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Macroscopic Manifestations of Neural Connectivity in EEG Signals

Cristian CARMELI†, Oscar DE FEO†, and Giorgio M. INNOCENTI‡

†Laboratory of Nonlinear Systems, Swiss Federal Institute of Technology Lausanne;
EPFL-IC-LANOS, CH-1015 Lausanne, Switzerland.
‡Department of Neuroscience, Karolinska Institutet;
Berzelius 3, S-17177 Stockholm, Sweden.
Email: oscar.defeo@epfl.ch, cristian.carmeli@epfl.ch, giorgio.innocenti@neuro.ki.se

Abstract—Cortical computation involves the formation of cooperative neuronal assemblies. Traditionally, these assemblies have been characterized by synchronous oscillatory activity, and the cortical connectivity organizing their formation has been assessed indirectly through measures of synchronization among cortex regions. However, a synchronization based definition of connectivity might be restrictive as weak, though important, interactions might remain unobservable under such a paradigm. Here, the macroscopic manifestation of functional cortico-cortical connectivity is assessed through a parametric identification method, out of the synchronization framework, applied to visual stimuli induced EEG signals.

1. Introduction

The operations performed by the cerebral cortex require the cooperative activity of neurons within distributed assemblies. Consequently, the study of the assemblies formation is of critical importance in neuroscience and questions like: “How and where assemblies form?”; “Under which condition (external stimuli)?”; “How different assemblies interact?”; etc., are central in brain studies.

In human studies, these assemblies have been identified with several methods as fMRI, EEG analysis, or combination of the two, see *e.g.* [1–3]. These studies have been guided by the assumption that the assemblies, at least certain types, are characterized by the synchronous activity of their constituent neurons [4] and, implicitly, defining the assemblies as synchronized clusters of neurons. Consequently, in these studies the cortical connectivity organizing the assemblies formation has been assessed indirectly through measures of synchronization among cortex regions [5]. On the other hand, it is usually unclear if the functional connectivity revealed by the increased synchronization reflects anatomical connectivity between the neurons of the assembly [6], and this assumption could be verified in a very restricted number of experimental and/or clinical conditions [7].

Though successful under the most varied experimental conditions, this paradigm might be too restrictive. Thinking neurons as dynamical systems, their interaction (connectivity) does not necessary imply their synchronization [8], still very strong interactions indubitably induce synchronization-like phenomena. However, weak though important interactions might remain unobservable under such a paradigm. Consequently, new connectivity studies outside the synchronization paradigm are needed to investigate the interactions among the cortex regions organizing the assemblies formation.

Along this line, by conceiving the brain as a heterogeneous network of interacting dynamical systems, here the macroscopic manifestation of functional cortico-cortical connectivity is assessed by applying the method (which is out of the synchronization framework) proposed in [9] to visual stimuli induced EEG signals. The experimental setup and the application of the method are described in Sec. 2. The results are reported in Sec. 3 and then discussed in Sec. 4.

2. Materials & Methods

The experimental setup is identical to that used in [2, 3, 10] to identify the synchronization-defined connectivity between the hemispheres. Here, on the contrary, the macroscopic manifestation of functional cortico-cortical connectivity is assessed by applying the method proposed in [9].

2.1. Experimentalia

The considered EEG recordings are from a normal right-handed women adult. The subject signed written informed consent, and all the procedures conformed to the Declaration of Helsinki (1964) by the World Medical Association concerning human experimentation and approved by the local ethical committee of Lausanne University.

During EEG recording session, the subject viewed the visual stimuli shown in Fig. 1 and was instructed to fix a point in the center of the screen. The stimuli were: iso-oriented gratings (*IG*) consisting of two identical patches of collinear, downwards-drifting horizontal gratings on both sides of the fixation point; and orthogonally-oriented gratings (*OG*) consisting of a patch of horizontal downwards-drifting grating on one side and a patch of vertical rightwards-drifting grating on the other. A uniform gray screen of the same space-averaged luminance as the stimuli with a fixation point in the center served as the background (*BGR*) stimulus. The vertical and horizontal

