp.*, vol. 28, pp. 1178-1193, Jan. 2007.

[24] G. Nolte, O. Bai, L. Wheaton, Z. Mari, S. Vorbach, and M. Hallett, "Identifying true brain interaction from EEG data using the imaginary part of coherency," *Clin. Neurophysiol.* vol. 115, no. 10, pp. 2292-2307, Oct. 2004.

[25] P. Tewarie, A. Hillebrand, E. van Dellen, M. M. Schoonheim, F. Barkhof, C. H. Polman, C. Beaulieu, G. Gong, B. W. van Dijk, and C. J. Stam, "Structural degree predicts functional network connectivity: a multimodal resting-state fMRI and MEG study," *Neuroimage* vol. 97, no. 15, pp. 296-307, Aug. 2014.

[26] M. Rubinov, and O. Sporns, "Complex network measures of brain connectivity: uses and interpretations," *Neuroimage* vol. 52, no. 3, pp. 1059-1069, Sep. 2010.