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FDI: A MATLAB tool for computing the fractal dimension index of sources reconstructed from EEG data

Juan Ruiz de Miras [a,*], Adenauer G. Casali [b], Marcello Massimini [c,d], Antonio J. Ibáñez-Molina [e], María F. Soriano [f], Sergio Iglesias-Parro [e]

[a] Department of Software Engineering, University of Granada, Granada, Spain
[b] Institute of Science and Technology, Federal University of São Paulo, São Paulo, Brazil
[c] Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy
[d] Fondazione Don Carlo Gnocchi, Milan, Italy
[e] Department of Psychology, University of Jaén, Jaén, Spain
[f] Mental Health Unit, San Agustín Hospital, Linares, Spain

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ABSTRACT

Background: The fractal dimension (FD) is a valuable tool for analysing the complexity of neural structures and functions in the human brain. To assess the spatiotemporal complexity of brain activations derived from electroencephalogram (EEG) signals, the fractal dimension index (FDI) was developed. This measure integrates two distinct complexity metrics: 1) integration FD, which calculates the FD of the spatiotemporal coordinates of all significantly active EEG sources (4DFD); and 2) differentiation FD, determined by the complexity of the temporal evolution of the spatial distribution of cortical activations (3DFD), estimated via the Higuchi FD [HFD(3DFD)]. The final FDI value is the product of these two measurements: 4DFD $\times$ HFD(3DFD). Although FDI has shown utility in various research on neurological and neurodegenerative disorders, existing literature lacks standardized implementation methods and accessible coding resources, limiting wider adoption within the field.
Methods: We introduce an open-source MATLAB software named `FDI` for measuring FDI values in EEG datasets.
Results: By using CUDA for leveraging the GPU massive parallelism to optimize performance, our software facilitates efficient processing of large-scale EEG data while ensuring compatibility with pre-processed data from widely used tools such as Brainstorm and EEGLab. Additionally, we illustrate the applicability of `FDI` by demonstrating its usage in two neuroimaging studies. Access to the MATLAB source code and a precompiled executable for Windows system is provided freely.
Conclusions: With these resources, neuroscientists can readily apply FDI to investigate cortical activity complexity within their own studies.

1. Introduction

The concept of fractal dimension (FD) serves as a numerical measure of an object's complexity [1]. The FD metric has been widely employed in neuroimaging studies to detect alterations in the structural composition and internal dynamical patterns of the human brain [2,3]. Due to its adaptability, the application of FD analysis to electroencephalogram signals (EEG) has led to the creation of numerous notable uses in many diseases such as epilepsy [4], sleep disorders [5], Alzheimer's disease [6], schizophrenia [7], depression [8] and attention-deficit hyperactivity disorder [9], among others.

Most of those studies compute the FD directly on the channels of the EEG signal by means of metrics such as Higuchi FD, Katz FD and correlation dimension [2]. There are also studies where fractal analysis is performed on neural oscillations extracted from sources reconstructed from the EEG signal [10]. Nevertheless, there has been recent progress towards developing a new high-resolution assessment method for FD, combining both the temporal and the spatial dimensions. This novel technique, known as FDI, is calculated based on the sources reconstructed from the EEG data [11]. Two different FD measures are used for calculating FDI: the 3D fractal dimension (3DFD) and the 4D fractal dimension (4DFD) of cortical activations derived from the EEG signal

* Corresponding author. Department of Software Engineering, University of Granada, Periodista Daniel Saucedo Aranda s/n, 18071, Granada, Spain.
E-mail address: demiras@ugr.es (J. Ruiz de Miras).

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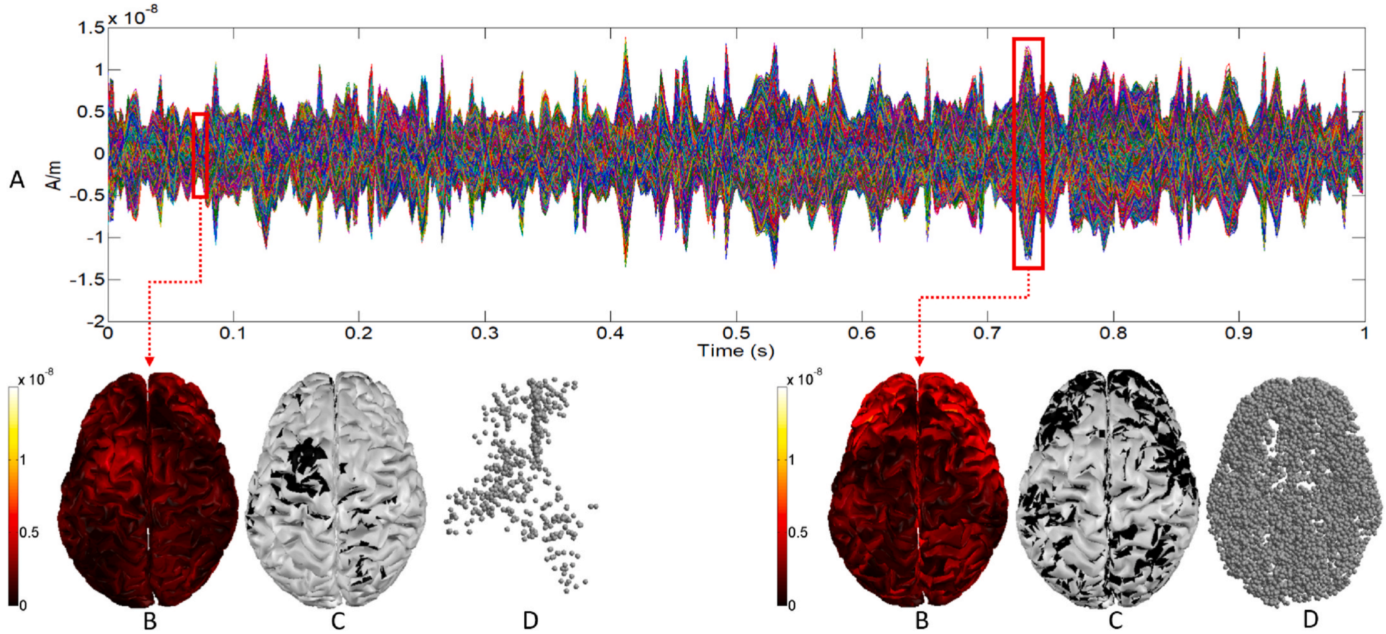

Fig. 1. Sources activity for 1 s in resting-state (A). 3D visualization of source activity at two distinct time samples (B). 3D visualization after binarization (C). Point cloud representations of cortical activations resulting from binarized sources (D). Adapted from Fig. 1 in Ref. [19].

using source reconstruction methods. The 3D coordinates of the cortical activations in the epoch being studied form a sequence of 3D point clouds. From these point clouds, the 3DFD and 4DFD values are computed by using the box-counting method [12]. FDI is then calculated as the product of: 1) the 4DFD of the spatiotemporal set comprising all of the 3D point clouds in the epoch, which quantifies the integration of cortical networks; and 2) the Higuchi FD [13] of the curve defined by the 3DFD values in the epoch, which measures cortical differentiation [11].

