



STRUCTURAL ANALYSIS AND APPLICATION TO BRAIN IMAGING

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Abstract – Our goal is to organize the ElectroEncephaloGram (EEG) signal so as to describe and image various brain activities. Our work is based on a data structure, a graph, which sums up the brain activity in the spatial, temporal and frequency domains. From the information contained in the time-frequency map of EEG signals, a graph is constructed. In order to analyze the complexity of the signal, our method is based on a multi-scale approach with several levels of information extraction. To compare different EEG signals, we use techniques of graph-matching with our data structure. The developed algorithm is based on the A* algorithm that allows us to compare variations of the recorded EEG in term of latency, frequency, energy and activated areas. The results of this project show first, that the graph is an appropriate tool to reduce the cortical activity complexity, and second, that graph-matching offers some interesting perspectives in order to describe functional brain activity.

Key words: EEG, Wavelet, Graph-matching, ERD/ERS.

INTRODUCTION

Our goal is to describe brain functioning from cognitive tasks to low-level cerebral activations. For that purpose, we develop a generic analysis methodology based on a data structure holding all information arranged in a hierarchical way. By this structure, we consider the brain dimensions in terms of time, frequency or space. One of our preoccupations is to validate this methodology with classical approaches.

Electromagnetic activations are essential to brain functioning comprehension as they directly reflect information transmission between neurons. Thus it is possible to observe very short activations with duration of only a few milliseconds by means of ElectroEncephaloGram (EEG) or MagnetoEncephaloGram (MEG), whereas duration of the hemodynamic activation of several seconds is required in Positron Emission Tomography (PET) and Functional Magnetic resonance Imaging (fMRI) [3].

In addition to good time resolution, the EEG presents a good spatial distribution (with up to 256 electrodes on the scalp). It allows us to record cortical activity in a powerful way. The EEG principle is based on the fact that populations of neurons form complex neuronal networks whereby feedback loops are responsible for the generation of oscillatory activity and determine its resonance frequency. [2].

Even if only a small fraction of the total population of neurons is synchronized, the resulting oscillations may well outweigh the rest of non-synchronized neurons

[4,6]. This small fraction of synchronized neurons generates a specific signal at high frequency (>100Hz) with a low energy. Upon the task, a large neuron assembly could be necessary and synchronizes itself inducing an increase of energy [22]. As a reaction to an external event, the brain generates evoked responses in specific frequency bands and related brain areas. Thus, the information contained in EEG signals is coded in amplitude, frequency and spatial position. Therefore, the EEG presents a high level of complexity. Different methods, from parametric ([11,21]) to nonparametric methods (spectral analysis [9], coherence [8]) via time-frequency analysis [3,12,13,19], are investigating brain electrical signals.

The main idea of our approach is that the brain response to excitation is not linear but is a sum of linear responses in a non linear structure. The hypothesis is that the low level activity producing synchronization could be modeled by a linear response. These synchronizations are linked in a non linear structure. This non linear aspect is embedded in a graph and the continuous aspect in a time-frequency analysis. In practice, we construct a graph simplifying the data by keeping only the pertinent information and the link between the various components thereof. The information is extracted via time-frequency analysis (using the complex Morlet wavelet transform). Finally, the matching is the instrument to measure similarities between graphs. The matching step, performed by algorithms such as A* [15] is used to compare, to classify signals, to follow the cortical activity evoked by the stimulation, or to better understand the information contained in the signals.

The strategy followed is, first, to perform EEG signal modeling by a time-frequency representation. In the second step, we present the graph built in order to obtain a data structure including the spatial contents. To validate this process, we establish comparisons between our structure and a classical approach based on statistical techniques (Event-Related Synchronization, ERD and Event-Related Synchronization, ERS). Before presenting the results, we develop the methodology used to compare two graphs. The interest comparison is demonstrated at the end of the discussion section. Finally, we conclude with our current developments and prospects in brain activity analysis.

