GENERALIZED SPECTRAL-ANALYTICAL METHOD FOR BIOMEDICAL DATA PROCESSING

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Summary. An article presents a new method of processing, analysis, storage and conversion of data sets of different nature. It is based on an approximation of one- and multi-dimensional array in orthogonal functional bases. Details of method use in the problems of magnetoencephalography data processing and biomagnetic sources localization are given.

1 INTRODUCTION

The report presents a new method of processing, analysis, storage and conversion of data sets of different nature. It is based on an approximation of one- and multi-dimensional array in orthogonal functional bases:

$$f(x)=\sum_{i=0}^{n} A_i \varphi_i(x)$$

As a result of this procedure, the transition is made from a point-wise signal recording to its spectral representation. All further analysis and processing operations are performed over the spectrum. Proposed technique is adaptive to the class of signals. It consists in preliminary assessment of data type and on its results a choice of the optimal basis is performed. The correctness of the choice provides an approximation of maximal simplicity in this class of data. Approximation tuning to the desired function system is performed by the signal's vector K of "aspect ratios" [1, 2]. Its components are the set of signal features. The problem of spectral expansion optimization is reduced, in fact, to the problem of optimal basis recognition in the feature space of coefficients:

$$K_i = \frac{(g_i, f)}{(h_i, f)}$$

(*,*) – scalar product or projection of function f on the template functions g_i, h_i with mutually contrasting properties. They may be, for example, the first basis functions of estimated basic systems. The use of adaptive procedures increases the efficiency of analytical description, and provides a high rate of data volume compression.

As will be shown in the report, it is convenient for these purposes as the basis functions to apply the modified classical orthogonal polynomials and functions. They may be of

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continuous and discrete arguments. Orthogonal decompositions based on classical orthogonal bases have relatively simple form, that is convenient to make analytical data transformations.

After the conversion from the original recordings to the coefficients of expansion, all operations on the signals are carried in the space of spectral features. They include pattern recognition, data classification and diagnosis, as well as the more common mathematical operations: integration, differentiation, multiplication, division, raising to integer and non-integer degree, optimal filtering, calculation of statistical moments, dimensional characteristics, and so on. For these purposes, the special library of mathematical transformations has developed for different bases (including those for functional systems of several variables). To obtain needed characteristics of the original record we have standard method of orthogonal series segments calculation. This finite orthogonal series is the required approximation of the signal characteristics. The procedures of computational technology are efficiently realized on parallel computers. So that we have practically linear scaling of both spectrum calculation and subsequent operations on the spectrum. Some basic procedures can be implemented in hardware in the form of special expansion computing devices for mainframes.

2 MAGNETOENCEPHALOGRAPHY DATA

Magnetoencephalography (MEG) is a recently developed experimental technique for studying human neural activity, mapping functional brain areas, and diagnosing various disorders. Research in this area is motivated by the possibility of noninvasive imaging of cortical and subcortical processes.

Until recently, the technique was difficult to apply because of the extreme weakness of both spontaneous and evoked neuromagnetic fields generated by current sources. Accordingly, the measuring apparatus to be employed must meet particularly stringent requirements.

Despite technical difficulties and the high cost of the required apparatus, this technique can be used as complementary or alternative to electroencephalography because magnetic field is much less perturbed by intracranial inhomogeneities and integumentary tissues than electric field, and the accuracy of source localization can therefore be substantially improved without detailed knowledge of the intracranial structure.

The input experimental data used in the present study were obtained by means of a 148-channel Magnes 2500 WH neuromagnetometer (a highly sensitive SQUID-based magnetic field measurement system) at the New York University School of Medicine. The system was housed in a magnetically shielded room.

The analysis presented in this paper is focused on recognition and classification of patterns of magnetic field distribution over the subject's scalp for localizing neuromagnetic activity sources. This problem arises from the complex variability of an MEG signal during the measurement time (approximately 10-20 min), which includes alternating intervals of abnormal and normal activity. Intervals of abnormal and normal activity can easily be identified visually when they differ by the mean amplitude of the signal. Otherwise, visual inspection cannot be reliably used to identify intervals corresponding to different activity modes, and the dominant type of activity can be determined by analyzing the spatial field

pattern, which strongly correlates with the number, location, and orientation of the current sources responsible for magnetic field generation.