Many studies in neuroscience have used the FD in 3D for analysing the brain morphology from structural magnetic-resonance (MRI) data, as in Refs. [14–16], for citing some of the most recent works. The temporal component was also included in some previous works based on functional MRI (fMRI) data, where maps of FD were constructed for analysing the spatial distribution of the complexity of the neural oscillations [17,18]. However, the studies performing FD analyses of 3D and 4D models representing brain activations are much more novel [11,19,20].

The primary strength of the FDI method lies in its ability to analyse brain complexity in two complementary ways: firstly, by examining the fractal structure of brain activity, and secondly, by tracking its evolution over time using the FD parameter.

FDI has two major advantages compared to FD metrics based on direct analysis of the EEG signal. Firstly, FDI offers more comprehensive information because it is constructed as a product of both 4DFD (integration FD) and HFD of 3DFD (differentiation FD). As such, not only does FDI offer a complete picture, but it also reveals distinct aspects of spatiotemporal complexity. Secondly, FDI allows evaluation of individual contributions from various brain regions towards overall spatiotemporal complexity. This capability could prove especially useful when studying conditions involving damage to particular parts of the cortex or diseases primarily impacting certain brain regions [19].

The novel FDI method has been increasingly employed in recent neuroimaging studies involving EEG. Researchers have utilized FDI to distinguish between conscious and unconscious states in healthy subjects through high-density EEG measurements taken after transcranial magnetic stimulation (TMS) [11]. According to Ref. [19], the FDI technique is also valuable when studying long resting-state EEG signals; it can capture dynamic shifts in various functional networks influenced by schizophrenia, a mental illness marked by disrupted information flow in the spontaneous brain networks. Furthermore, FDI has proven beneficial in identifying distinctive alterations in brain dynamics associated with Parkinson's disease, particularly through its successful application in analysing resting-state EEG data [20].

Prior investigations relied on tailored, per-study techniques for calculating the FDI due to the absence of readily accessible software tools. Consequently, our primary objective in the current study is to develop and share an easy-to-use software solution with the neuroscience community, enabling efficient computation of the FDI for future studies. To achieve this goal, we developed our `FDI` computer program using MATLAB (The MathWorks Inc., Natick, MA, US), a very popular platform in the biomedical field due to its compatibility across systems. The program `FDI` offers dual functionality, allowing users to interact with it via a graphical user interface (GUI) as well as through commands entered at the MATLAB prompt. Given that calculating 3DFD and 4DFD metrics for long EEG epochs requires significant computational power, we optimized these algorithms by implementing them in CUDA and integrating them into the MATLAB code. This integration enables us to leverage the immense parallelism offered by current graphics processing units (GPUs). Furthermore, our `FDI` software is compatible with the file formats used by common EEG source reconstruction pipelines in Brainstorm [21] and EEGLab [22], making it accessible and convenient for researchers utilizing these popular tools for EEG data analysis.

In subsequent sections, we first outline the methodology behind computing the FDI measure. We then present an overview of our software's primary modules, illustrate the capabilities of its user interface, and evaluate its performance on two distinct hardware-software configurations. Following that, we detail instructions for obtaining, installing, and running `FDI`. Lastly, we offer a comprehensive guide on employing `FDI` to analyse two different types of EEG recordings: event-related potentials induced by TMS, and periods of resting-state activity. By providing these detailed descriptions and practical examples, we aim to make the tool accessible to the neuroscientific community, enabling them to effectively harness its potential in their studies involving the analysis of brain dynamics complexity from EEG signals.

2. Computational methods and theory

This section focuses on explaining the process of estimating the FDI

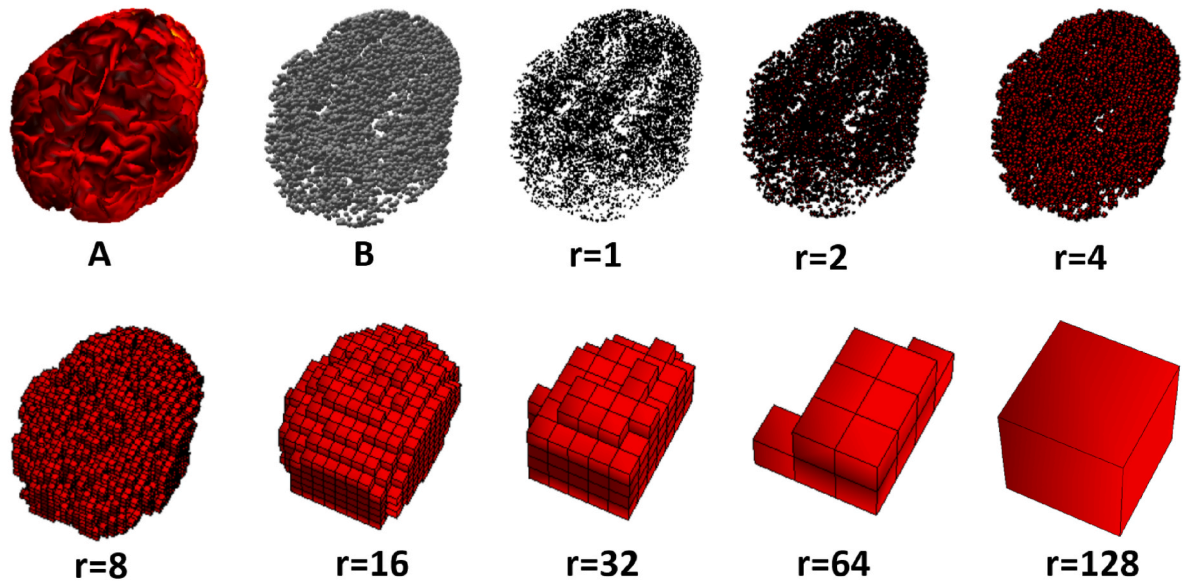

Fig. 2. Sources activity at a time sample (A). Point cloud defined by sources binarization (B). 3D voxelizations of the point cloud from $r = 1$ to $r = 128$. Adapted from Fig. 2 in Ref. [11].

measure for sources reconstructed from EEG epochs. For those interested in the underlying technicalities of FDI calculation, we refer to prior publications [11,19,23]. As a quick reference, we include here a succinct reiteration of the essential steps involved in the procedure.

2.1. Extraction of brain activations from EEG

An initial preprocessing requirement for computing the FDI involves performing source modelling of the EEG signal. Common software suites, including Brainstorm and EEGLab, generally follow a multi-stage pipeline comprising: 1) construction of a forward EEG model [24] using tools such as OpenMEEG [25], wherein the model conforms to either the individual subject's unique anatomy or a preexisting template [26] supplied by the software suite; and 2) solving the inverse problem of determining the 3D distribution of electrical sources (current dipoles) through techniques such as Weighted Minimum Norm constraint [27] or LORETA (Low Resolution Brain Electromagnetic Tomography) [28]. Once completed, the source modelling phase generates a matrix (#sources × #samples) containing the amplitude of brain electrical current at each source location for each time sample.