MATERIAL AND METHODS

Data Set and Acquisition

Subjects and stimulus material

Ten subjects, between 30 and 50 years of age, participated in this study. All subjects were right handed as confirmed by a standard test for handedness, had no hearing impairment, had normal vision or were corrected to normal vision, and were without past history of abnormalities of the central nervous system.

The participants had to apply a certain cognitive strategy, known to involve the frontal lobes in particular. They answered questions of approximation asked in the course of the paradigm (for instance "How many oranges in a kilogram?").

Experimental Procedure

Subjects sat in front of a computer screen and were confronted sequentially with the stimulus material, presented via loudspeakers positioned on both sides of the screen. In detail, the temporal sequence of the trials is (see Fig.1):

1. a question known to involve the frontal lobe,
2. the thinking useful to elaborate a solution to the question raised,
3. the answer to the question ,
4. a pause of 5 seconds at the minimum.

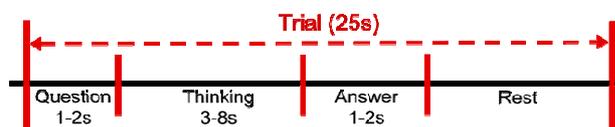


Figure 1. The temporal sequence of the experimental procedure.

The EEG was recorded from 25 Ag-AgCl electrodes positioned on the scalp in proportion to a 5x5 matrix (Fig 2). Uniform spacing was allowed between the electrodes. The band pass filter of the amplifier was set between 0.54 and 60Hz, with a 50 Hz notch filter included.

The EEG was recorded with a sampling rate of 250 Hz during the presentation of stimulus blocks. Individual

EEG recordings were scanned visually for artifacts. Only answered trials, free of artifacts were included in the subsequent analysis. Individual recordings were scanned visually for question and answer trigger marks. Then the recordings were trimmed to keep from 5 seconds before the beginning up to 5 seconds after the end of the answer.

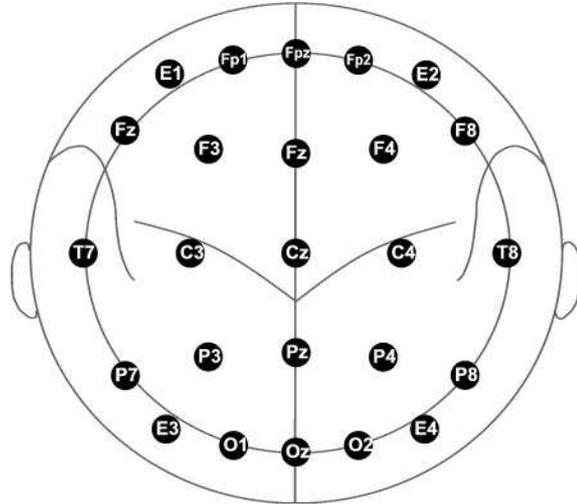


Figure 2. Positioning of the 25 EEG electrodes on the scalp. Only the E1-4 electrodes do not follow the conventional electrode placement.

Signal Modeling

For a good understanding of cortical functioning, it is important to simplify the complex EEG signal. The simplification process we use is based on neuronal information coding. The amplitude, the frequency and the spatial position had to be investigated. Therefore a time-frequency transform is applied to extract the frequency, latency and duration of oscillatory phenomena as accurately as possible. The choice of the time-frequency transform was concerned with wavelet decomposition. The wavelet interest is its dual temporal/frequency representation that can tell when is which frequency, i.e. a technique in which the frequency resolution changes with the temporal localization.

Time-frequency representation

Wavelets are mathematical functions that decompose data into different frequency components, and then study each component with a resolution which is adapted to its scale [5]. This approach is well suited to our problem to describe EEG synchronization as precisely as possible.

A *mother wavelet* [14] is a function $\varphi \in L_1 \cap L_2$ with $n+1$ null moment (L_1 is the space of integrable functions on \mathfrak{R} and L_2 is the space of square integrable functions on \mathfrak{R}). n acts on the shape of φ curve representation (the larger the value of n , the more oscillations φ will have).