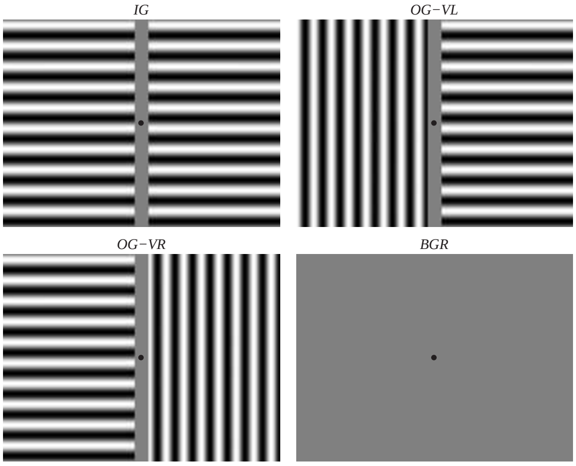

Figure 1: The four different types of visual stimulus.

gratings of the *OG* stimulus appeared in the left or right hemifield at random. Type of stimulus (*OG*, *IG*, and *BGR*), stimulus exposure (2.2–2.6 *s*), and inter-stimulus intervals (1.8–2.2 *s*) were also randomized.

The EEGs were recorded with the 128-channel Geodesic Sensor Net. The signals were digitized with a 12-bit analog-to-digital converter at a rate of 500 $samples/s$, band-pass filtered (FIR, 3–70 *Hz* and notch at 50 *Hz*), and re-referenced against common average reference. In order to assess only the steady-state, the first 200 *ms* after stimulus onset were excluded, removing stimulus-onset artifacts, response-onset transients, and stimulus-locked synchronization. Then, the signals were segmented into 100 non-overlapping artifact-free epochs of 1 *s*. Finally, in order to make the measurement of connectivity independent from the absolute energy of the signals, each epoch was mean de-trended and scaled to unit time variance.

2.2. Assessing cortico-cortical connectivity from high surface sampling EEG

The experimental setup considered here was designed to assess interhemispheric connectivity within the synchronization framework. The present study also addresses interhemispheric connectivity, though under a more general definition of it, which is still dynamical system oriented. The method for assessing this connectivity is described in detail in [9]. Although mathematically convoluted, the method soul is rather simple. Starting from a multivariate (vector) measured time series, it assumes a local dynamical system behind each (scalar) variable and it proceeds along two steps. In the first step, for each local variable (measure), a deterministic black-box model of the local system is identified solely from the time courses of the variable at issue. In the second step, a linear model of the dynamical interaction among the local variables, *i.e.* the topology and strength of the influences graph, is fitted cross relating all the measured variables to the modelling residuals (dynamics unjustified by the local models), providing in this way the connectivity matrix K.

For the considered stimuli, previous synchronization-defined studies of connectivity [2, 10] showed that an interhemispheric synchronization, probably implemented via callosal connections, can be detected at occipital electrodes close to the midline, *e.g.* electrode pairs 71-84 and 70-90 in Fig. 2. Coherently, this study considered the connectivity within the left and right cluster of electrodes shown in Fig. 2, *i.e.* [70, 71] and [84, 90], respectively. However, it is clear that through the same method other connectivity issues are assessable.

The close interhemispheric connectivity has been assessed as follows.

Firstly, the connectivity matrix among the four electrodes were estimated for each of the epochs i and stimulus ST, obtaining a set of matrices $\left\{K^{(i)}_{ST}\right\}$. The connectivity matrix estimation was performed with the following parameters [9]: state space dimension, equal for all electrodes, $m_i = 4$; delay and window for the PCA state space reconstruction automatically determined through self-mutual-information; and 100 points used for the RBF fitting.