The proposed approach was validated against data derived from a reference group of healthy individuals and a group of patients suffering from Parkinson's syndrome. The signal was a 148-dimensional time series measured at 148 points on the head surface at a sampling rate of 500 Hz per channel.

The data analysis can be divided into the following tasks:

- detection of a signal associated with a particular type of brain activity (e.g., response to auditory, visual, tactile, or other stimulation; generation of Parkinson's tremor or auditory hallucinations; etc.);
- selection of instants for sampling the spatial field distribution over the head surface to be used as input in solving the inverse problem of current source localization;
- solution of the inverse problem of source localization in the cases of abnormal and normal activity;
- the use of fMRI data as physiological constraints.

2.1 Measurements with phantom sources

For the setting of algorithms for inverse problem solving the preliminary measurements were carried out. Here the data used have been obtained in measurements with phantom spherical conductor and were generated by 10 fixed dipoles of variable moments. Figure 1 demonstrates this case. On the right figure points correspond to sensors positions, black and white are for positive and negative flux of the magnetic induction respectively.

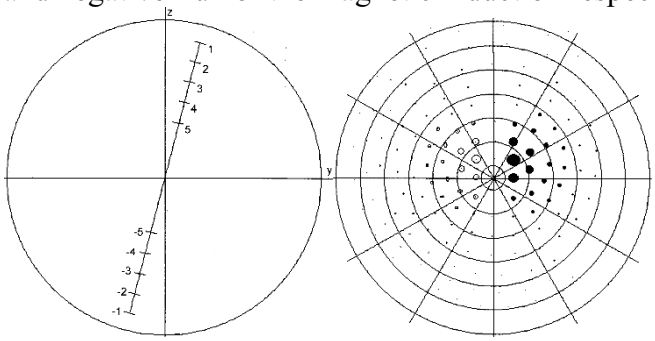


Figure 1: Test dipoles 1 - 5 and their antipodes (left) and experimental data set for dipole 1 (right)

2.2 MEG data preprocessing

The preprocessing refers to the reading, segmenting around interesting events such as triggers, temporal filtering and optionally re-referencing of the data set. In the work preprocessing implements a Fourier transform filter, a Butterworth and a FIR filter for low-pass, high-pass and band-pass filtering.

Detection of artefacts can be done by using manual or automatic artefact detection and visual identifying independent components (ICA). There are two ways to remove artefacts: 1) rejecting trial or the piece of trial containing the artefact; 2) subtracting the spatio-temporal contribution of the artefact from the data. ICA is most widely used for cleaning from cardiac,

eye movements and blinks artefacts.

The application of transcranial magnetic stimulation (TMS) pulses during the data acquisition poses some specific challenges. This is an occurring of TMS artefact right after TMS pulse (pulse artefact, ringing/step response artefact, cranial muscle artefact) and recharging artefact in 500 ms after stimulation onset. There is a general trend for increase in artefact magnitude with TMS intensity. The following artefacts removal methods were used: removal large muscle artefacts from TMS by ICA [3], adapted recording system with software artefact correction [4], off-line removal of TMS-induced artefacts on human magnetoencephalography by Kalman filter, based on cross-correlation coefficients of ICA [3]. Then time average ERP/ERF for all trials is computed and baseline correction can be applied.

2.3 Frequency analysis

It can be shown by means of spectral routines that oscillatory components contained in the MEG signal power changes regarding the system status. For this purpose frequency or time-frequency analysis based on Fourier bases and wavelets were used.

As an example, monaural audible stimulus was applied. Pulsing frequency was 7 Hz, while the response was localized at frequencies near 10 and 20 Hz. Fig. 2 shows this situation on the wavelet diagram [5, 6].

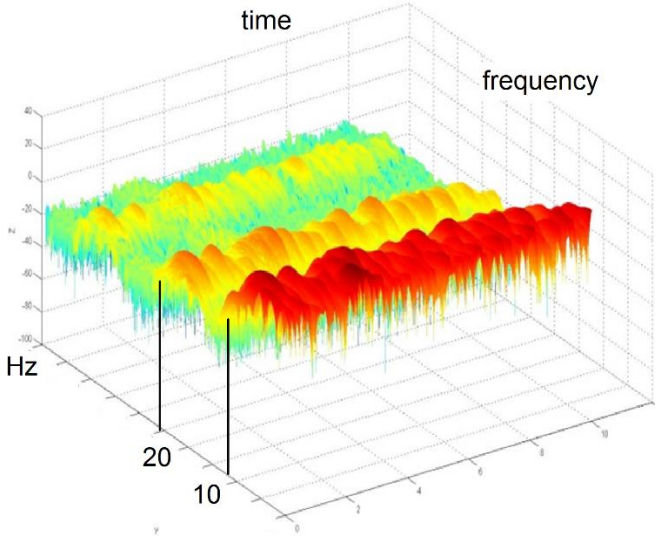


Figure 2 : Haar wavelet diagram of MEG response for 7 Hz pulsing audible stimulation.

