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Partial Spectroscopy of the Human Brain Based On the Joint Analysis of MEG and MRI Data. Application to the CamCAN Data Array

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Abstract. The new technology was developed to calculate spectral characteristics of various compartments of the human brain. This technology combines two types of spatial data: 1) MEG-based functional tomogram presenting spatial distribution of the electric sources and 2) anatomical structure of the brain estimated by the magnetic resonance imaging. Multichannel magnetoencephalograms were used to calculate the functional tomogram by the precise frequency-pattern analysis, decomposing brain activity into a set of elementary oscillations. In the functional tomogram, unique spatial location corresponds to each spectral component, generated by the equivalent current dipole. Based on this fact, we calculated partial spectra – sets of frequencies, generated by various anatomical regions of the brain. Individual spatial structure of the brain compartments was determined by the annotated segmentation of magnetic resonance tomogram for each subject under study. The partial spectrum of the brain compartment was composed of the set of frequencies, localized into this compartment. Here we calculated partial spectra of 15 compartments of the brain for 600 subjects, using MEG and MRI datasets obtained from the open archive CamCAN. Average spectra were calculated and the distribution of the spectral power between brain compartments was estimated.

Key words: *magnetic encephalography, Fourier transform, frequency-pattern data analysis, functional tomogram, magnetic resonance imaging, partial spectrum*

INTRODUCTION

One of the basic problems of neuroscience is to determine the place of electric signals origination in the human brain. For a long time, researchers were trying to estimate it by the analysis of time series or spectra in particular channels of encephalography, distributed over the head. Then the implantable microelectrodes technique was invented, providing information about the internal electrical activity of the brain [1, 2]. In electrocorticography, electrodes are placed directly on the surface cerebral cortex, such procedure is performed on the open brain and may be dangerous for subjects, but is used during operations, when necessary [3]. Also, it is used in animal research such as the study of the processing of pain signals by the rat's brain [4]. Electrocorticography measures electrical activity directly at the place of its origin, however, due to its invasiveness, it is not suitable for large scale studies.

Here we propose a new method of coupled analysis of magnetic encephalograms and MRI images. This method makes it possible to split the general spectrum into partial spectra of the brain compartments. The term “partial” (fractional, from Latin “*partialis*”) is widely used in science and engineering and means “relating to the separate parts” of the complex system. One example of this term usage is partial pressure, meaning the pressure of separate component in the mixture of gases. Another example is partial epilepsy, affecting the part of the brain (in contrast with generalized epilepsy). Partial spectroscopy studies the frequency distribution of

some or other parameter describing the part of complex system. In solid-state physics and crystallography, partial spectra make it possible to determine the role of different elements in the energy distribution of oscillations. In papers [5, 6] those spectra were estimated experimentally. When the brain is modelled by means of neural networks, partial spectra can serve to measure the connectivity between the different network elements [7, 8].

In current study, we use the term “partial spectrum” to denote the fraction of the general spectrum, which is generated by the sources, located in some anatomical part of the brain. Partial spectra of the brain spontaneous activity are calculated from the coupled analysis of two principally different experiments. Magnetic encephalography (MEG) registers magnetic fields, produced by electrical sources in the brain, and characterizes the function of the brain. Magnetic resonance imaging (MRI) produces the spatial distribution of hydrogen atoms and characterizes the anatomical structure of the brain. Method to noninvasively estimate partial spectrum of the arbitrary parts of the brain, includes the following steps [9–15]: detailed spectral analysis, calculation of the functional tomogram, calculation of the brain part spatial mask from annotated MRI segmentation, and assembling of the partial spectrum from frequency components, covered by the spatial mask. Here we apply this method to analyze MEG and MRI experimental data, obtained from large scale CamCAN archive [16].

1 MATERIALS AND METHODS

1.1 Data acquisition

In this study we used MEG and MRI data downloaded from CamCAN [16] data repository. The Cambridge Center for Aging and Neuroscience Research (Cam-CAN) Phase 2 cohort study archive is a large-scale (approximately 700 subjects), multimodal (MRI-magnetic resonance imaging, MEG-magnetic encephalography, cognitive study), cross-sectional population-based study of the mechanisms of cognitive aging spanning adult life expectancy (18–87 years). All MRI datasets were collected at a single location (MRC-CBSU, Cambridge, England) using a 3T Siemens TIM Trio with a 32-channel head coil. The scanner used memory foam cushions for comfort and to minimize head movements. All MEG data sets were collected at a single location (MRC-CBSU, Cambridge, England) using a 306-channel VectorView MEG system (Elekta Neuromag, Helsinki) consisting of 102 magnetometers and 204 orthogonal planar gradientometers located in a magnetically shielded room (MSR). Data were sampled at 1 kHz with a 0.03 Hz upper-pass filter. Recordings were made in a sitting position. During the resting state recording, participants sat motionless with eyes closed for at least 8 minutes and 40 seconds.

