FUNCTIONAL BRAIN MAPPING WITH HIGH-TEMPORAL RESOLUTION: INTRODUCING "EVOLUTIONARY ACTIVATION CELLS"

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ABSTRACT

Functional image sequences obtained from image reconstruction techniques applied to Magneto and Electroencephalography (M/EEG) data convey a large amount of information in the space and time domains. Conventional approaches to their analysis necessitates considerable input from an expert to extract pertinent information. We introduce in this paper an automatic data sequencing procedure of these brain activation maps. Our main objective consists in facilitating and accelerating the extraction of spatiotemporal activation patterns of interest called *activation cells*. These cells are tracked across time with consistent labeling that follows a small set of predefined evolutionary scenarios. Resulting graphical synopsis are exemplified on epileptic spike analysis and indicate satisfactory consistency with human expertise.

1. INTRODUCTION

Image reconstruction techniques applied to scalp Electro and Magnetoencephalography (E/MEG) data produce brain activation maps with excellent time resolution at the infra millisecond scale. This results in series of image activation sequences of typically 1000 images per second of recording. This information rate makes the analysis cumbersome to experimentalists. The choice of salient features of interest for subsequent analysis and inferences may even end-up being very subjective. The E/MEG expert usually describes the instantaneous activation maps obtained in terms of number of activation sources. For each source, the location, amplitude and occasionally spatial extension of the cortical areas involved are reported and considered for subsequent inference and classification across subjects and/or conditions. Though E/MEG benefits from unique time resolution, the very description of the evolution of brain activations with time is usually discarded from further consideration and exploration. This paper introduces a systematic approach to the automatic analysis of these brain image sequences. We exemplify the concepts and methodology in the context of epileptic spike classification.

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Epileptic spike-wave complexes in partial epilepsy are often rapidly initiated and resolved within an epileptogenic network of brain areas. These fast propagation and interplay of cortico-cortical activations are excellent candidates to E/MEG imaging. In this context, there is a primary need for spike classification as each patient may be subjected to multiple types of spikes in terms of E/MEG topography and dynamics. Expert neuro-electrophysiologists are trained to classify epileptic spikes – most notably from signals at EEG scalp electrodes – and have accumulated considerable empirical knowledge to infer e.g. the number of possible foci from which the spikes may originate [1]. Because daily human classification of scalp recordings has revealed to be tedious and highly-subjective (see e.g. [2]), a great number of automatic techniques have been proposed and are often integrated in commercial software solutions to the neurologist [3]. E/MEG source reconstruction approaches have the potential to improve the elucidation of the spatial origins of the spikes and represents an active field of research ([1],[2],[4]) but most of them still require considerable input from an expert. Recently, Ossadtchi et al. proposed a fully-automatic combination of spike detection, source localization and classification techniques [5]. However, this approach – like most of the published material – was built on equivalent focal dipolar models, therefore has a limited potential to elucidate the time evolution and propagation of the cortical activations involved as the spike-wave complex unfolds.

The methodology presented here aims at approaching some of these issues with simple topological considerations, which elementary building-blocks are called *evolutionary activation cells*.

2. METHODS

2.1. Objectives and basic principles

The primary objective of our approach consists in reaching significant dimension reduction in the description of the original data (i.e. spatiotemporal sequences of cortical currents). Space and time must therefore be compactly encoded in 2D graphs that need to be easily understood by an operator with minimum training. Beyond human readability, specifications also enforce that data decomposition will be subjected to quan-

titative analysis for e.g. data classification such epileptic spike sorting. Therefore, instantaneous activation maps that support a dense distribution of currents need to be efficiently resampled through a segmentation into elementary spatiotemporal blocks that will be evolving in space and time according to a set of admissible scenario.

These specifications translate into a sequential process that unfolds as the following:

1. Cortical current map at each time instant $t+1$ is spatially segmented into elementary activation cells;
2. For each activation cell at time t, its descent is identified from the activation cells at $t+1$ through a set of evolutionary scenarios;
3. Cells are tracked from t to $t+1$ with consistent labeling; newborn cells obtain new labels.

The entire process from 1 to 3 is then repeated for all $t \in \tau$. Once the process is completed on all available time samples, the corresponding spatiotemporal decomposition into activation cells with their associated genealogy is synthesized in a graphical synopsis. We shall now describe each of these elementary steps in details.