Atoms of the wavelet transform are defined by the translation and the dilation of φ . For any scale factor

$a \in \mathfrak{R}^{+*}$ and any position factor $b \in \mathfrak{R}$, an atom is defined by:

$$\varphi_{a,b}(t) = \frac{1}{\sqrt{a}} \varphi\left(\frac{t-b}{a}\right)$$

The family $\{\varphi_{a,b}\}_{a,b \in \mathfrak{R}^{+*}, \mathfrak{R}}$ is the wavelets family associated to φ .

The *continuous wavelet transform* of the function f of finite energy is the family of the coefficients $C_f(a, b)$ defined by:

$$C_f(a, b) = \int_{-\infty}^{+\infty} f(t) \overline{\varphi_{a,b}(t)} dt$$

The chosen mother wavelet $\varphi_{a,b}(t)$ is the complex Morlet wavelet which has a simple analytic form and has a good time and frequency resolution [6]. The complex Morlet function is defined as the product of a complex exponential wave and a Gaussian envelope.

$$\varphi(t) = \pi^{-\frac{1}{4}} e^{ikt} e^{-\frac{t^2}{2}}$$

where constant k is the wavenumber defined in accordance with the signal length.

The wavelet estimate of the energy density in time-scale plane -*scalogram*- is given by:

$$E^{a,b} = |C_f(a, b)|^2$$

This estimate can be translated to the time-frequency plane:

$$E^{a,b} = |C_f(f, a)|^2 = \left| \sqrt{\frac{2\sqrt{\pi}f}{k}} \int_{-\infty}^{+\infty} f(t) e^{-\frac{1}{2}\left(\frac{2\pi f}{k}(t-a)\right)^2} e^{i2\pi f(t-a)} dt \right|^2$$

By this translation, we can represent our EEG signal in a time-frequency map as shown on the figure 3 (b); the high energy level is represented by a red color and the low one by a blue color. Consequently, if a red burst appears on the map, it means that this frequency is strongly presents at this given time (for instance, lots of 10 Hz at 0.2 sec).

Conserved information

With the use of the wavelet transform, the frequency, latency and duration of the oscillatory phenomena are identified on a map. This map is composed of pixels. Each pixel represents the energy of a defined frequency at a precise time (see fig3 (b)). The next step is to extract the interesting pixels to model the EEG signal only with its main characteristics. A threshold is applied on the time-frequency map to remove the noise and background activity. This threshold is defined for each map according to the pixel level. After a well study of the

map composition, we observe that the map histogram is bimodal, one mode, in the low level, pixel represents the noise and the background activity and the other mode, in the high level pixel, represents the event-related activity. A bi-Gaussian modeling is used to define the threshold level. Consequently by removing low level pixels we only keep the interesting EEG features (Fig. 3 (c)).

After all, a watershed algorithm [1, 18] is use to segment the thresholded map into bursts of interest. This algorithm performs segmentation by labeling connected areas within the gradient of the time-frequency image. Regarding the morphological gradient of the original image as a topographic surface, the rule of assigning labels can be derived from physics: a particle in free fall on a topological surface will move due to gravity downward to the deepest neighboring location. The task performed by the present algorithm is to trace a path for each non-minimum point on the surface (origin) to a minimum (destination), and to mark all pixels along the path with label of the minimum. This path is the final boundary of each burst of the time-frequency map (Fig. 3 (d)). Each segmented burst i is individually characterized by four features:

- t_i : time position on the energy maximum of the burst,
- f_i : frequency position of the energy maximum of the burst,
- \hat{E}_i : maximum energy of the burst,
- \bar{E}_i : averaged energy of the burst.

By this signal modeling, we have extracted and characterized each oscillation of interest represented by a burst in our time-frequency map. Consequently a signal S can be sum by a set of bursts features, with the burst set B and $|B|$ its cardinal:

$$S = \bigcup_{i=0}^{|B|} (t_i, f_i, \hat{E}_i; \bar{E}_i)$$

Even if the amplitude and frequency information has been investigated, we have no information about the spatial position. The link between burst along time and frequency and its spatial position should be also modeled. In a first approximation, it would be possible to sum up the brain activity from an electrode by a set of energy bursts, but this approach could not easily describe the dependence relation between bursts. Consequently, we chose to use a graph structure able to describe on the one hand the energy burst localization in time, frequency and spatial space and, on the another hand the dependence relation.