After performing source modelling, a process of binarization is needed to determine cortical activations at each time sample. FDI uses the box-counting algorithm to compute 3DFD and 4DFD, and this algorithm requires binary matrices as input data. `FDI` offers the binary classification of input sources by using a threshold based on the mean plus a specified number of standard deviations of the absolute values over the epoch. This method is usually employed with resting-state EEG recordings where cortical activations are identified as sources with intensity values significantly higher than the average within the epoch [19,20]. See Fig. 1 for an example of the outlined binarization process. Other binarization methods may be employed when EEG is recorded in the presence of an external stimulus, as is the case of TMS-evoked potentials. In this type of recording, activation thresholds are usually extracted from the pre-stimulus signal using nonparametric statistical approaches such as bootstrapping [29]. In `FDI` users can provide pre-binarized matrices obtained with specific statistical approaches when needed. Refer to **Section 5** for detailed instructions on these features.

2.2. FDI computation

Upon completion of the binarization process to extract the matrix depicting the spatiotemporal dynamics of brain activations, the subsequent step involves calculating FDI according to the complexity of the spatiotemporal distribution of the sources.

FDI can be expressed as:

$$FDI = 4DFD \times HFD(3DFD) \tag{1}$$

where: *4DFD* represents the fractal dimension of the 4D matrix consisting of the temporal evolution of brain activations (3D point clouds) at every time sample; *3DFD* denotes the curve described by the sequence of fractal dimension values computed individually for the 3D point cloud at each sample; and *HFD* refers to the Higuchi FD [13] of that curve.

FDI combines two measures of complexity in a single number. 4DFD captures the complexity of the temporally integrated spatial distributions of cortical activations, reflecting the dispersion of these activations. Meanwhile, the HFD(3DFD) quantifies the complexity of the states the system goes through as it evolves over time. In this way, FDI integrates both spatial and temporal domains, and combining these two domains is crucial to capture brain complexity as the balance of integration and differentiation. These two measures of information are related to the Integrated Information Theory of consciousness [30,31]. Therefore, FDI is an empirical measure, theoretically rooted, which provides a comprehensive assessment of how the complexity of the brain's dynamical system changes over time.

We estimate the FD values of both 3D and 4D point clouds by employing the box-counting algorithm [12]. Specifically, we calculate the FD value as the slope of the linear regression line fit to the plot of log ($n(r)$) versus log($1/r$), where $n(r)$ represents the count of boxes with size r^d required to cover the entire point cloud (with d set equal to 3 for 3D point clouds and 4 for 4D point clouds). Fig. 2 illustrates this voxelization process of covering a 3D point cloud (cortical activations at a given time sample) with boxes of varying sizes ranging from $r = 1$ to $r = 128$.

Performing the box-counting algorithm in three and four dimensions can be computationally intensive, making it a potential bottleneck when calculating FDI values for long EEG epochs or large-scale studies with numerous EEG records. In an effort to mitigate this issue, we used a CUDA GPU-optimized parallel implementation of the box-counting algorithm provided in Ref. [23]. This CUDA code was then compiled as a *mexcuda* function within MATLAB to seamlessly integrate with our

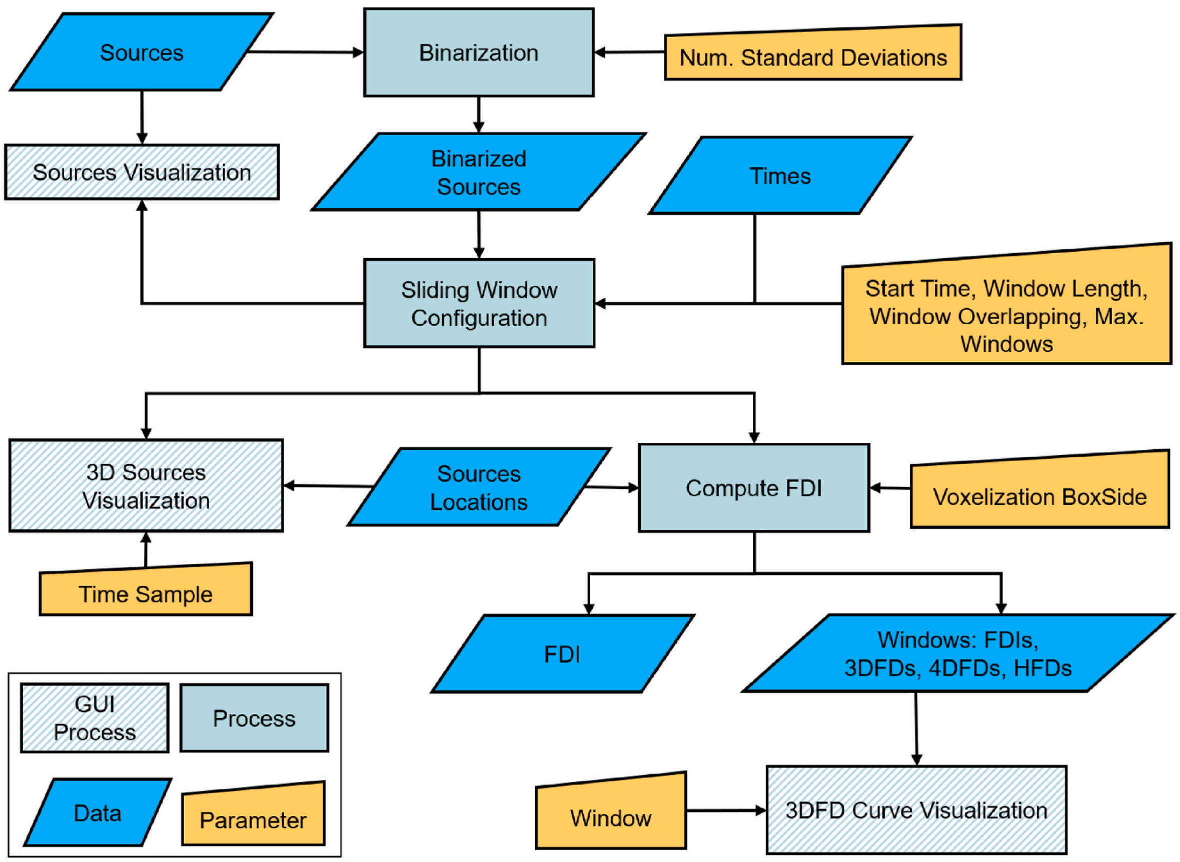

Fig. 3. Data-flow diagram of FDI.