Secondly, the connectivity arrangement in the two actively stimulated situations *IG* and *OG* were compared statistically and graphically. The connectivity matrices of epochs corresponding to identical active stimulus condition, *i.e.* $K^{(i)}_{OG}$ and $K^{(i)}_{IG}$, were considered as random samples. These matrices were averaged obtaining the statistics of the connectivity topography corresponding to each one of the two active visual stimuli, *i.e.* the mean matrices $\bar{K}_{IG}$ and $\bar{K}_{OG}$ and the corresponding matrices of standard deviations. Before averaging, the estimated entries of the connectivity

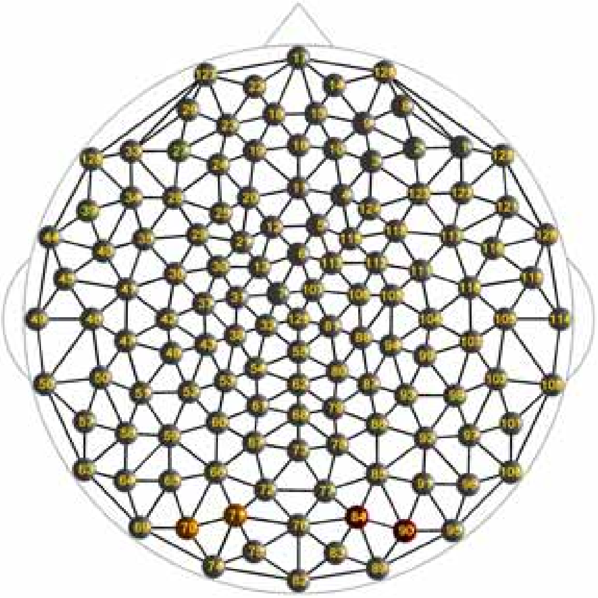

Figure 2: Spatial localization of the electrodes. Those considered for the connectivity analysis are from the left (orange) and right (red) occipital region.

matrices $\left\{K_{ST}^{(i)}\right\}$ below a threshold or with uneven covariance have been removed, considering in this way only the reliable part of influences graphs. Afterwards, the remaining entries of the average connectivity matrices have been tested to be significantly different in statistical sense. This was performed by means of the one-way ANOVA (tailed two-sample *t*-test assuming unequal variances) test. Finally, the most statistically significant changes between the two average connectivity matrices were extracted.

3. Results

The visual stimuli used in this study were chosen primarily because it was previously found that they could reliably modify interhemispheric spectral coherence in animals and men [2, 3]. The stimulus *IG* conforms to the Gestalt principle of perceptual grouping by collinearity and common fate and is likely to generate cooperative activity in the two hemispheres. The stimulus *OG*, instead, presumably places the visual area of the two hemispheres in a condition of perceptual rivalry. Consequently, according to the cooperative-assemblies-based solution to the binding problem, different interhemispheric connectivity is predicted within the brain regions processing the two stimuli.

The result of the procedure described in Sec. 2.2 is summarized in Tab. 1. The average connectivity matrices induced by the two active stimuli *IG* and *OG* were tested for statistical significance. About an half of them proved to be reliable at least at 95 %, hence showing stimulus-specific changes in the arrangement of brain connectivity within the visual area. Furthermore, the statistically significant changes have been relativized (*cf.* $\Delta\bar{K}_{IG\ vs\ OG\%}$ in Tab. 1) in order to highlight the topology, directionality, and strength of these changes. The result is summarized in Fig. 3.

$$\bar{K}_{IG} = \begin{bmatrix} 0 & 274.52 & 152.55 & 131.22 \\ 212.40 & 0 & 153.89 & 107.15 \\ 129.06 & 188.92 & 0 & 201.50 \\ 86.70 & 134.28 & 201.84 & 0 \end{bmatrix}$$

$$\bar{K}_{OG} = \begin{bmatrix} 0 & 299.72 & 136.87 & 116.74 \\ 191.45 & 0 & 141.56 & 105.37 \\ 112.76 & 162.56 & 0 & 165.18 \\ 130.76 & 194.35 & 211.81 & 0 \end{bmatrix}$$

$$\Delta\bar{K}_{IG\ vs\ OG\%} = \begin{bmatrix} \text{—} & -8.4 & 11.5 & 12.4 \\ \mathbf{10.9} & \text{—} & 8.7 & 1.6 \\ 14.5 & \mathbf{16.2} & \text{—} & \mathbf{22.0} \\ \mathbf{-33.7} & \mathbf{-30.9} & -4.7 & \text{—} \end{bmatrix}$$

Table 1: $\bar{K}_{IG,\ OG}$ are the average connectivity matrices induced by the two active stimuli *IG* and *OG*. $\Delta\bar{K}_{IG\ vs\ OG\%}$ is the relative variation in the connectivity matrix induced by the iso-oriented grating *IG* with respect to the orthogonally oriented grating *OG*; in bold are the most statistically significant variations.