1.2 Data preprocessing

1.2.1 MEG data

To suppress external noises, we applied Maxwell filter [17, 18] routine from MNE [19] package to the raw MEG data. Time series of magnetometer channels were selected for further analysis. On the next step time series were trimmed to 300 seconds length, starting from 100th second of recording. Using the FFTW library [20], multichannel spectra were computed over the entire length (300 sec) of the time series. Data structures describing the spatial configuration of the magnetic encephalograph and its position in space relative to the subject’s head were constructed using the FieldTrip package [21].

1.2.2 MRI data

MRI images were realigned to CTF-like coordinate system¹ with 2 mm spatial resolution. To construct an annotated brain map, we segmented magnetic resonance images of the human head using a pre-trained UNesT neural network [22, 23]. The weights for this network were taken from the Project MONAI [24] repository. The ANTsPy [25] package was used for

translation into MNI (Montreal Neurological Institute coordinate system [26]) space and vice versa.

1.3 MEG-based functional tomography

Let us consider the theory of the MEG-based functional tomography, as it was set out in the works [9, 10, 14]. The encephalograph simultaneously records the values of magnetic field induction in K channels during time T producing a set of experimental vectors $\{B_k(t)\}$, $k = 1, \dots, K$. The field is recorded at H points in time with a constant step T/H . As a result of the measurements, we obtain a two-dimensional data array B_{hk} , where $h = 0, \dots, H-1$, $k = 1, \dots, K$. Multichannel discrete Fourier transform can be written as:

$$b_{nk} = \sum_{h=0}^{H-1} B_{hk} e^{-\frac{i2\pi hn}{H}} \sin(2\pi v_n t + \varphi_{nk}), \quad n = 0, \dots, \left\lfloor \frac{H+1}{2} \right\rfloor \quad (1)$$

where b_{nk} – complex Fourier amplitude for frequency v_n in a channel with a number k , and $v_n = \frac{n}{T}$. All spectra are computed for the full measurement time T , which reveals the detailed frequency structure of the system. Frequency resolution is equal to $\delta v = v_n - v_{n-1} = 1/T$, thus, it is determined by the registration time. The phase and amplitude of the n -th component of the Fourier series are written as: $\varphi_{nk} = \text{atan2}(\text{Im}b_{nk}, \text{Re}b_{nk})$, $\rho_{nk} = \frac{1}{H} \sqrt{(\text{Re}b_{nk})^2 + (\text{Im}b_{nk})^2}$, where $\text{Re}b_{nk}$ – real part of b_{nk} , $\text{Im}b_{nk}$ – imaginary part.

Knowing the multichannel spectrum, the inverse Fourier transform can be performed on all channels:

$$B_k(t) = \sum_{n=0}^N \rho_{nk} \sin(2\pi v_n t + \varphi_{nk}), \quad v_n = \frac{n}{T}, \quad N = \left\lfloor \frac{H+1}{2} \right\rfloor. \quad (2)$$

To study the detailed frequency structure of the brain, we reconstruct the multichannel signal at each frequency and analyze the obtained time series. Reconstructed multichannel signal of frequency v_n in all channels:

$$B_{nk}(t) = \rho_{nk} \sin(2\pi v_n t + \varphi_{nk}) \quad (3)$$

where $t \in [0, T_{v_n}]$, $T_{v_n} = 1/v_n$ – period of that frequency.

Formula (3) can be written as

$$B_{nk}(t) = \rho_n \hat{\rho}_{nk} \sin(2\pi v_n t + \varphi_{nk}) \quad (4)$$

where $\rho_n = \sqrt{\sum_{k=1}^K \rho_{nk}^2}$ – amplitude of the frequency v_n , $\hat{\rho}_{nk} = \frac{\rho_{nk}}{\rho_n}$ – value of normalized pattern

$\hat{\rho}_n$ of this oscillation in k -th channel. In multichannel measurements, the space is determined by the channel arrangement. The use of normalized patterns makes it possible to determine the spatial structure of the signal sources by the solution of the inverse problem.

The theoretical foundations for the reconstruction of static functional entities (neural circuits, or sources) were outlined in [9, 10]. This reconstruction is based on detailed frequency analysis and the selection of frequency components with similar patterns. Algorithm for this method can be written as:

- 1) Fourier transform of the input multichannel signal.
- 2) Inverse Fourier transform – reconstruction of the signal at each frequency.

3) Calculation of phase, normalized pattern and its amplitude for each frequency component.

4) Solution of the inverse problem for all of the components.