3 THE DIRECT PROBLEM

Consider the dipole current density J generated in an active region G of conductive brain tissue characterized by conductivity σ. Assuming a constant permeability μ = μ0, we write the quasi-static Maxwell equations as

$$\begin{aligned} \mathbf{E} &= -\nabla\phi, \\ \nabla\cdot\mathbf{B} &= 0, \\ \mathbf{J} &= \mathbf{J}_p + \sigma\mathbf{E}, \end{aligned} \tag{1}$$

where ϕ is the electric potential and **J** is the total current density. The magnetic field is calculated by the Biot- Savart law:

$$\mathbf{B}(r) = \frac{\mu_0}{4\pi} \int \mathbf{J}(r) \times \frac{(\mathbf{r} - \mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|^3} dv' . \quad (2)$$

The variable of integration $\mathbf{r}'$ is dipole radius-vector. Here we assume that the conductive region is a sphere and the source is a current dipole $\mathbf{J}(\mathbf{r}) = \mathbf{Q}\delta(\mathbf{r} - \mathbf{r_0})$ with dipole moment $\mathbf{Q}$ and position vector of a source $\mathbf{r_0}$.

According to [7], the magnetic induction on a homogeneous sphere enclosing the dipole can be calculated as

$$\mathbf{B}(\mathbf{r}) = \frac{\mu_0}{4\pi} F^2 (F\mathbf{Q} \times \mathbf{r}_0 - \mathbf{Q} \times \mathbf{r}_0 \cdot \mathbf{r} \nabla F) \quad (3)$$

with $F = a(ra + r^2 - \mathbf{r_0} \cdot \mathbf{r})$, $\mathbf{a} = \mathbf{r} - \mathbf{r_0}$, $a = |\mathbf{a}|$, $r = |\mathbf{r}|$, $\mu_0 = 4\pi \cdot 10^{-7}$

$\nabla F = \left(r^{-1}a^2 + a^{-1}\mathbf{a} \cdot \mathbf{r} + 2a + 2r\right)\mathbf{r} - \left(a + 2r + a^{-1}\mathbf{a} \cdot \mathbf{r}\right)\mathbf{r_0}$.

For the case of point sensors we can write the magnetic induction magnitude, measured by j-th sensor in the form

$$B_j = \mathbf{B}(\mathbf{r_j}) \cdot \mathbf{n} . \quad (4)$$

It is clear that the outer magnetic field generated by a radially oriented source vanishes.

Therefore, the inverse problem is ill posed: the source characteristics can be determined only up to an arbitrary radial component of the current dipole moment. Note also that the contribution of volume currents to the magnetic induction given by Eq. (3) does not depend on the conductivity σ.

4 THE INVERSE PROBLEM

The locations and orientations of the sources of spontaneous activity are determined by using the magnetic field values at the measurement points to solve the inverse problem for Eq. (3). For the adopted model of brain activity and head geometry, the inverse problem can generally be reformulated as a nonlinear optimization problem for calculation of the locations and moments of the set of dipoles that provides the best approximation of the measured MEG data with respect to RMS deviation. The inverse problem is difficult solve primarily because it is ill posed: there exist infinitely many solutions consistent with the experimental data. The computational complexity of the nonlinear optimization problem is explained by the existence of multiple local extrema of the objective function, particularly when the number of dipole sources is large [8].

There also exist technical difficulties due to the weakness of both spontaneous and evoked magnetic fields generated by brain current sources against a high background noise level in MEG measurements.