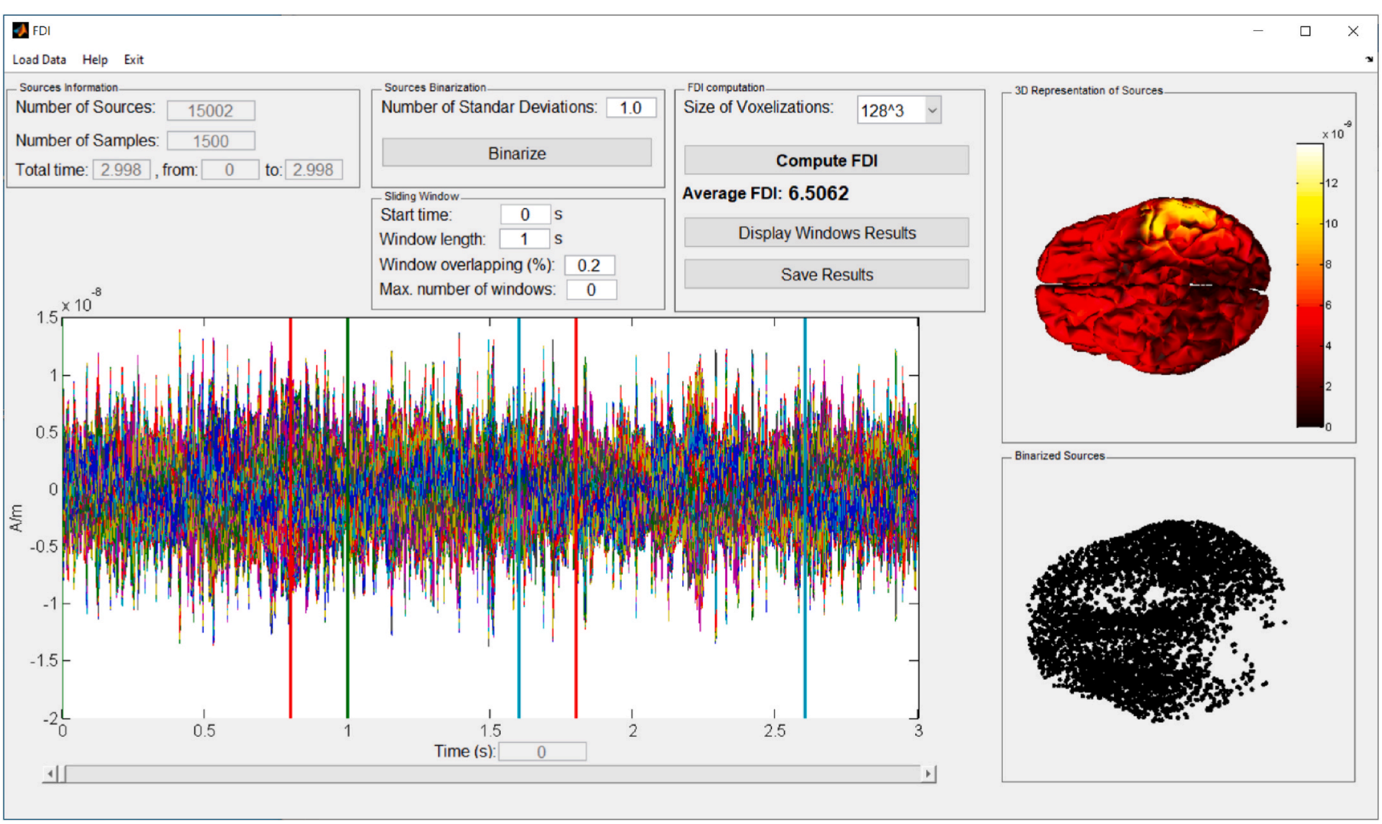

Fig. 4. FDI GUI displaying the FDI (6.5062) of the cortical activations obtained from a resting-state EEG record of 3 s with a sliding window of 1 s and 20 % of overlapping.

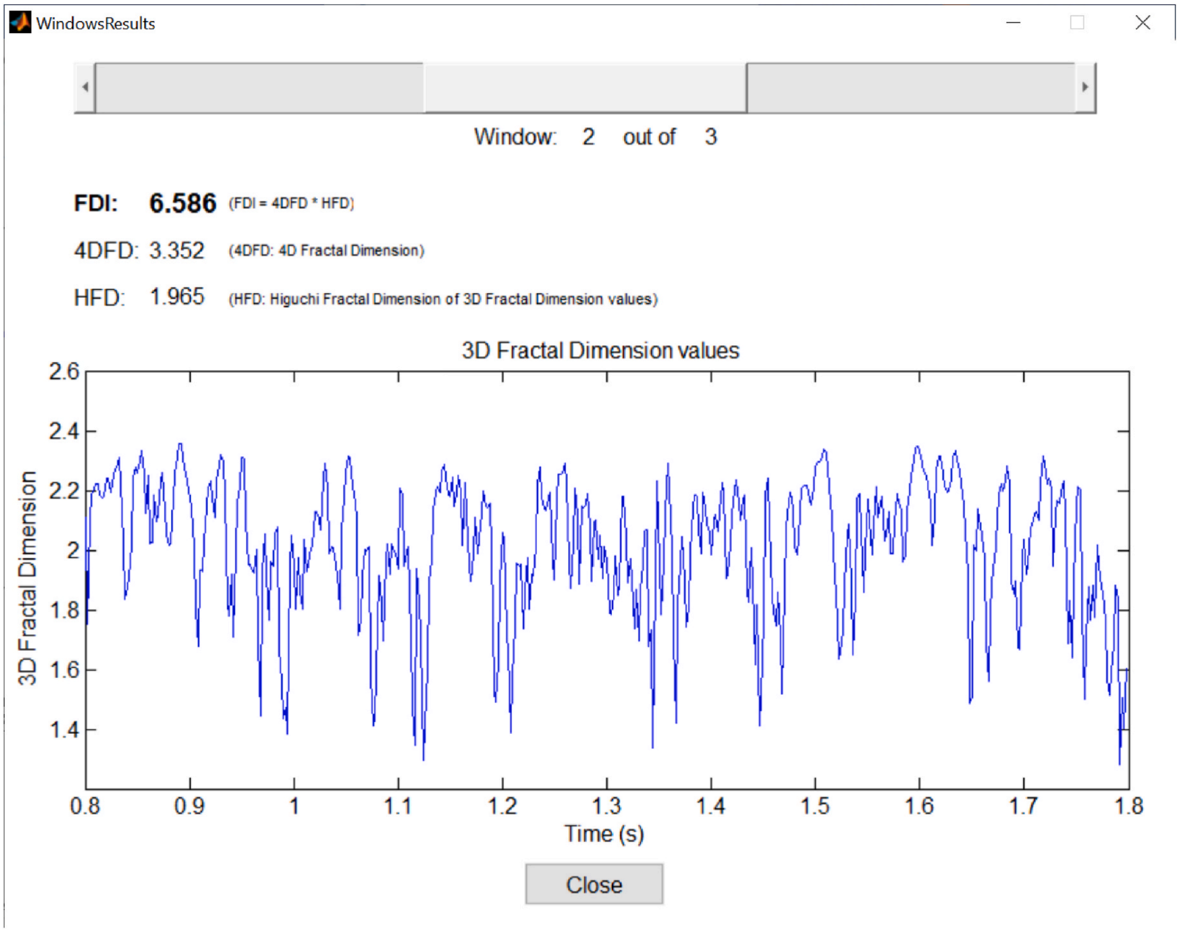

Fig. 5. Interactive display of FDI, 4DFD, HFD and 3DFDs values for each window in GUI mode.

existing FDI calculation pipeline, allowing users to transparently benefit from its improved performance. Section 4 details the performance analysis of `FDI` comparing the computational efficiency in two different platforms.