Each elementary oscillation is characterized by frequency ν_n , phase Φ_n , amplitude ρ_n , normalized pattern $\hat{\rho}_n$, and its source is a functional entity with a permanent spatial structure. The functional tomography method reconstructs the structure of the system by analyzing a set of normalized patterns ρ_n . A functional tomogram shows a three-dimensional map of the distribution of energies produced by sources located at a given position in space. To construct a functional tomogram, the investigated region of space is divided into $N_x \times N_y \times N_z$ elementary cubic cells with centers at $\mathbf{r}_{ijs}$. The length of the cube edge is chosen according to the desired accuracy, in this study it was 2 mm. In each cell set of test dipoles $\mathbf{Q}_{ijsl}$ with direction $\mathbf{L}$ is constructed. The magnetic induction generated by the test dipole $\mathbf{Q}_{ijsl}$, located at the point $\mathbf{r}_{ijs}$ is recorded by a sensor with the number k , located at the point with coordinates $\mathbf{r}_k$ and having the direction $\mathbf{n}_k$, k -th component ρ_{ijslk}^{tr} of the test pattern ρ_{ijsl}^{tr} is calculated using the model of the current dipole in a spherical conductor [27]:

$$\rho_{ijslk}^{tr} = \frac{\mu_0}{4\pi F^2} \left(\left(\mathbf{F}(\mathbf{Q}_{ijsl} \times \mathbf{r}_{ijs}) - (\mathbf{Q}_{ijsl} \times \mathbf{r}_{ijs}, \mathbf{r}_k) \nabla F \right), \mathbf{n}_k \right) \quad (5)$$

where $F = a(ar_k + r_k^2 - (\mathbf{r}_k, \mathbf{r}_{ijs}))$,

$$\begin{aligned} \nabla F &= (a^2 r_k^{-1} + a^{-1}(\mathbf{a}, \mathbf{r}_k) + 2a + 2r_k) \mathbf{r}_k - (a + 2r_k + a^{-1}(\mathbf{a}, \mathbf{r}_k)) \mathbf{r}_{ijs}, \\ \mathbf{a} &= \mathbf{r}_k - \mathbf{r}_{ijs}, \quad a = |\mathbf{a}|, \quad r_k = |\mathbf{r}_k|, \quad |\mathbf{n}_k| = 1, \quad \mu_0 = 4\pi \cdot 10^{-7} \end{aligned}$$

The normalized pattern is calculated as:

$$\hat{\rho}_{ijslk}^{tr} = \frac{\rho_{ijslk}^{tr}}{|\rho_{ijsl}^{tr}|} \quad (6)$$

where $|\rho_{ijsl}^{tr}| = \sqrt{\sum_{k=1}^K (\rho_{ijslk}^{tr})^2}$. All test dipoles located at the point $\mathbf{r}_{ijs}$, lie within the same plane orthogonal to $\mathbf{r}_{ijs}$, since the result of the vector product $\mathbf{Q}_{ijsl} \times \mathbf{r}_{ijs}$ is non-zero only for such dipoles. The test dipoles cover the circle in $Lmax$ directions in $360/Lmax$ degree increments, $Lmax = 72$ was used in this study. For each of the dipoles, a set of normalized patterns is computed using formula (5):

$$\{\rho_{ijsl}^{tr}\}, \quad i = 1, \dots, N_x; \quad j = 1, \dots, N_y; \quad s = 1, \dots, N_z; \quad l = 1, \dots, L_{max} \quad (7)$$

For each of the normalized experimental patterns $\hat{\rho}_n$ the following function is computed to determine the difference between that pattern and one of the test patterns:

$$\chi(i, j, s, l) = \sum_{k=1}^K (\hat{\rho}_{ijslk}^{tr} - \hat{\rho}_{nk})^2, \quad (8)$$

where $\hat{\rho}_{ijslk}^{tr}$ – k -th component of the normalized trial pattern $\hat{\rho}_{ijsl}^{tr}$, $\hat{\rho}_{nk}$ – k -th component of the normalized experimental pattern $\hat{\rho}_n$, k – channel number. Position and direction of the source corresponding to the pattern $\hat{\rho}_n$, is determined by the numbers (I, J, S, L) , corresponding to the minimum of the function $\chi(i, j, s, l)$ on variables

$i = 1, \dots, N_x; j = 1, \dots, N_y; s = 1, \dots, N_z; l = 1, \dots, L_{max}$. The minimum of this function is found by the method of exhaustive search, i.e., by selecting the smallest of several million values of the function χ for each pattern $\hat{\rho}_n$. This procedure determines the position $\mathbf{r}_{IJS}$ – solution of the inverse problem for pattern $\hat{\rho}_n$ without spatial filtering of channels and without introduction of weight functions. The energy of this source ρ_n^2 is added to the energy produced from the cubicle with the center at $\mathbf{r}_{IJS}$. Performing this procedure for all normalized patterns $\hat{\rho}_n$, it is possible to distribute in space the energy of all oscillations from formula (2). The result of such distribution is the functional tomogram of the brain, reconstructed from MEG.