To classify the types of neuromagnetic activity and identify abnormal intervals in MEG records, we use the feature space spanned by the spectral expansion coefficients of the total magnetic field on a sphere, which are invariant under rotation. The natural basis for describing the spatial field distribution is the set of spherical harmonics:

$$f(\theta, \varphi) = \sum_{n=0}^{N} \sum_{s=0}^{n} \left(a_{ns} p_n^s(\cos\theta) \cos s\varphi + b_{ns} p_n^s(\cos\theta) \sin s\varphi \right).$$

Here p_n^s are associated Legendre functions, a_{ns} and b_{ns} are expansion coefficients. Relevant features are extracted at the training stage of the algorithm by estimating the variability of the expansion coefficients for the class of objects under analysis. The upper bound for the dimension of the feature space depends on the length N of the Fourier expansion. There exists a simple analytical relationship between the expansion coefficients of functions whose arguments are related by an SO(2) transformation [9], which makes it possible to develop a fast search procedure for functions in a particular class.

A most straightforward way to solve an inverse problem consists in multiple direct problem solution. On each step we substitute the trial parameters set (dipoles coordinates and moments), calculate the magnetic field in the sensors positions, and construct the residual function

$$\Delta = \sum_{i=1}^{N_s} \left| B_i - B_i^e \right| . \tag{5}$$

Here N_s = 148 is the total number of sensors. Parameters, for which this value is minimal for all possible coordinates and moments constitute the solution of the inverse problem.

An absolute value of the moment on each iteration is determined by the fitting of calculated magnitude $\overline{B} = \sum_{i=1}^{N_s} |B_i|$ to appropriate experimental value $\overline{B}^e = \sum_{i=1}^{N_s} \left| B_i^e \right|$. Final moment modulus is

$$Q = Q_0 \frac{\overline{B}^e}{\overline{B}} . \tag{6}$$

A mean error in the second column is calculated by equation

$$\text{mean error} = \frac{\sum_{i=1}^{N_s} \left| B_i^e - B_i \right|}{\sum_{i=1}^{N_s} \left| B_i^e \right|} \cdot 100\% . \tag{7}$$

A dependence of mean error data approximation on search step in x-, y-, z- coordinates is represented on Figure 3.

Another way of the inverse problem solution consists in fast minimization of the sum

$$S(\vec{\beta}) = \sum_{i=1}^{N_s} \left[B_i(\vec{\beta}) - B_i^e \right]^2 , \tag{8}$$

were $\vec{\beta}$ is the parameters vector $(x_0, y_0, z_0, q_x, q_y)^T = (\beta_1, \ldots, \beta_5)^T$

The extremum condition for the functional S can be written as

$$\begin{cases} \dfrac{\partial S(\vec{\beta})}{\partial \beta_j} = 0, \; j=1,\ldots,5. \end{cases} \tag{9}$$

This method is realized in program MRIAN [8].

4.1 Source analysis

Source estimation comprises two steps: 1) estimation of the potential or field distribution

for a known source and for a known model of the head is referred to as direct modelling; 2) estimation of the unknown sources corresponding to the measured MEG is referred to as inverse modelling.

The head model specifies how currents that are generated by sources in the brain, e.g. dipoles, are influenced by the tissue properties and how these result in externally measureable MEG fields. For MEG the following head models are used: analytical single sphere model; local spheres model for MEG, one sphere per channel; realistically shaped single shell approximation, based on the implementation from Guido Nolte; magnetic dipole in an infinite vacuum. In the earliest studies, head models with simple geometries and homogeneous parameters were used, permitting many simplifications in the computation. When using models with spherical symmetry, solving the direct problem can be reduced to evaluating an analytic expression in Eq. (3).