2.2. Spatial segmentation into cells

The M/EEG inverse problem from scalp surface data consists in modelling the corresponding distribution of cortical currents. Our approach operates in the context of distributed dipole models for which image reconstruction techniques applied to M/EEG data produce at time t an activation map $\mathcal{A}(t)$. $\mathcal{A}(t)$ is the set of local neural current estimates $a(\mathbf{r},t)$ on Γ, a manifold of $\mathbb{R}^3$:

$$\mathcal{A}(t) \doteq \{a(\mathbf{r},t), \mathbf{r} \in \Gamma\}. \quad (1)$$

Our main objective consists of the spatiotemporal characterization of the entire sequence of activation maps $\mathcal{A} = \{\mathcal{A}(t), t \in \tau\}$, τ a time-window of interest, by tracking activation cells in the spatial and temporal domains. The segmentation of $\mathcal{A}(t)$ into elementary spatial clusters – the activation cells – is guided by the following working hypothesis:

$\mathbf{Hyp.1}$: instantaneous brain activation $\mathcal{A}(t)$ is sparse and focal. Therefore, the spatial distribution of activation cells is also sparse and focal.

While some approaches to the resolution of the M/EEG inverse problem may explicitly consider sparse-focal source models [6], statistical inference across experimental conditions define thresholds that isolate significant current amplitudes [7]. The thresholded current maps can subsequently be segmented into a set of cells that are spatially connex. We then suggest a new definition for $\mathcal{A}(t)$ as a set of $N(t)$ activation cells:

$$\mathcal{A}(t) \doteq \{a(\mathbf{r},t), \mathbf{r} \in \mathcal{C}(t)\}, \quad (2)$$

where:

$$\mathcal{C}(t) \doteq \{\mathrm{C}_i(t), i \in [1, N(t)]\}, \quad (3)$$

and:

$$\mathrm{C}_i(t) \doteq \{\mathbf{r}, a(\mathbf{r},t) \in \mathcal{A}(t) \text{ and } \mathrm{C}_i(t) \text{ connex}\}. \quad (4)$$

In practice, Γ is sampled with spatial elements such as voxels (volumic case) or triangle vertices (surfacic case). Cells in $\mathcal{C}(t)$ are obtained by the exploration of the connectivity tree of the spatial elements in $\mathcal{A}(t)$.

2.3. Tracking cells across time: evolutionary scenarios

Tracking of activations cells from t to $t+1$ observes the following hypothesis:

$\mathbf{Hyp.2}$: The high temporal resolution of M/EEG translates into a high degree of similarity between $\mathcal{A}(t+1)$ and $\mathcal{A}(t)$. Consequently, mutations of each element in $\mathcal{C}(t)$ to elements in $\mathcal{C}(t+1)$ follow a small set of predefined evolutionary scenario: i) survival in $\mathcal{C}(t+1)$, ii) dissociation into multiple elements of $\mathcal{C}(t+1)$, iii) merging into one single cell of $\mathcal{C}(t+1)$, and iv) elimination. The fifth scenario concerns the identification of cells that are newborn at time $t+1$.

To sort out the scenario than may relate any element $c \in \mathcal{C}(t)$, to $c' \in \mathcal{C}(t+1)$, the normalized rate of spatial overlap between c and c' is introduced and is defined as:

$$V(c,c') \doteq \frac{S(c \cap c')}{\max_{c'' \in \mathcal{C}(t+1)} S(c'')}, \quad (5)$$

where $S(c)$ is the surface area of cell c.

c' is considered a priori as a breed of c if $V(c,c') > 0$ and the entire descent of c is defined as:

$$\mathcal{D}(c) = \{c' \in \mathcal{C}(t+1), V(c,c') > 0\}, \quad (6)$$

which has the following properties:

1. $\{\cup \mathcal{D}(c), c \in \mathcal{C}(t)\} \subset \mathcal{C}(t+1)$;
2. There is no guarantee that: $\forall c_1, c_2 \in \mathcal{C}(t),\ \mathcal{D}(c_1) \cap \mathcal{D}(c_2) = \emptyset$.