1.4 MRI segmentation and calculation of partial spectra

The first step in partial spectra calculation is the annotated segmentation of the subject's MRI. It was described in Section 1.2.2 and included several open access programs. The result of the segmentation is the annotated 3D map of the brain, where each MRI voxel corresponds to particular anatomical compartment of the brain.

Let us denote the set of all voxels belonging to the compartment C_m as Ω_{Cm} . The solution of inverse problem for frequency ν_n is $\mathbf{r}_{IJS}$. The rule of the partial spectrum extraction can be formulated as follows:

$$\text{if } \mathbf{r}_{IJS} \in \Omega_{Cm}, \text{ then } \rho_n^{(Cm)} = \rho_n, \text{ if } \mathbf{r}_{IJS} \notin \Omega_{Cm}, \text{ then } \rho_n^{(Cm)} = 0. \quad (9)$$

After checking all frequencies in the formula (2), the initial spectrum will be split into the set of partial spectra $\{\rho_n^{(Cm)}\}$ where $m = 1, \dots, M$. In this work we considered 15 compartments (see Table 1).

1.5 Calculation of the average partial spectra

The procedure described in Sections 2.3-2.4 was applied to experimental datasets of MEG+MRI for N_s subjects. In this study $N_s = 500$.

Average spectra for all compartments were calculated:

$\bar{\rho}_n^{(Cm)} = \frac{1}{N_s} \sum_{n_s=1}^{N_s} \rho_n^{(Cm)}(n_s)$, where n_s – number of subjects, and $\{\rho_n^{(Cm)}(n_s)\}$ – partial spectrum of the compartment C_m for that subject.

2 RESULTS AND DISCUSSION

Figure 1,A shows the result of segmentation, where different colors correspond to different anatomical compartments of the brain. Figure 1,B represents the average spectrum of magnetic encephalogram, produced by the whole brain.

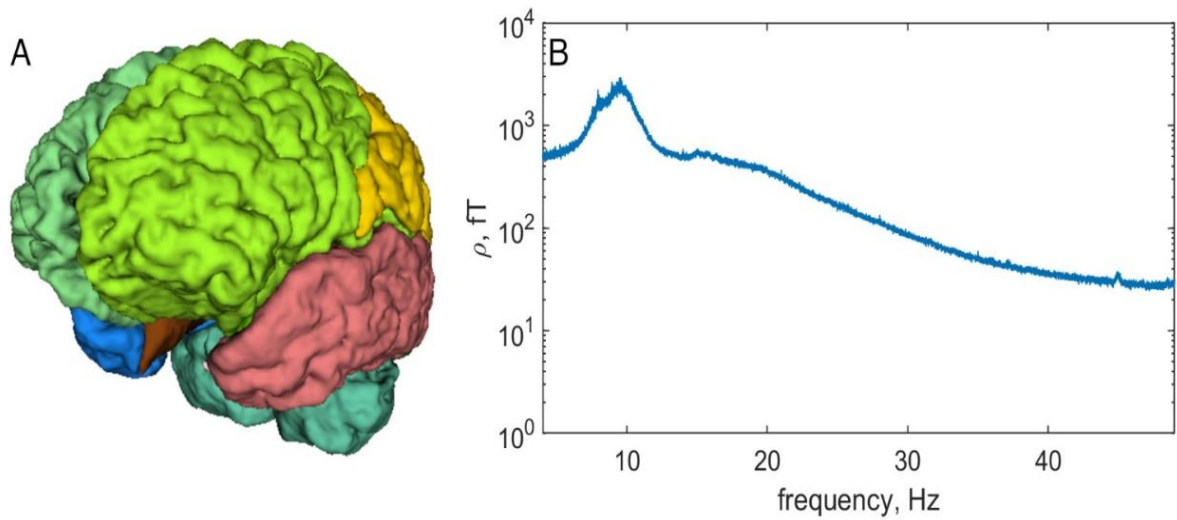


Fig. 1. Annotated segmentation of the brain (A) and average spectrum (B) produced by the whole brain.

Table 1 represents the distribution of the average partial energy between brain compartments. The left column of the table shows brief denomination of the compartments (C1-C15) for the further consideration. Figures 2–5 illustrate anatomy of compartments together with partial spectra.