The box-counting algorithm features two main configuration parameters: 1) the maximum size r for computing voxelizations (referred as *boxSide* in `FDI`), and 2) the range of box sizes to choose for fitting the linear regression line. Users can select either *boxSide* = 128 (the default setting) or *boxSide* = 256. Based on prior studies [11,19,20], the following predefined ranges of box sizes are empirically established in `FDI` for 3D FD computation: when *boxSide* = 128, the range goes from $r = 8$ to $r = 64$, whereas when *boxSide* = 256, the range extends from $r = 16$ to $r = 128$. Similarly, for 4D FD computation, the chosen ranges span from $r = 4$ to $r = 64$ (for *boxSide* = 128) and from $r = 8$ to $r = 128$ (for *boxSide* = 256).

3. Program description

Fig. 3 illustrates the data-flow diagram for `FDI`, highlighting its primary components. Note that the striped-shaded processes in this figure (*Sources Visualization*, *3D Sources Visualization* and *3DFD Curve Visualization*) are only available in the GUI mode of the application, while the remainder of the processes are available in both modes GUI and console.

The first input to the program is a file containing the sources to process (a matrix of number of sources × number of time samples in MATLAB format). This file could contain the original sources as generated from software such as Brainstorm or EEGLab or a previously generated binarization (matrix with entries 0 and 1 for inactive and active spatiotemporal samples, respectively) according to any specific algorithm to extract the cortical activations. In case the original sources were provided, then a binarization process must be applied to each source, as shown in Fig. 1, using as threshold the mean plus the desired number of standard deviations of the absolute values of the source.

A times file is also required to properly configure the sliding window generator. This file must include a MATLAB vector containing the actual time for each time sample. Then, a sliding window is created with the following parameters: 1) the starting time of the sliding window, 2) the duration of each window, 3) the overlap percentage between consecutive windows (a value between 0 and 1), and 4) the maximum number of windows to generate. Sliding windows enable adequate processing of sources extracted from long EEG recordings, such as resting-state sessions [19,20]. Within each window, the FDI is calculated independently, and the average across all windows is taken to represent the FDI for the entire epoch. Users can inspect both the sources activity and the sliding window in the GUI mode (see the *Sources Visualization* process in Figs. 3, and Fig. 4).

Calculating the FDI also requires the 3D location of each cortical activation (*Sources Locations* in Fig. 3). This MATLAB file is provided by the software used to obtain the sources from the EEG data, and contains

Table 1
Average computation times for calculating the FDI for: Case #1) the pre-binarized sources of 130 ms TMS-evoked EEG (1 window × 47 samples), and Case #2) the original sources of 3 s resting-state EEG (3 windows × 500 samples). Average times (in seconds) for 10 executions.

Process	Computation Time			
	PC		Server	
	Case #1	Case #2	Case #1	Case #2
Binarization	–	0.572 s	–	0.815 s
3DFDs computation	0.438 s	14.676 s	0.539 s	12.327 s
4DFD computation	0.412 s	3.273 s	0.489 s	2.893 s
Total time	0.850 s	18.521 s	1.027 s	16.530 s

the X, Y and Z coordinates for each source. From this data, two distinct voxelizations of the cortical activations are created: 1) the 3D voxelization at each individual time sample and 2) the 4D voxelization for each window. Both voxelizations are generated with the desired maximum resolution (parameter *Voxelization BoxSide* in Fig. 3: 128 or 256). The source locations (X, Y and Z coordinates) are always the same since they are predefined from anatomy. However, the 3D voxelization at each sample time and the 4D voxelizations for each window are different, since they are constructed from the cortical activations obtained in the binarization process of the reconstructed sources at each sample time. When operating in GUI mode, the 3D visualization of both the sources activity and cortical activations for the selected time sample appears (see *3D Sources Visualization* in Figs. 3, and Fig. 4).

Finally, the FDI value is obtained for each window according to **Equation (1)** (*Compute FDI* in Fig. 3). After processing, the average FDI across all windows and the individual FDI, 4DFD, HFD and 3DFDs values for each window are jointly saved in a MATLAB file. `FDI` stores the 4DFD and 3DFD values alongside their respective correlation coefficients calculated when performing linear regression fitting.

`FDI` in GUI mode enables users to interactively examine the FDI, 4DFD, HFD and 3DFDs values for each individual window (*3DFD Curve Visualization* process in Fig. 3). Fig. 5 displays the `FDI` interface containing the FDI, 4DFD, HFD and 3DFDs results for the second window of the sliding window depicted in Fig. 4.

4. Software/hardware specifications and performance analysis

`FDI` is a MATLAB program. 3DFD and 4DFD values are computed in GPU through both MEX (MATLAB executable) functions compiled in C++/CUDA with the MATLAB command *mexcuda*. The graphical user interface of `FDI` was designed using MATLAB GUIDE (https://www.mathworks.com/discovery/matlab-gui.html).

`FDI` was tested on two different platforms: a desktop computer (PC) and a high-performance computing server (server). The PC operates on the Microsoft Windows 10 OS, featuring an Intel Core i7-9700 3.0 GHz CPU (8 cores – 8 threads), 64 GB of RAM, and an NVIDIA RTX 3060 GPU with 3584 CUDA cores and 12 GB of dedicated memory. On the other hand, the server platform uses Debian Linux 5.10 and boasts two Intel Xeon Silver 4210 2.20 GHz processors (20 cores – 40 threads), accompanied by 96 GB of RAM, and an NVIDIA RTX 3090 GPU with 10,406 CUDA cores and 24 GB of dedicated memory.

In order to analyse the computational performance of `FDI`, Table 1 shows the average times (for ten executions) needed for computing the FDI value in two different conditions: Case #1) pre-binarized sources from 130 ms of TMS-evoked EEG with one window containing 47 samples; and Case #2) original sources from 3 s of resting-state EEG with a sliding window of 1 s and 0 % overlapping (3 windows × 500 samples = 1500 samples). Computation times were obtained by executing `FDI` on our two testing platforms in console mode with no user interaction.

The calculation of 3DFD values for cortical activations at every time sample represents the most compute-intensive part of the entire process. Specifically, for Case #1, calculating 3DFD values accounts for 51 % of the total time on the PC platform and 52 % on the server platform. For Case #2, this step takes up 79 % of the total time on the PC platform and 75 % on the server platform.

Higher percentages of 3DFD computation time were observed for Case #2 compared to Case #1 due to the larger number of time samples in Case #2 (1500 vs. 47). Nevertheless, the use of parallel GPU computing enabled the application to scale efficiently. Specifically, the total processing time for Case #2 was just 21.8 times longer on the PC and 16.1 times longer on the server compared to Case #1. Given that the ratio of time samples between the two cases was 31.9, this suggests that the computation time increases by almost half the increase in time samples to process, indicating a highly efficient scaling behaviour.