Graph structure and graph-matching

Graph definition

A *graph* is a pair $G = (V, E)$ of sets satisfying $|E| \leq |V|^2$, thus the elements of E are 2-element subsets of V . The elements of V are the vertices of the graph G , the elements of E are its edges. In a

directed graph, E is a set of directed edges. A labeled graph is a quad $G(V, E, \alpha, \beta)$, where α is the vertex labeling function and β the edge labeling function. Labels describe the vertices and edges properties.

Naturally, the main approach is to combine bursts extracted from the time-frequency map with the graph vertices. We obtain a directed labeled graph $G(V, E, \alpha, \beta)$ defined as following:

- V : non empty and finite set of vertices, each vertex represents an energy burst.
- $E \subset V \times V$: finite set of directed edges, each edge represents the link between two bursts.
- L_V : non empty and finite set of labels of one vertex defined by (\hat{E}, \bar{E}) .
- L_E : non empty and finite set of labels of one edge defined by (Δ_t, Δ_f) with Δ_t the time variation and Δ_f the frequency variation from the edge origin until the edge destination.
- $\alpha: V \rightarrow L_V$: vertex labeling function.
- $\beta: E \rightarrow L_E$: edge labeling function.
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Application to the EEG activity representation

To reduce the signal complexity, we use an abstraction through a simple model. For that, we conserved in the time-frequency representation the burst of significant energy level. To chain these bursts inside the graph representation is our main difficulty. As a connection between all bursts implies a huge complexity in the data structure and the graph manipulation, it is necessary to limit the edges number.

To respect the brain activity and enhance the structure ability, we only consider edges in which the time distance between the two bursts is low in accordance to the detail level (frequency domain). Consequently the structure allows us to manipulate 2-complex representation (fig 3(e)).

Graphs comparison

Comparing two cortical activities corresponds, in our case, to compare the variations of the recorded EEG answer in term of latency, frequency, energy and activated areas. Thus, estimate these variations, with our data structure, is equivalent to measure the graph similarity. For that two steps are necessary, the first one is to find the most common subgraph in the two graph candidates, it is the graph matching problem. The second is the measure computation between these two common subgraphs. Generally a unique optimization algorithm is used to combine these two steps, the graph matching problem using a similarity measure.