Table 1. Average energy of the brain compartments

Denomination of the compartment	Brain compartment	Average energy produced by the compartment	% from total brain energy
C1	Left Frontal	$2.74 \cdot 10^6$	0.41
C2	Right Frontal	$2.49 \cdot 10^6$	0.37
C3	Left Parietal	$3.15 \cdot 10^7$	4.69
C4	Right Parietal	$2.87 \cdot 10^7$	4.27
C5	Left Temporal	$3.26 \cdot 10^6$	0.49
C6	Right Temporal	$2.43 \cdot 10^6$	0.36
C7	Left Occipital	$4.98 \cdot 10^7$	7.41
C8	Right Occipital	$7.26 \cdot 10^7$	10.81
C9	Left White Matter	$1.75 \cdot 10^8$	26.05
C10	Right White Matter	$1.91 \cdot 10^8$	28.40
C11	Left Limbic	$2.24 \cdot 10^6$	0.33
C12	Right Limbic	$2.04 \cdot 10^6$	0.30
C13	Left Subcortical	$2.88 \cdot 10^6$	0.43
C14	Right Subcortical	$2.54 \cdot 10^6$	0.38
C15	Cerebellum	$1.03 \cdot 10^8$	15.29

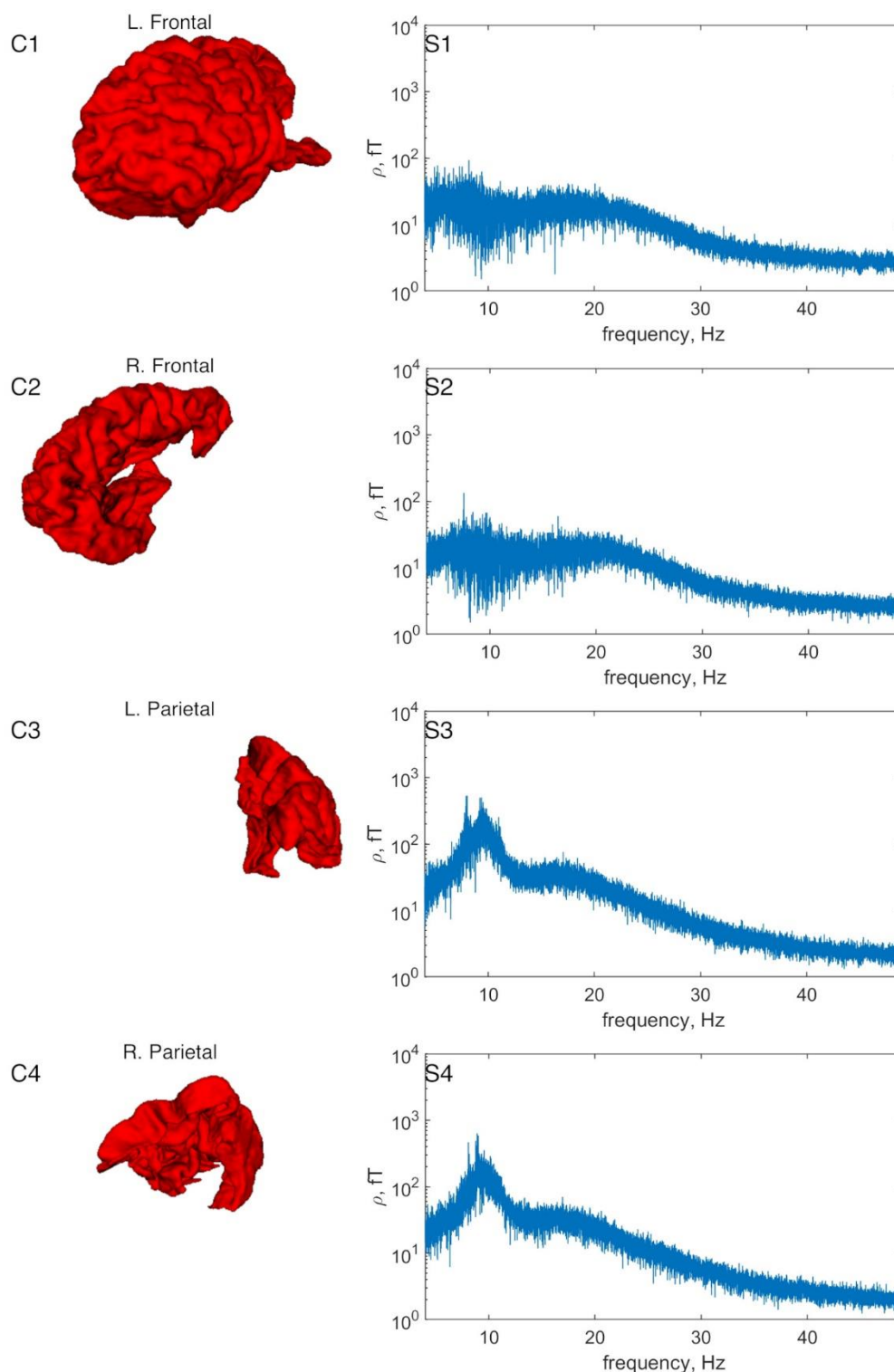


Fig. 2. Panels C1 and C2 illustrate left and right frontal compartments. Panels S1 and S2 show average spectra produced by these areas of the brain. It can be concluded that spectral amplitude and summary power (see Table 1) of frontal area is rather low, with some additional decline in the alpha band. Panels C3 and C4 illustrate left and right parietal compartments. Panels S3 and S4 show average spectra produced by these areas of the brain. It can be concluded that spectral amplitude and summary power (see Table 1) of parietal area is rather high (ten times greater than frontal), with definite peak in the alpha band and some increase in the beta band.