Based on the reported computation times, calculating the FDI for large datasets with long epochs would require huge processing times, unless these epochs are computed concurrently on multi-core systems. As we will show in **Section 6**, FDI can be applied to a large-scale study involving 31 EEG records of 150 s, where five distinct regions of interest were analysed. In this study, a total amount of 11,625,000 3DFD values and 23,250 4DFD values were computed. This example additionally supplies detailed scripts for running `FDI` on multiple EEG registers in parallel.

5. Availability of the program: download, installation, and usage

The source code for `FDI` is publicly available and can be accessed at https://www.ugr.es/~demiras/fdi/. To use `FDI` on a Windows system, the Microsoft Visual C++ 2019 Redistributable Libraries (available for download at https://learn.microsoft.com/en-US/cpp/windows/latest-supported-vc-redist?view=msvc-170#latest-microsoft-visual-c-redistributable-version) are required to run the `FDI` MEX-files. Additionally, `FDI` requires a computer equipped with an NVIDIA CUDA-compatible GPU and the corresponding NVIDIA CUDA Runtime (version 11.6 or higher), which can be obtained from the NVIDIA website at https://developer.nvidia.com/cuda-11-6-0-download-archive. MEX files are pre-compiled for both 64-bit Linux (Debian Linux 5.10) and Windows systems within the `FDI` source code. In order to compile these files on other platforms, users must use the *mexcuda* command provided by the Parallel Computing Toolbox in MATLAB.

FDI can be executed in one of two ways: either at the MATLAB command prompt or as an independent operating system process. Using the former approach is suitable for single-epoch processing, while the latter allows for efficient parallelization of multiple epochs, as demonstrated in **Section 6**. Here is the syntax for calling `FDI` from the MATLAB command prompt.

>> `FDIgui`: Start `FDI` in GUI mode.

>> `FDIConsole parameters`: Start `FDI` in console mode. The `parameters` syntax is: `sources times frequency vertices windowTime windowOverlapping iniTime [optional parameter-value pairs]`

where the parameters are:

`sources`: MATLAB .mat file containing a matrix named *sources* and dimensions number of sources × number of time samples. This matrix contains the amplitude of brain electrical current for each reconstructed source at each sample time, or the pre-binarized sources (1's and 0's),

`times`: MATLAB .mat file containing a vector named *times* and dimensions 1 × number of time samples. This vector contains the time (in seconds) for each time sample,

`frequency`: the frequency at which the signal was sampled (number of time samples per second),

`vertices`: MATLAB .mat file containing a matrix named *vertices* and dimensions number of sources × 3. This matrix contains the X, Y and Z coordinates of each source,

`windowTime`: duration in seconds of the sliding window,

`windowOverlapping`: value between 0 and 1 indicating the percentage of overlapping between consecutive windows,

`iniTime`: scalar value specifying the starting time of the initial time window, expressed in seconds.

The optional parameter-value pairs are:

`'maxWindows' max number of windows`: default value is 0 (number of windows is set to the maximum possible according to the values of `windowTime` and `windowOverlapping`),

`'boxSide' voxelization resolution`: possible values are 128 (default) or 256,

`'subjectId' string identification for the epoch`: default value is *FDIResults*,

`'nStd' number of standard deviations to binarize the sources`: by default (-1) no binarization is performed, assuming that the sources were previously binarized,

`'silent' true/false`: if true, no messages are displayed at the console. Default value is false.

Two different examples for testing `FDI` can be found at https://www.ugr.es/~demiras/fdi/. The first example includes the reconstructed sources of a TMS-EEG measurement spanning 1 s, with 0.5 s before the TMS stimulation and 0.5 s after the TMS stimulation. This EEG originated from a prior investigation on sleep and consciousness that we conducted [11]. The second example comprises 3 s of the reconstructed sources derived from a 150-s resting-state EEG recording taken from a previous study on schizophrenia [19]. Additional details regarding the EEG data associated with these two examples are presented later in **Section 6**. **Listing 1** shows the MATLAB code to test `FDI` using these two epochs.

MATLAB files specified in lines 2, 3 and 4 in Listing 1 contain the matrices with the pre-binarized sources (cortical activations) of the

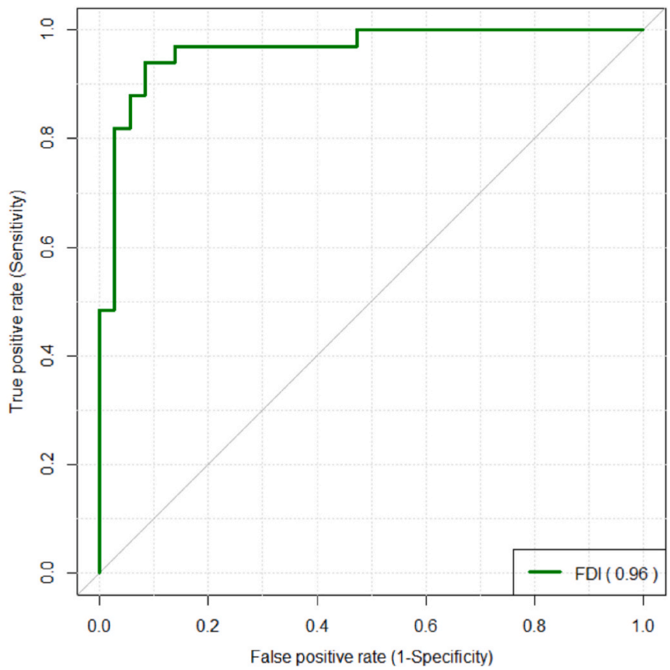

Fig. 6. Performance evaluation of FDI as classifier for consciousness through receiver operating characteristic (ROC) curve analysis. The area under the ROC curve (AUC) value for FDI is indicated in brackets [11].

TMS-EEG epoch, the time for each sample, and the 3D coordinates of the cortical activations, respectively. Then, lines 5 through 11 configure parameters required to calculate FDI: processing one window (*maxWindows*) of 0.130 s (*windowTime*), starting from time 0 s (*iniTime*) and covering the cortical activations with a voxelization of size 128 voxels (*boxSide*). Finally, the FDI is computed through the *FDIConsole* function in lines 12 and 13. Results are saved as a MATLAB structure in the file *1_TMS_BinarizedSources_Results.mat*, containing the FDI, 4DFD, HFD and 3DFDs values for the analysed window.

Similarly, lines 16 through 27 in Listing 1 show the code for computing the FDI of the second example: the 3-s resting-state EEG epoch. In this case, sources are not pre-binarized, so the optional parameter *nStd* must be set (lines 23 and 27). The sliding window is configured starting at time 0 (*iniTime* in Line 22), with a duration of 1 s (*windowTime* in line 20) and 0 % of overlapping (*windowOverlap* in line 21). This configuration generates three windows because the duration of the epoch is 3 s and the *maxWindows* parameter is not set. Call to *FDIConsole* in lines 26 and 27 computes the FDI for each window, and results are saved in the file *2_Resting_State_Original_Sources_Results.mat*. This file contains the MATLAB structure with the average FDI value and, for each window, the FDI, 4DFD, HFD and 3DFDs values obtained.