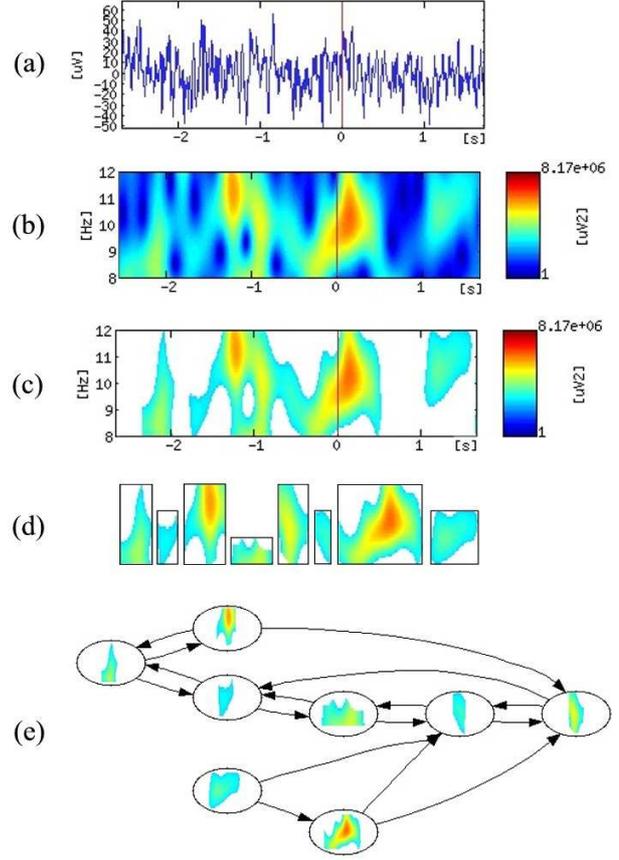


Figure 3. EEG signal modeling. (a) the raw EEG signal, (b) the time-frequency map from a Morlet wavelet decomposition between 8-12Hz, (c) the adapted thresholded time-frequency map, (d) the bursts extracted from the thresholded time-frequency map by a watershed algorithm, (e) the graph built from the extracted bursts, each burst is linked with its two nearest bursts in time and frequency.

This matching is done by isomorphism, we are looking for the best association between the vertices and the edges of $G_1(V_1, E_1, \alpha, \beta)$ and the vertices and the edges of $G_2(V_2, E_2, \alpha, \beta)$. A graph isomorphism between G_1 and G_2 is a bijective mapping $f: V_1 \rightarrow V_2$ such that

1. $\forall v \in V_1, \alpha_1(v) = \alpha_2(f(v))$
2. $\forall (v, e) \in V_1 \times V_1, \beta_1(v, e) = \beta_2(f(v), f(e))$.

For the same brain process, the neuronal oscillations and the number of oscillations are not totally identical. So the two brain processes that we want to compare have not necessarily the same length, it means trying to match a graph with a subgraph of a larger graph. To get this isomorphism, similarity distances have to be defined to know how similar two bursts or edges are. For each label l , a similarity S_l is defined: $S_l \in [0, 1]$ with $l \in \{L_V, L_E\}$.

By the mean of these similarities, it is possible to estimate the similarity $S_{G_1-G_2}$ between two graphs G_1 and

G_2 . The goal is to maximize this similarity to find the most similar common subgraph.

$$S_{G_1-G_2} = \frac{\sum_{l \in L_V} \sum_{v_1 \in V_1} \sum_{v_2 \in V_2} M(v_1, v_2) \times S_l(v_1, v_2)}{\sum_{l \in L_V} \sum_{v_1 \in V_1} \sum_{v_2 \in V_2} M(v_1, v_2)} + \frac{\sum_{l \in L_E} \sum_{e_1 \in E_1} \sum_{e_2 \in E_2} M(e_1, e_2) \times S_l(e_1, e_2)}{\sum_{l \in L_E} \sum_{e_1 \in E_1} \sum_{e_2 \in E_2} M(e_1, e_2)}$$

M is the result matrix of the best matching between G_1 and G_2 .

The implemented matching algorithm is based on the A* algorithm which is a graph search algorithm that finds a path from a given initial vertex to a given goal vertex [15]. It employs a heuristic estimate that ranks each vertex by an estimate of the best route that goes through that vertex. It visits the vertices in order to this heuristic estimates. Consequently the A* algorithm permits to find the optimal solution, however it is not optimized in term of computation time ($O(\log(|V|))$ complexity, with $|V|$ the number of graph vertices). Some algorithms as those proposed by Gold or Ranganath [10,17] could be more optimized.

Similarity formulation

The similarity functions are defined for all labels $(a) l \in \{L_V, L_E\}$. These functions need normalized measures between two labels. In this case, the normalization is done by using the distance maximum between two labels in destination $V_1 \times V_2$ or $E_1 \times E_2$, for instance:

$$S_{\Delta_t}(e_1, e_2) = 1 - \frac{\Delta_t(e_2) - \Delta_t(e_1)}{\Delta t_{\max}}$$

$$S_{\Delta_f}(e_1, e_2) = 1 - \frac{\Delta_f(e_2) - \Delta_f(e_1)}{\Delta f_{\max}}$$

The Δ_t and Δ_f functions used l_t expression in time and frequency domain. The purpose was to validate the structure and the approach, not the distance functions or similarity formulation. Moreover numerous existing formulations are possible from Minkowski Norm to fuzzy expressions [20]. A specific work on this question is in process.