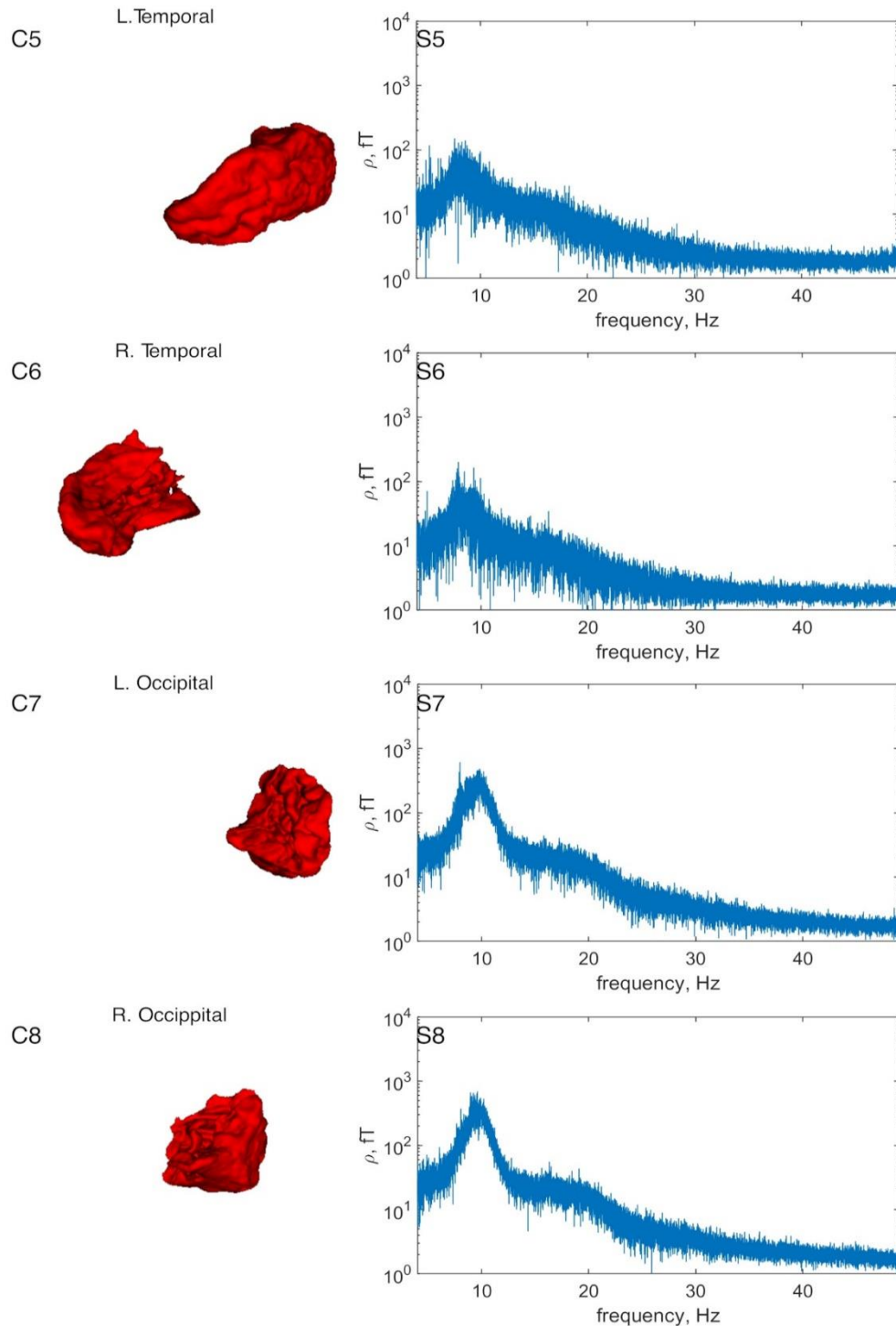


Fig. 3. Panels C5 and C6 illustrate left and right temporal compartments. Panels S5 and S6 show average spectra produced by these areas of the brain. It can be concluded that spectral amplitude and summary power (see Table 1) of temporal areas is rather low (comparable with frontal area), with definite peak in the alpha band. Panels C7 and C8 illustrate left and right occipital compartments. Panels S7 and S8 show average spectra produced by these areas of the brain. It can be concluded that spectral amplitude and summary power (see Table 1) of occipital area is of the highest in the brain, with definite peak in the alpha band and rather asymmetric (right occipital power is 1.45 greater than left, see Table 1).