Authorized evolutionary scenarios can now be expressed using $\mathcal{D}(c)$:

1. c is a survivor from $\mathcal{C}(t)$ in $\mathcal{C}(t+1)$ if card$(\mathcal{D}(c)) = 1$;
2. c splits in new cells if card$(\mathcal{D}(c)) > 1$;
3. c merges with other elements of $\mathcal{C}(t)$ if $\exists\, \alpha \subset \mathcal{C}(t)$ and $\exists!\ c' \in \mathcal{C}(t+1)$, $\forall c \in \alpha, c' \subset \mathcal{D}(c)$;
4. c is eliminated if $\mathcal{D}(c) = \emptyset$;
5. c' is a newborn if $c' \cap \{\cup \mathcal{D}(c), c \in \mathcal{C}(t)\} = \emptyset$.

2.4. Tracking cells across time: labeling

Time-tracking of cells from t to $t+1$ necessitates consistent labeling of i) surviving cells; ii) cell breeds following cell splitting and iii) newborn cells with new labels. We therefore introduce the labeling operator $\mathrm{L}(\cdot)$ defined as:

$$\begin{array}{rcl} \mathrm{L} : \mathcal{A} & \rightarrow & \mathbb{N} \\ c & \mapsto & j \end{array} \tag{7}$$

Consistent labeling with L is enforced by the following labeling rules:

1. Scenario sorting: any cell of $\mathcal{C}(t+1)$ either originates from a single ascent in $\mathcal{C}(t)$ according to the *split* or *merge* evolutionary scenario, or is a newborn cell;

2. Instantaneous label unicity: $\forall t \in \tau$, all cells in $\mathcal{C}(t)$ must wear a different label;

3. Consistency rule:

$$\begin{array}{c} \forall t \in \tau, \forall c \in \mathcal{C}(t), \forall c' \in \mathcal{C}(t+1), \\ \mathrm{L}(c') = \mathrm{L}(c) \Leftrightarrow c' = \underset{c'' \in \mathcal{D}(c)}{\arg\max}\, \mathrm{V}(c, c''). \end{array} \tag{8}$$

These labeling rules are applied sequentially to all cells in $\mathcal{C}(t+1)$ once labeling of cells in $\mathcal{C}(t)$ is completed. Newborn cells with no ascent and cells resulting from cell splitting with no available ascent label are tagged with a new label.

2.5. Synopsis: building the genealogy tree

This last step in the exploration of activation maps consists of the generation of a compact graphical synopsis. This new object can be interpreted as a genealogy graph of all cells in $\mathcal{A}$ and may serve as both a 4D data visualizer to the human operator and as a graph tree in subsequent quantitative analysis and contrast inference between e.g. experimental conditions. Each activation cell is represented as an horizontal bar which length encodes its lifespan. Its color encodes the instantaneous location of its centroid (Fig. 1). Position of the bar on the y-axis encodes its label. Additional graphical items may be added to the synopsis to represent for the scenarios that ruled cell evolution from t to $t+1$.

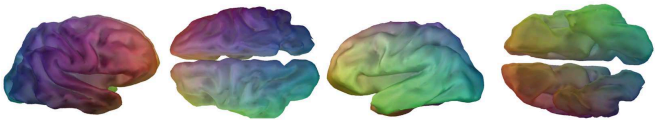

Fig. 1. Colormap used for the encoding of the locations of cortical activation cells.

3. RESULTS

The method is illustrated on a small set of averaged interictal epileptic spikes recorded from a voluntary patient on the 151-channel whole-head array at the La Salpêtrière hospital (VSM MedTech). Spikes were subsequently classified in two classes by a neurologist in accordance to their clinical relevance. To increase SNR, 20 spikes from the same class were then averaged, time-locked to the spike peak latency.
Manual data exploration of the corresponding MEG source maps indicated that the two types of spikes originated from the lateral right temporo-occipital junction (T spikes) and the right hippocampal region (H spikes), respectively.
The cell sequencing approach was applied to the H-spike average (Fig. 2) and two distinct T-spike averages (T1 & T2, Fig. 3) obtained from two separate acquisition runs for consistency checking of the method.
Fig. 3 shows great similarity between the T1 and T2 cell genealogy graphs, thereby confirming the consistency of the cell decomposition with the outcome of human expert identification. About $t = 0$, a waterfall of short activation cells marks