`FDI`, like any MATLAB program, can be run as an independent process to perform batch or parallel processing of multiple EEG epochs. To do this, MATLAB must be started without its GUI (*-nodisplay*, *-nosplash* and *-nodesktop* parameters) and including `FDI` as the script parameter as follows:

```
matlab -nojvm -nodisplay -nosplash -nodesktop -r
"FDIConsole parameters"
```

6. Application of the program: FDI for characterizing consciousness states and schizophrenia

This section demonstrates how to use FDI to process the EEG data for two separate studies involving large sample sizes. Since these two studies by our group were previously published in Refs. [11,19], we now briefly describe the aims, materials, methods and results of these studies, focusing the explanation on how to perform these studies with the new `FDI` tool.

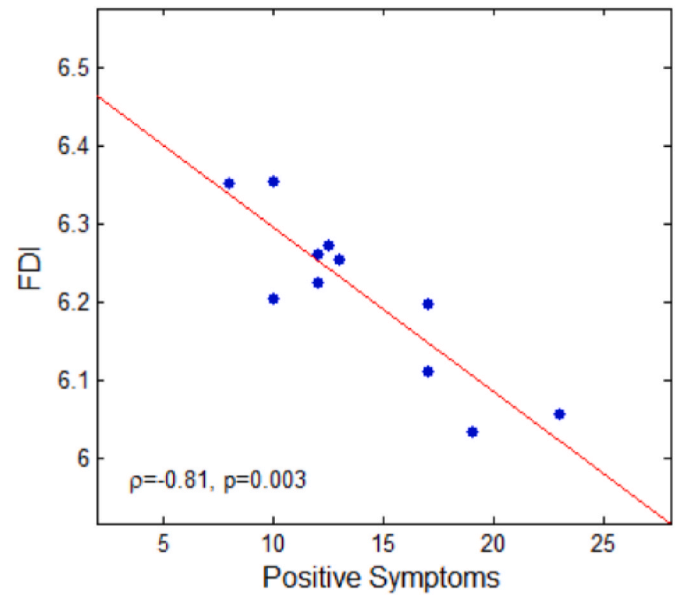

Fig. 7. Correlation between schizophrenia positive symptoms and FDI values for the whole brain.

6.1. *FDI for determining states of consciousness*

Determining the level of consciousness is a complex and multifaceted challenge with numerous clinical applications [32]. One approach involves exploring the complexity content of EEG signals during conscious and unconscious states [33]. Our metric, FDI, was designed upon this approach by utilizing FD as the reference measure to estimate signal complexity.

We applied the FDI methodology to analyse the complexity of 69 high-density EEG recordings after TMS collected from 18 healthy participants progressing from wakefulness to natural sleep and chemically-induced sedation via xenon and propofol exposure. TMS induces a non-invasive cortical perturbation which allows to measure the resulting electrical responses to causal interactions between neural areas. Our analysis revealed that FDI values were consistently and significantly lower during both sleep and sedation phases compared to wakeful periods, suggesting that FDI may serve as a reliable indicator of diminished consciousness [11].

To conduct this study, we first performed source modelling to localize the primary electromagnetic sources by using the MATLAB packages Brainstorm and SPM (https://www.fil.ion.ucl.ac.uk/spm/). Subsequently, we estimated the deterministic brain responses (cortical activations) caused by the TMS perturbation by applying nonparametric bootstrapping procedures on the corresponding TMS-evoked current distributions. The c-shell script for processing in parallel those 69 EEG epochs with the new `FDI` tool is shown in **Listing 2**.

In Listing 2, the parent directory pointed by *$EEGS_DIR* in line 2 contains individual folders for each registered EEG measurement. Within each subject-specific folder, the corresponding cortical activation estimates are stored as a MATLAB file named *Sources.mat*. Calls to `FDIConsole` use the parameters `'$eeg/Sources.mat'` (cortical activations), `'Times.mat'` (times), `362.5` (signal frequency), `'Vertices.mat'` (3D coordinates of cortical activations), `0.130` (window duration), `0` (starting time), `0` (window overlapping), `'maxWindows'` `1` (number of windows), `'subjectId'` `'$eeg'` (EEG register identification). Default values were used for parameters `'boxSide'` (128) and `'nStd'` (−1, no binarize).

Fig. 6 shows the receiver operating characteristic (ROC) curve and the area under the ROC curve (AUC) value obtained for the FDI measure as classifier for consciousness. An impressive AUC value of 0.96 was

```
% 1: TMS EEG: sources pre-binarized, 1 window from time 0s to time 0.130s
sources = './examples/1_1_TMS_preBinarized_Sources.mat';
times = './examples/1_2_TMS_Times.mat';
vertices = './examples/1_3_TMS_Vertices.mat';
frequency = 362;
windowTime = 0.130;
windowOverlap = 0;
iniTime = 0;
maxWindows = 1;
boxSide = 128;
subjectId = '1_TMS_BinarizedSources_Results';
FDIConsole(sources, times, frequency, vertices, windowTime, windowOverlap, iniTime, ...
           'maxWindows', maxWindows, 'boxSide', boxSide, 'subjectId', subjectId);

% 2: resting-state EEG: original sources, 3 windows of 1 second each, 0% overlapping
sources = './examples/2_1_Resting_State_Original_Sources.mat';
times = './examples/2_2_Resting_State_Times.mat';
vertices = './examples/2_3_Resting_State_Vertices.mat';
frequency = 500;
windowTime = 1;
windowOverlap = 0;
iniTime = 0;
nStd = 1; % number of standard deviations for binarization
boxSide = 128;
subjectId = '2_Resting_State_Original_Sources_Results';
FDIConsole(sources, times, frequency, vertices, windowTime, windowOverlap, iniTime, ...
           'boxSide', boxSide, 'subjectId', subjectId, 'nStd', nStd);
```

Listing 1. MATLAB code to test FDI.

```
#!/bin/csh
foreach eeg ($EEGS_DIR/*)
  matlab -nojvm -nodisplay -nosplash -nodesktop -r \
         "FDIConsole '${eeg}/Sources.mat' 'Times.mat' 362.5 'Vertices.mat' 0.130 0 0 \
                     'maxWindows' 1 'subjectId' '$eeg'" < /dev/null &
end
```