4. Discussion

By conceiving the brain as a heterogeneous network of interacting dynamical systems, here the macroscopic manifestation of functional cortico-cortical connectivity has been assessed applying the method proposed in [9] to visual stimuli induced EEG signals. Still dynamical system inspired, this method lays outside the synchronization framework, and can detect weak though important interactions, which might remain unobservable under the synchronization paradigm.

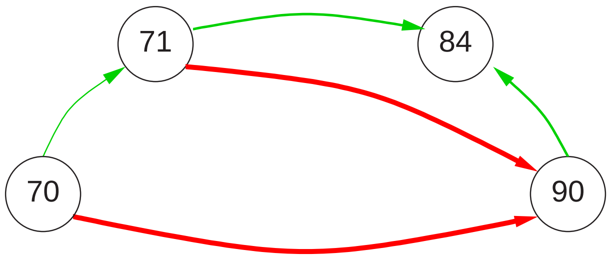

Figure 3: Topology and strength of the most significant changes in the influences graphs induced by the iso-oriented grating *IG* with respect to the orthogonally oriented grating *OG*. Red (green) links highlight statistically significant diminished (augmented) connectivity, whilst the width of the links reflect the intensity of the change.

The experimental setup considered here is identical to that used in [2, 3, 10] to identify the synchronization-defined connectivity between the hemispheres. This has the advantage of testing the new paradigm within an experimental framework known to result in reproducible synchronization dynamics; hence, it allows the comparisons between the results within the two paradigms.

Similarly to the results obtained within the more traditional synchronization paradigm, the results presented here (*cf.* Sec. 3) allows demonstrating stimulus-specific changes in the arrangement of brain connectivity within the visual area, albeit independently from any form of synchronization. However, the main difference between the synchronization-based assessment of connectivity and the one applied here lays in the determination of both strength and directionality of the dynamical interactions. Indeed, within the former framework, connectivity is assessed indirectly through measures of synchronization between cortex regions. Several of these synchronization estimators (surely coherence, the most used in EEG studies) are bivariate, symmetric, and relative (incommensurable). Namely, they ascertain the coupling between two sites as a function of temporal/spectral correlations, without providing neither a cause-effect relation nor a relative order among the couplings between different sites.

On the contrary, the entries of the connectivity matrix obtained here provide a whole picture of the influence graph; hence, both strength and directionality of the interactions. In particular, being the method implicitly multivariate, the entries remain all commensurable, *i.e.* the couplings strengths can be directly compared to each other. In this way, an order among the couplings and their changes, with respect to their relative strength, can be obtained. Indeed, the results reported in Fig. 3 illustrate not only stimulus specific changes in the interhemispheric connectivity, but also the direction and the intensity of these changes. In particular, it may be observed that, under the *IG* stimulus, the interhemispheric connectivity is weakened between the most occipital electrodes (70 and 90) and strengthened between those upper positioned (71 and 84). At the same time, intrahemispheric connectivity in the upward direction is also strengthened, somehow suggesting a displacement of the cooperative activity of neurons towards the upper visual areas. These results emphasize the complexity of the changes in the macroscopic manifestation of functional cortico-cortical connectivity induced even by very simple stimuli. This has potentially interesting consequences for the interpretation of the EEG data, which are however beyond the aims of the present study.

5. Conclusions

A new paradigm for extracting connectivity from multivariate time series has been applied to visual induced EEG signals. The study shows that different visual stimuli induce different macroscopic manifestations of neural connectivity, confirming the results obtained under the synchronization paradigm albeit going beyond them. Evidently, as only one subject has been studied, no further conclusions can be drawn, and the application on several subjects is in progress in order to extract population, as well as individuals, statistics.

Finally, because of its intrinsic multivariate nature, this non-synchrony defined connectivity paradigm is particularly suitable for multichannels EEG analysis, and a good candidate for clinical applications, such as online analysis and monitoring of the state of functional connectivity.

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