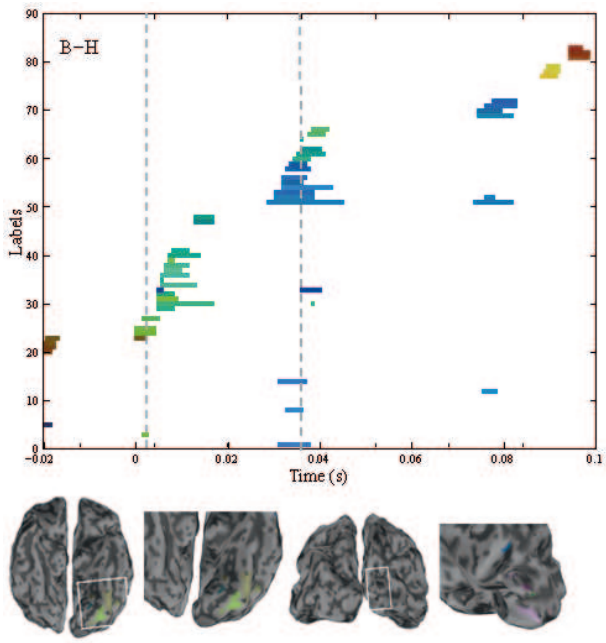

Fig. 2. Type-H hippocampic spike. Top: the graphical synopsis of the corresponding cortical activation maps. Bottom: activation cells are represented on a smoothed tessellation of the subject's cortical surface. Color encodes the label of each cell. From left to right, view of the ventral cortical surface at time $t = 0$s and a zoomed view of the same cells. Last two images represents the activation cells at time t =350ms (posterior and zoomed views).

the spike lifespan in a small network of neighboring temporo-occipital cortical regions. The graphical synopsis later shows the resurgence of activity in similar regions during the subsequent wave of the spike-wave complex but with significantly slower dynamics.
As expected, the contrast in terms of location and dynamics of activations with the sequencing of the H-spike is quite striking (see Fig. 2).

4. CONCLUSION

We have presented a new tool for the facilitated exploration and quantitative analysis of functional brain mapping data at high-temporal resolution. This tool is based on the spatial segmentation of activation maps into activations cells. These cells are tracked across time with consistent labeling that follows a small set of predefined evolutionary scenarios. Resulting graphical synopsis was exemplified on epileptic spike analysis and indicate satisfactory consistency with human expertise.
Ongoing research is now focussing on larger-scale evaluation of this method and on specific quantitative tools for the analysis of cross-condition contrasts in functional imaging.

5. REFERENCES

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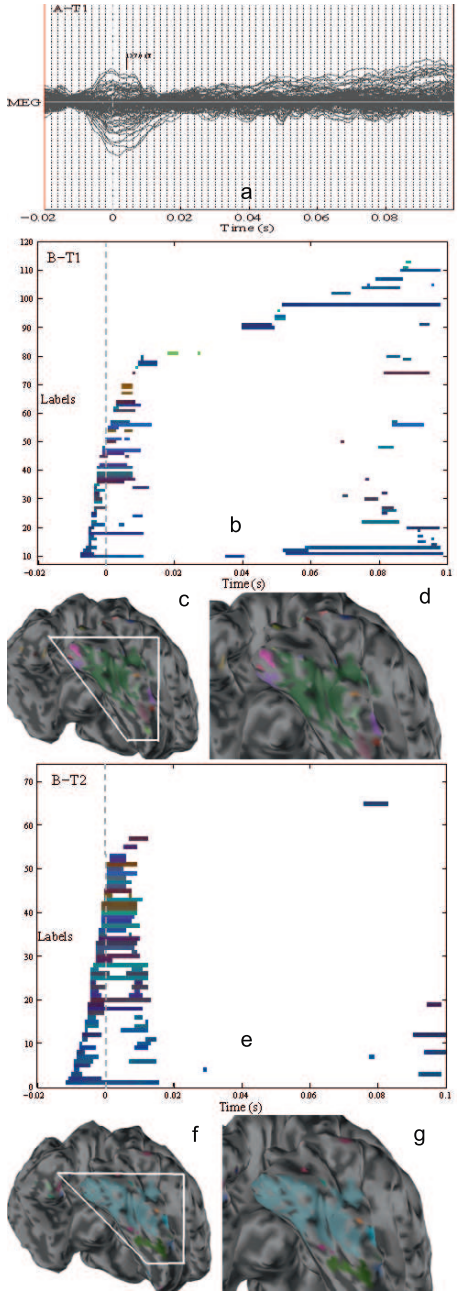

Fig. 3. Type-TO temporo-occipital spike. a.: a butterfly plot of times series on the 151 MEG channels; b. (res. e.) the graphical synopsis for spike T1 (res. T2); c. and f.: a display of cortical cells at time $t = 0$s with the associated zoomed views (d. and g.).