Event-related De/Synchronization

To validate our approach, we need to compare our results with results from a well-known technique. The event-related phenomena represents frequency specific changes of the ongoing EEG activity and may consist in general terms, either of decrease or of increase of power

in a given frequency bands. This may be considered to be due to a decrease or an increase in synchrony of the underlying neuronal populations, respectively. The former case is called event-related desynchronization (ERD) and the latter event-related synchronization (ERS). A method has been developed, mainly by Pfurtscheller et al. [16], to measure these phenomena. The classical method to compute the time course of ERD includes the following steps (Fig. 4):

1. raw EEG epoch selection.
2. bands pass filtering of all event-related trials.
3. squaring of the amplitude samples to obtain power sample.
4. averaging of power samples across all trials.
5. averaging over time to smooth the data and reduce the variability.

This procedure results in a time course of band power values, including phase-locked power changes as well. To obtain percentage values for ERD/ERS, the power within the frequency band of interest in the period after the event is named A whereas that of the preceding baseline or reference period is named R . ERD or ERS is defined as the percentage of the power decrease or increase, respectively, according to the expression:

$$ERD\% = \frac{A - R}{R} \times 100$$

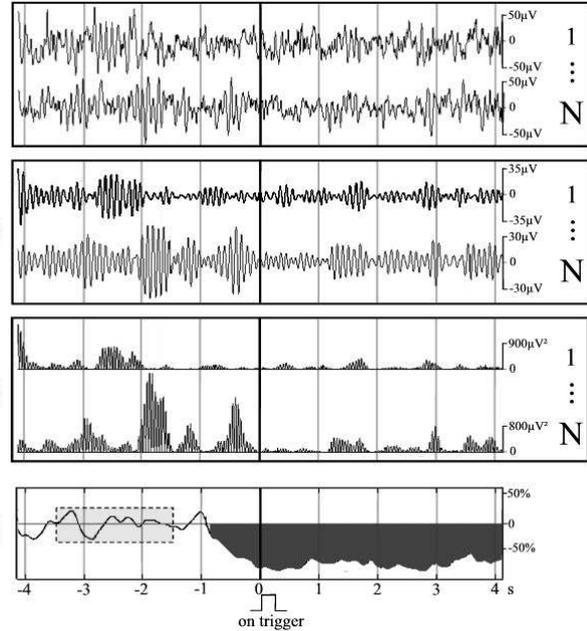


Figure 4. Principle of ERD processing. (a) Raw EEG signals, (b) bandpass filtered signals (8-12Hz), (c) squared samples, (d) relative power of the averaged squared samples on a chosen trigger, in black the significant difference from the reference (dashed rectangular).

The same kind of procedure can be applied by using the wavelet transform and the marginal density instead of the band pass filtering. The burst structure, issued of the

averaged time-frequency map, was a three dimension object (energy over time and frequency) whereas the classical ERD was a two dimension object (power over time). In order to compare them, we used the concept of marginal density in a chosen frequency band. This marginal density D_m sums up the energy of the burst over the time, with E the scalogram:

$$D_m(t) = \sum_{f=f_{\min}}^{f_{\max}} E(t, f)$$

The method adapted to the use of the wavelet transform can be computed by following the different steps (Fig 5):

1. raw EEG epoch selection.
2. wavelet transform of all event-related trials.
3. marginal density of the time-frequency map to obtain energy sample.
4. averaging of energy samples across all trials.
5. averaging over time to smooth the data and reduce the variability.