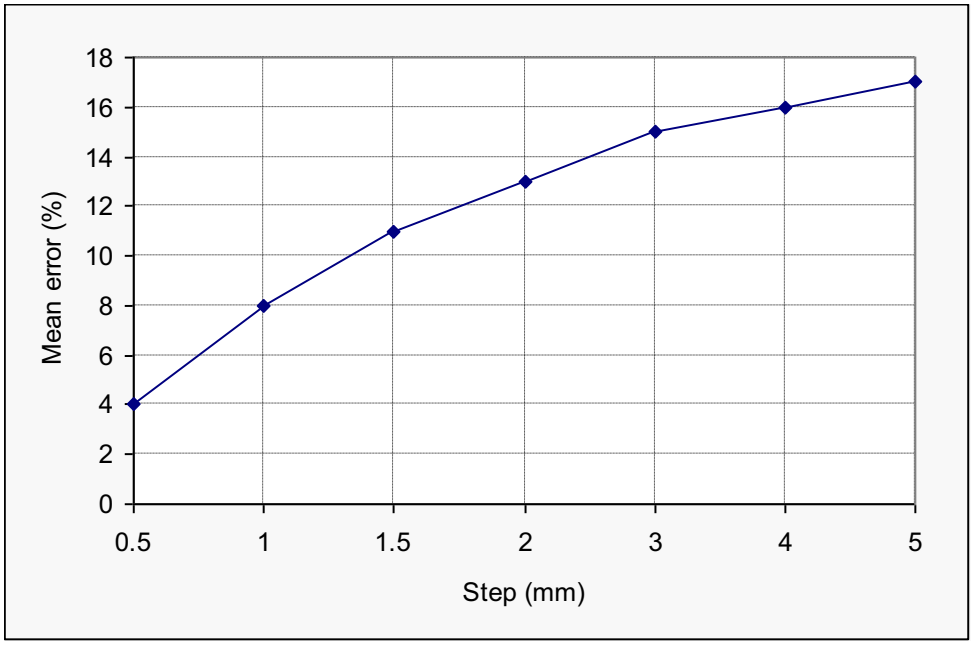


Figure 3

To reconstruct the location and the time-course or spectral content of a source in the brain, various source-localization methods are available. Here calculations with audible stimulation data and Parkinson patients' records used MRIAN software (Ustinin, Makhortykh et al., 2002). It is rather efficient for one- and two- dipoles problem with usage of structural restrictions by means of fMRI tomograms.

Results of spontaneous and induced sources localizations are presented by Figures 4 and 5. It shows the response on the monaural audible stimulus in auditory cortex: 10 Hz source is in the contralateral as long as 20 Hz source (see Figure 2) is in the ipsilateral hemispheres. Figure 4 a - d) demonstrates localized sources of pathological activity in different brain zones for the case of parkinsonian patient. Temporal dynamics of activity regimes switches is shown on Figure 6. Full description is brought out in [5].

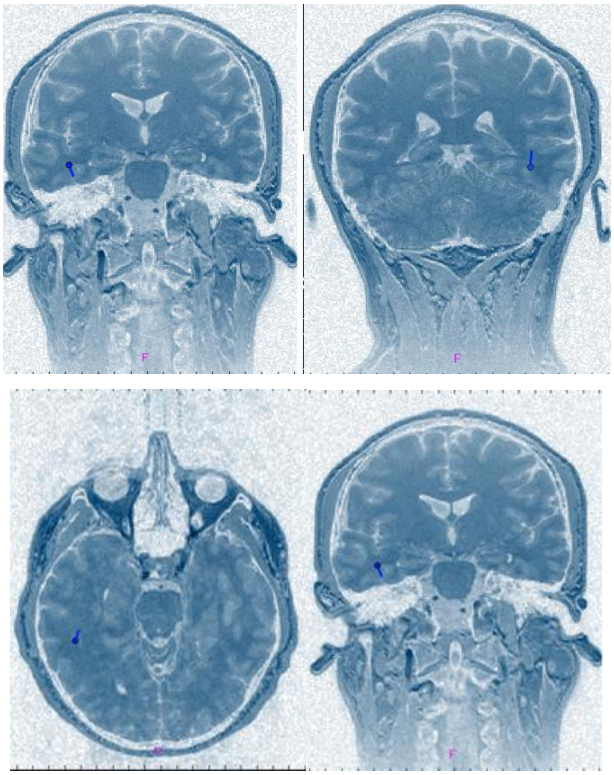
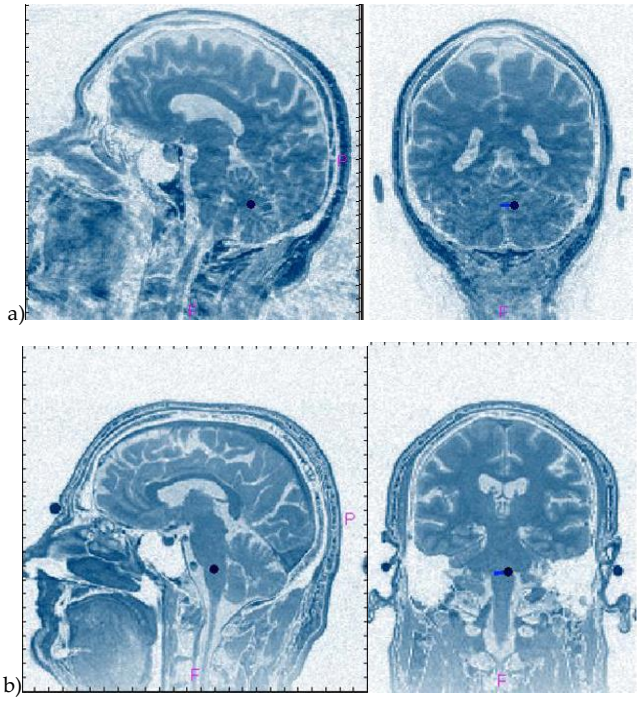


Figure 4: Sources localization (circles with rods) for induced activity (audible stimulus response).