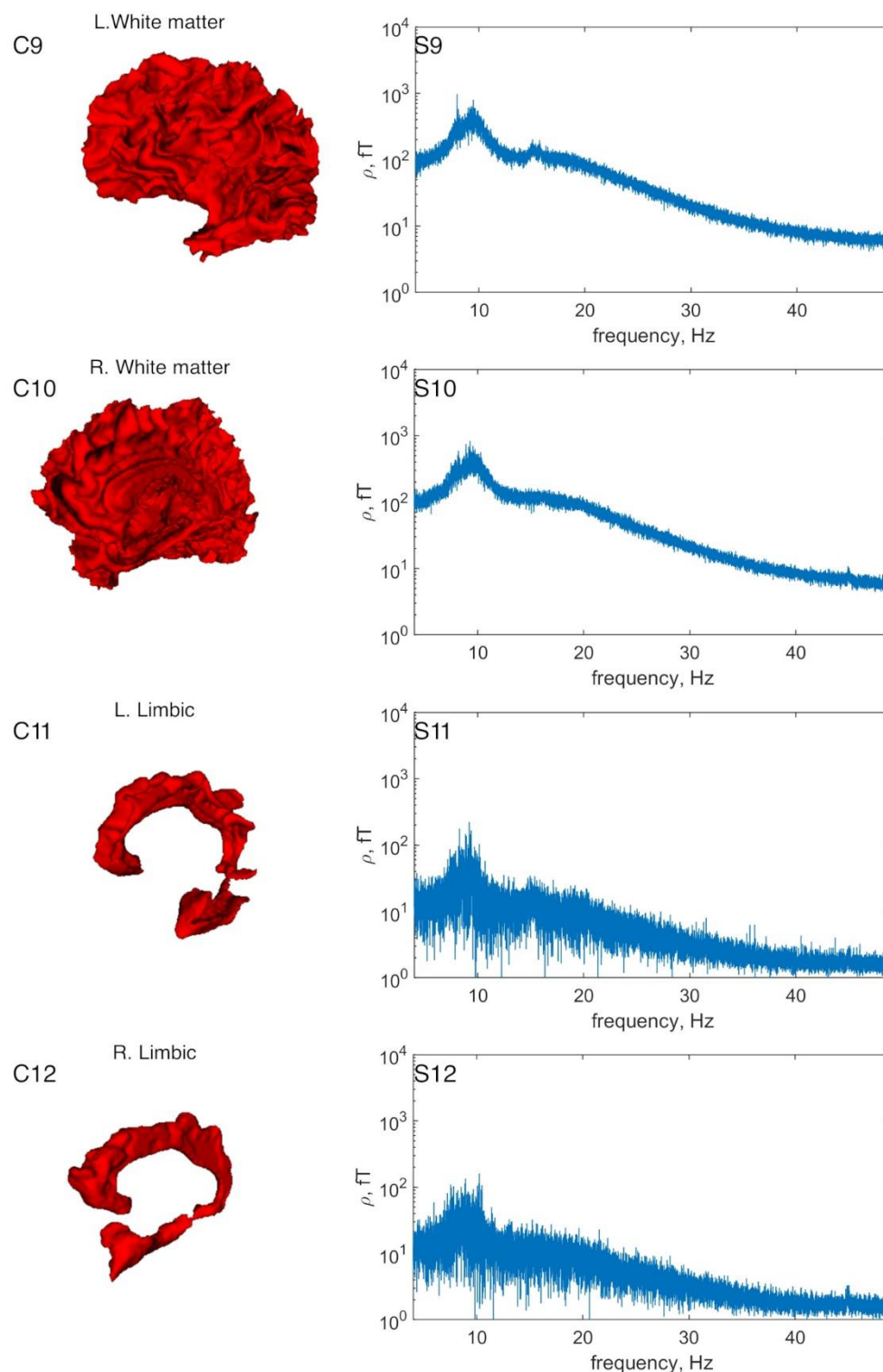


Fig. 4. Panels C9 and C10 illustrate left and right white matter compartments. Panels S9 and S10 show average spectra produced by these areas of the brain. It can be concluded that spectral amplitude and summary power (see Table 1) of these areas are the highest in the brain, with definite peak in the alpha band. Panels C11 and C12 illustrate left and right limbic compartments. Panels S11 and S12 show average spectra produced by these areas of the brain. It can be concluded that spectral amplitude and summary power (see Table 1) of limbic area is the smallest in the brain, still with some peak in the alpha band.