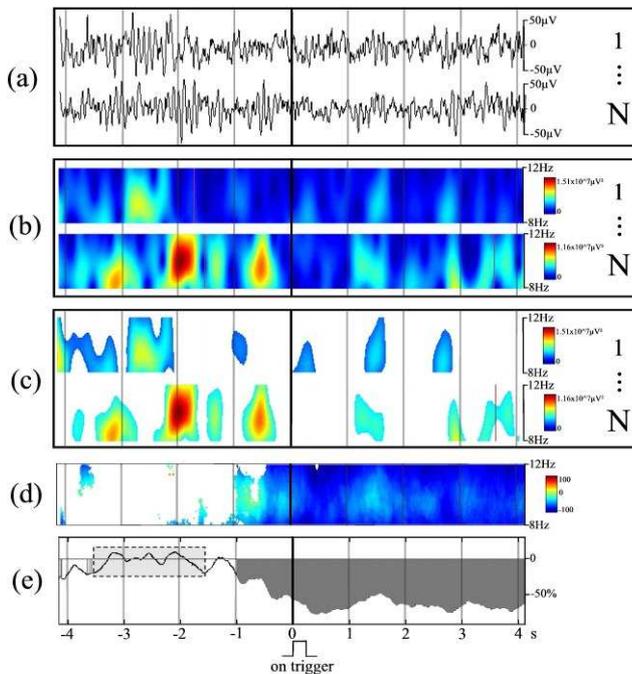


Figure 5. Principle of time-frequency ERD processing. (a) Raw EEG signals, (b) time frequency map (8-12Hz), (c) bursts map, (d) relative power of the averaged bursts map on a chosen trigger, only values significantly different from the reference are depicted, (e) relative power of the marginal density of the averaged map on a chosen trigger, in black the significant difference from the reference (dashed rectangular).

Both of these methods bring the description of the time course of the cortical activity in correspondence with a reference period. The following section describes the comparison of them.

RESULTS

Signal modeling validation

In order to validate the chosen model based on the extraction of the burst from a time-frequency map, we compared the event-related synchronization and desynchronization description from the classical method of Pfurtscheller and the one based on our burst structure (see the precedent section).

A statistical Wilcoxon parametric test was used to know if the two methods are significantly different or not. This Wilcoxon test was chosen as it is non parametric test (no hypothesis on the sample distribution) appropriated for paired samples. The test was performed on the 1000 original signals (40 trials on 25 electrodes, see Materials and methods, Experimental procedure).

The first time, the test was applied to compare the classical ERD and the marginal density of the time-frequency map. The result shows that they are not significantly different, with $\alpha=0.01$ and $p=0.8736$.

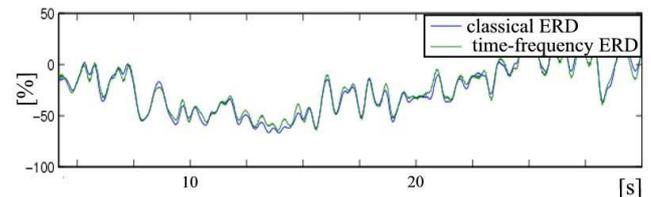


Figure 6. No significant difference between ERD from the classical method and ERD from the marginal density of the time-frequency map.

The second time, the test was applied in order to compare the classical ERD and the marginal density of the burst structure, i.e. the segmented time-frequency map. $\alpha = 0.01$ and $p = 0.4395$.

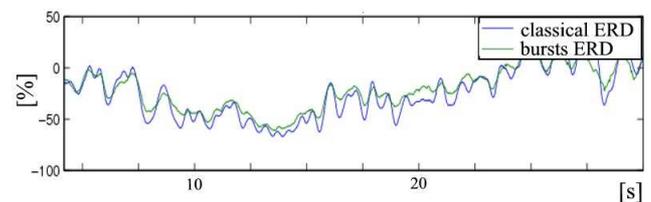


Figure 7. No significant difference between ERD from the classical method and ERD from the marginal density of the segmented time-frequency map (burst structure).

As we have proved that the data structure did not loose important information, indeed we are able to observe the same phenomena as with the classical ERD, we can go further in the use of this structure. The next section gives an example of this use.

First result of graph matching

Afterward we evaluated the graph-matching method interest. Indeed this latter is able to compare two cortical activities and, in the same time, to precise the going evolution. We looked on the functional evolution of the cortical activity according to the data protocol.

The neurophysiologic knowledge brought some information about the well known cortical activation. In our case, three main tasks should be found, first the question hearing activating the auditory cortex then the thought activating the prefrontal lobe and last the answer enunciation activating the motor cortex.