Listing 2. C-shell script for processing the TMS-evoked EEG dataset in parallel.

```
#!/bin/csh
foreach eeg ($EEGS_DIR/*)
  matlab -nojvm -nodisplay -nosplash -nodesktop -r \
         "FDIConsole '${eeg}/Sources.mat' 'Times.mat' 500 'Vertices.mat' 1 0 0 \
                     'nStd' 1 'maxWindows' 150 'subjectId' '${eeg}'" < /dev/null &
  matlab -nojvm -nodisplay -nosplash -nodesktop -r \
         "FDIConsole '${eeg}/SourcesAUD.mat' 'Times.mat' 500 'VerticesAUD.mat' 1 0 0 \
                     'nStd' 1 'maxWindows' 150 'subjectId' '${eeg}AUD'" < /dev/null &
  matlab -nojvm -nodisplay -nosplash -nodesktop -r \
         "FDIConsole '${eeg}/SourcesDAN.mat' 'Times.mat' 500 'VerticesDAN.mat' 1 0 0 \
                     'nStd' 1 'maxWindows' 150 'subjectId' '${eeg}DAN'" < /dev/null &
  matlab -nojvm -nodisplay -nosplash -nodesktop -r \
         "FDIConsole '${eeg}/SourcesDMN.mat' 'Times.mat' 500 'VerticesDMN.mat' 1 0 0 \
                     'nStd' 1 'maxWindows' 150 'subjectId' '${eeg}DMN'" < /dev/null &
  matlab -nojvm -nodisplay -nosplash -nodesktop -r \
         "FDIConsole '${eeg}/SourcesSAN.mat' 'Times.mat' 500 'VerticesSAN.mat' 1 0 0 \
                     'nStd' 1 'maxWindows' 150 'subjectId' '${eeg}SAN'" < /dev/null &
  matlab -nojvm -nodisplay -nosplash -nodesktop -r \
         "FDIConsole '${eeg}/SourcesVIS.mat' 'Times.mat' 500 'VerticesVIS.mat' 1 0 0 \
                     'nStd' 1 'maxWindows' 150 'subjectId' '${eeg}VIS'" < /dev/null &
end
```

Listing 3. C-shell script for processing the resting-state EEG dataset in parallel.

obtained, demonstrating excellent discrimination capabilities between conscious and unconscious states [11]. Moreover, examination of the ROC curve, reveals a rapid ascent towards the upper-left quadrant, indicating a robust discriminative ability of the classifier for the dataset in question. The steepness of the curve in its initial phase suggests a high true positive rate, or sensitivity, achieved at low false positive rates, implying a commendable specificity concurrently. Specifically, the classifier demonstrates a heightened ability to detect the presence of the condition with minimal misclassification of the negative instances at lower decision thresholds.

6.2. Analysing resting state functional networks in schizophrenia using `FDI`

We evaluated the utility of the FDI methodology for analysing resting-state EEG signals in Ref. [19]. This study aimed to characterize the dynamic changes in various functional networks affected by schizophrenia, a neurological disorder characterized by impairments in how information flows through the spontaneous brain networks [34].

Our analysis included 31 resting-state EEG recordings of 150 s, comprising 20 healthy subjects and 11 patients with schizophrenia. In order to assess psychopathology in the group of patients suffering schizophrenia, the Spanish version of the Positive and Negative Syndrome Scale (PANSS) was used [35]. The PANSS Positive Scale consists of 7 items that measure the severity of positive symptoms such as delusions, hallucinations, speech disorders, and thought disorder. Each item is scored from 1 (absent) to 7 (extreme), yielding a total Positive Scale score ranging from 7 to 49. Source modelling was performed in Brainstorm as described in **Section 2.1**. To obtain the brain activations at each time sample, we applied a binarization process using a threshold equal to the mean plus one standard deviation of the absolute values of the corresponding amplitudes of brain electrical currents across all time samples in the epoch. We then processed the brain activations in each resting-state functional network separately, following the cortical parcellation scheme proposed in Ref. [36], which identifies five distinct resting-state functional networks: AUD (auditory network), DAN (dorsal attention network), DMN (default mode network), SAN (salience network), and VIS (visual network).

To compute the FDI, we used a sliding window with a window length of 1 s and no overlap. The c-shell script for computing the FDI for each functional network in all subjects with the new `FDI` tool is shown in Listing 3.

In Listing 3, each subject-specific folder stores the cortical activations for the whole brain and the five functional networks, stored as MATLAB files named *Sources.mat*, *SourcesAUD.mat*, *SourcesDAN.mat*, *SourcesDMN.mat*, *SourcesSAN.mat* and *SourcesVIS.mat*, respectively. The 3D coordinates of the sources in each functional network are stored in files *Vertices.mat*, *VerticesAUD.mat*, *VerticesDAN.mat*, *VerticesDMN.mat*, *VerticesSAN.mat* and *VerticesVIS.mat*, while the times file (*Times.mat*) is the same for all networks. All calls to `FDIConsole` use the same parameters: `500` (signal frequency), `1` (window duration), `0` (starting time), `0` (window overlapping), `'nStd' 1` (number of standard deviations for binarization). and `'maxWindows' 150` (number of windows).

Our analysis of covariance (ANCOVA) revealed statistically significant reductions in FDI for schizophrenia patients compared to healthy controls in three networks [19]: AUD ($F = 7.72$, $p < 0.05$), DAN ($F = 7.33$, $p < 0.05$), and SAN ($F = 8.19$, $p < 0.05$). Furthermore, our findings demonstrated strong negative correlations between positive symptoms and FDI in both the whole brain and all resting-state networks, excluding VIS [19]. Fig. 7 shows the results for the non-parametric Spearman correlation (ρ) analysis performed on the FDI values for the whole brain. These results suggest that FDI has the potential to serve as a reliable biomarker for diagnosing schizophrenia and monitoring its severity based on clinical symptomatology.

7. Conclusions

`FDI` is a MATLAB program created to compute the fractal dimension index of brain activations derived from EEG signal source reconstruction. Designed with compatibility in mind, `FDI` works with popular platforms like Brainstorm and EEGLab to process their output files. Using GPU programming techniques, `FDI` efficiently computes the 3DFD and 4DFD values needed for determining FDI, as our performance analysis on two different hardware/software platforms indicated.

`FDI` prioritizes user experience by offering interactive capabilities via an easy-to-use graphical interface. Moreover, users can also opt for increased automation and flexibility through command-line invocation, enabling them to execute batch or parallel operations across multiple datasets and parameter configurations. To the best of our knowledge, `FDI` is the first publicly available software for computing the fractal dimension index of cortical activations extracted from EEG recordings.

To facilitate adoption in diverse research settings, we include detailed steps illustrating the application of `FDI` in two neuroimaging studies [11,19]. With these resources, neuroscientists can readily apply `FDI` to investigate cortical activity complexity within their own studies.

8. Institutional review board statement

This study was conducted in accordance with the Declaration of Helsinki. The EEG data used in the present study was acquired as part of prior publications [11,19]. Specifically, the protocol and informed consents for TMS-EEG data collection were approved by the Ethical Committee of "Ospedale Luigi Sacco" in Milan, Italy (Reference: 2012). Additionally, the acquisition and processing of resting-state EEG data were approved by the Institutional Ethics Committee of the University of Jaén in Spain (Reference: November 2016).

CRediT authorship contribution statement

Juan Ruiz de Miras: Writing – original draft, Validation, Software, Methodology, Funding acquisition, Formal analysis, Conceptualization. **Adenauer G. Casali:** Writing – review & editing, Validation, Software, Resources, Investigation, Data curation. **Marcello Massimini:** Writing – review & editing, Resources, Investigation, Data curation. **Antonio J. Ibáñez-Molina:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **María F. Soriano:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Sergio Iglesias-Parro:** Writing – review & editing, Validation, Resources, Investigation, Funding acquisition, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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