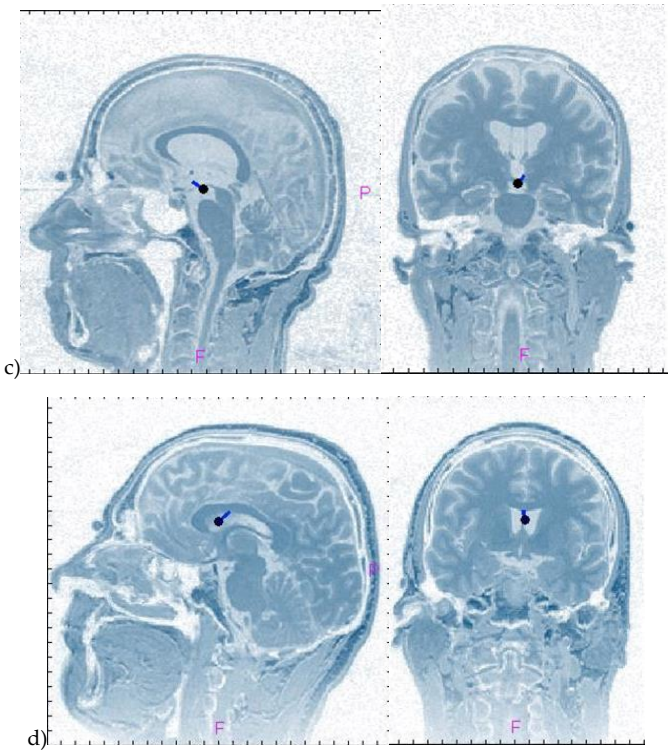


Figure 5: Sources localization for spontaneous parkinsonian signal: a) source in the cerebellum; b) … in the brainstem (pons); c) … in substantia nigra; d) … in the caudate nucleus.

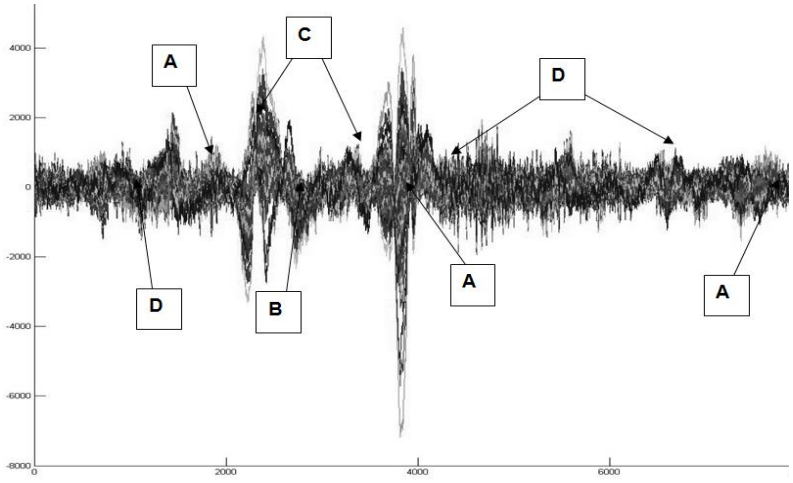


Figure 6: Temporal dynamics of activity regimes switches on time series of MEG records.

5. CONCLUSIONS

Analysis of MEG records and localization of brain biomagnetic activity are the bases of the cerebral processes functional mapping. Data preprocessing by means of generalized spectral

method (Dedus, Makhortykh et al.,) allows to remove noise, highlighting the desired signal and in many cases determines the success of the solution. It uses a set of orthogonal bases so that spectral description can be scaled down to fit a particular class of signals. In many cases correct source localization and model parameters estimates can be obtained only after projection of the signal on the proper basic function (as on Figure 2). Also expansion coefficients can be used as features for the system control and signal type recognition.

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