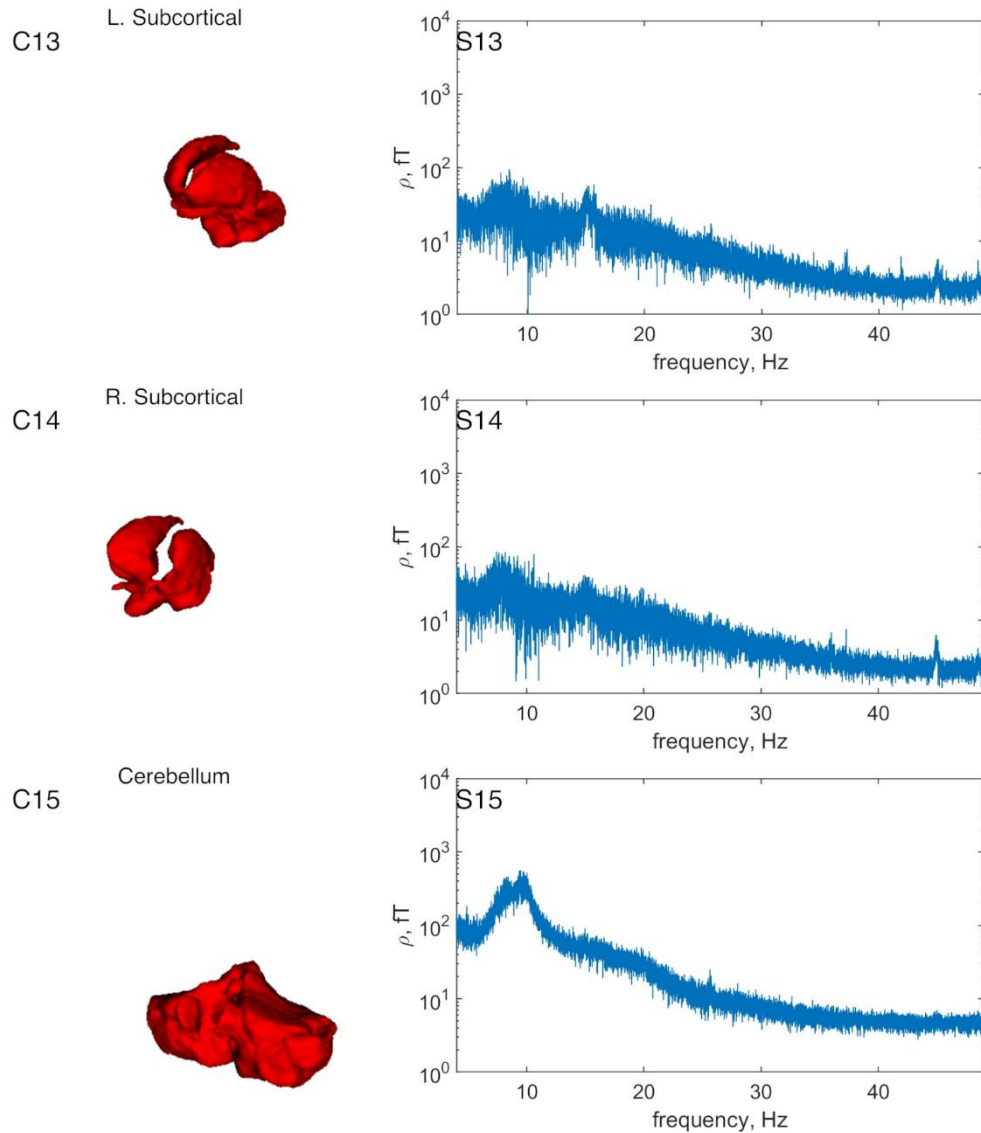


Fig. 5. Panels C13 and C14 illustrate left and right subcortical compartments. Panels S13 and S14 show average spectra produced by these areas of the brain. It can be concluded that spectral amplitude and summary power (see Table 1) of these areas are of the smallest in the brain, with some peaks in the alpha and beta band. Panel C15 illustrates Cerebellum compartment. Panel S15 shows an average spectrum produced by this area of the brain. . It can be concluded that spectral amplitude and summary power (see Table 1) of cerebellum area is of the highest in the brain, with definite peak in the alpha band.

CONCLUSION

The novel methodology was used to analyze spontaneous brain activity in humans from the large-scale CamCAN archive [16]. Spectral analysis of the prolonged time series made it possible to extract detailed frequency structure of the MEG signal and to localize the sources of elementary oscillations. After the annotated segmentation of individual brains those sources were distributed between the brain compartments, providing their partial spectra. Average partial spectra were calculated, and conclusions about the power and place of origin were made. The proposed method makes it possible to further study in detail electrical sources of brain activity.

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