The objective of the experimentation was to measure the activation delay between each area of interest. We chose the middle electrode of each area: P3 in the auditory cortex, F4 in the prefrontal lobe and Cz in the motor cortex. Then we matched the burst structure issued of these three electrodes. The matching uses the vertices and edges labels (time, frequency, averaged energy and maximum energy burst). These labels give us similarity values which are interpreted in accordance to the physiological data.

The following results are one example of what could be obtained. By studying the time shift between each graph we found a delay of 0.9s from P3 to F4 and of 3.8s from P3 to Cz (Fig. 8). So the time delay is going from P3 to F4 and later from P3 to Cz. We found again the same process as the one described by the neurophysiologist. And the results appear to be in the same range as the physiological expectations.

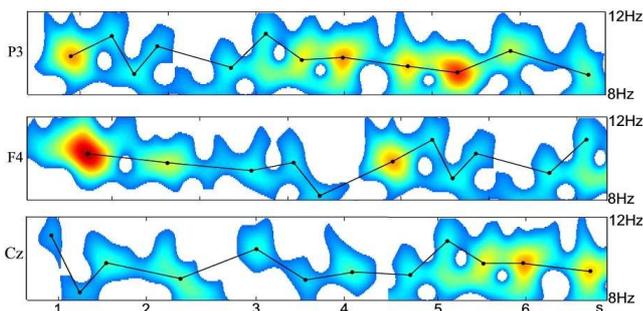


Figure 8. Description of cortical activity evolution from P3 to Cz via F4 by burst structure matching (trial 14, 7-13Hz). The evolution features are the following, between P3 and F4: 0.9s time shift, between P3 and Cz: 3.8s time shift.

DISCUSSION

Our goal is the description of brain functioning from cognitive tasks to low levels cerebral activations. For that purpose, we have developed a generic analysis methodology based on a data structure holding all information arranged in a hierarchical way. This structure -a graph- consists of information from the whole brain dimensionalities. The time and frequency and energy features are extracted from Morlet wavelet decomposition. The spatial dimension is considered by the signal origin, i.e. the spatial position of the acquiring electrode.

During a trial the recorded EEG signal comes from the confrontation with the stimulus. As the signal is represented in our case by graphs, the event-related brain activities can be associated to the set of independent graphs. Since these activities are related to one main task,

they are linked as the graphs are linked. The links between these graphs are studied by the graph-matching technique. Thanks to this technique we should be able to add some spatial edges linking the graphs themselves in the spatial domain.

The very important point after the methodology adjustment is the method validation. This one has been done in two steps. First we have computed the ERD/ERS technique on our data set and then we have compared these results with those obtained in the same way with our signal abstraction. A wilcoxon statistical test has demonstrated that they are not significantly different. This proves that the data reduction has correctly been carried out. Therefore the used of this abstraction decreased hugely the amount of data, for instance the raw data size was about 20MB for a recording of thirty minutes and the reduced data about few kilo bytes. Moreover we can study all conventional EEG waves (alpha, beta, gamma, ...) or subject adapted frequency band.

The second step was to demonstrate the graph-matching interest in brain activity description. The first computation, presented in the last section, showed it is possible to have different kind of brain functioning information. The time delay gives information about the information transfer from one brain area to another; the frequency delay shows the rhythm variations and the energy variations illustrate the size of the mobilized neurons population.

The results obtained with the presented method are encouraging. However some improvements had to be brought, mainly in the graph structuring and graph matching. First of all, the edge building is still a problem. How be sure that two vertices had to be linked? The different building possibilities had to be analyzed in a deeper way and tested with simulated data. Secondly the similarity functions used in the graph matching process are actually very simple. If they allow a structure validation they do not have an acceptable behavior. Our current work is based on a theoretical expression of the distance function on the time, frequency and spatial domain. As the physiological mechanisms are different for the information transfer (spatial aspect), transmission and reaction time (time aspect) or rhythm variations (frequency aspect), a specific formulation is needed for all these dimensions. The study complexity is linked to the non-linear behavior of brain activity for each of these dimensions. Lastly some optimized matching algorithm can improve the computation speed.

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