LOCALIZATION OF ELECTRICAL ACTIVITY SOURCES IN HUMAN BRAIN DURING EPILEPTIC SEIZURES WITH EEG ANALYSIS

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Abstract

The human brain consists of about 100 billions of neurons, which are highly interconnected. One of the most important characteristic of neural cells is that they can produce electrical signals, therefore, measurements of electrical activity of brain represents a possibility for brain exploration. Measuring scalp potentials is one of the most often used and one of the oldest non-invasive methods for studying brain activity. The method is known as Electroencephalography (EEG). Potentials on scalp carry the information on certain brain activity and by analyzing the time-series data the information can be extracted from the recorded potentials. This information can be used for monitoring and diagnosing certain clinical situations, such as epilepsy. Data from three persons during epileptic seizure was used in the study and Brainstorm software was used to localize dipole sources in the brain. In spite of the fact, that concentric-spheres model was used and that only 32 electrodes were used for EEG measurements and that general electrode positions were used, the system provided very realistic results. Nevertheless, it can occur that real source location is not the most probable-one suggested by the program, therefore, only the specialist can decide at the end what is most probable location of the source. Brainstorm provides a relatively fast tool for identification of sources under Matlab environment.

Keywords: electroencephalography, modelling, simulation, source localization, epilepsy

Presenting Author's Biography

Ilka Peyrer-Heimstätt was born on the 06.12.1982 in Vienna, Austria. After she finished school in 2001, she stared studying technical mathematic of natural science on the University of Vienna. She stayed half a year in Ljubljana, Slovenia to write her diploma thesis at the University of Ljubljana, Faculty of Electrical Engineering. She graduated in june 2007. Beside the study of technical mathematic she is an ambitious amateur photographer. Her first exhibition was shown in 2005 in Vienna.

1 Introduction

The human brain consists of about 100 billions of neurons, which are highly interconnected. One of the most important characteristic of neural cells is that they can produce electrical signals, therefore, measurements of electrical activity of brain represents a possibility for brain exploration. Measuring scalp potentials is one of the most often used and one of the oldest non-invasive methods for studying brain activity. The method is known as Electroencephalography (EEG). Potentials on scalp carry the information on certain brain activity and by analyzing the time-series data the information can be extracted from the recorded potentials [1]. This information can be used for monitoring and diagnosing certain clinical situations, such as epilepsy.

An active neuron or small group of neurons can be approximated with electrical dipole under specific conditions. The dipole changes the characteristics of the surrounding space, which is known as electromagnetic field. If the dipole is located within the material that has some measurable electrical conductivity, potential differences in the surrounding electric field will cause electrical currents in the material. If the physical dimensions of the material are known, together with electrical properties, as well as dipole position, strength, and orientation, the electrical potentials and currents throughout the material can be calculated. This is the so called forward problem. It is also possible to identify the position, orientation and strength of dipole within the material from the measured potentials and currents in the material. In the case of brain research, only the potentials on the surface are known, however, the dipole position, strength, and orientation are not, as well as currents and potentials within the brain. This is so called inverse problem. The difficulty of solving the inverse problem is that potentials and currents within material are not measurable which results in multiple solutions of inverse problem. This ambiguity of the solution can only be reduced with physiological background of the underlying system. Thus, unlikely positions and orientations of dipole are discarded. There are several algorithms to calculate the solution of the inverse problem. The goal of this study was to test the Brainstorm software for identification of sources of the electrical signals measured on the human scalp by electroencephalography (EEG), during epilepsy seizures.

2 Human head model

When considering electrical properties of human head, it can be modelled as an inner sphere surrounded by three concentric spherical shells, each having a different conductivity. In the case of epileptic seizures, it is typical, that origin in the brain is very localized, therefore it can be modelled as a single dipole. The inner sphere represents brain, next spheres represent brain membrane, liquor and scalp. In spite extremely simplified geometry, clinically useful results can be obtained from the model [1, 2].

To calculate the electric potentials in the spheres the Poisson's (eq. 1) and Laplace's (eq. 2) equation are used.

$$\nabla^2 u = u_{xx} + u_{yy} + u_{zz} = f \tag{1}$$

$$\nabla^2 u = u_{xx} + u_{yy} + u_{zz} = 0 \tag{2}$$

In case of symmetrically positioned dipole somewhere on z-axis, the potential u, which than depends only on the two spherical coordinates r and θ, the formal analytical solution for the Laplace's equation can be expressed in each sphere as

$$u_L(r,\theta) = \sum_{n=0}^{\infty} [A_n r^n + B_n r^{-(n+1)}] P_n(\cos\theta) \tag{3}$$

The functions $P_n(\cos\theta)$ are the Legendre polynomials of order n. The coefficients A_n and B_n depend on the sources and boundary conditions of continuous tangential electric field (or continuous potential) and radial current flow at the interface between spheres. In addition, the solution has to be to be finite at $r = 0$ and as $r \to \infty$. The former condition requires that $B_n = 0$ in the innermost sphere and the latter condition requires that $A_n = 0$ in the infinite medium surrounding the outer surface (air).

The potential in the innermost sphere u_1 can be written as

$$u^1(r) = \tag{4}$$

$$= \frac{Id_z}{4\pi\sigma_1 r_z^2} \sum_{n=1}^{\infty} \left[A_n^1 \left(\frac{r}{r_1}\right)^n + \left(\frac{r_z}{r}\right)^{n+1} \right] n P_n(\cos\theta);$$

$$r_z < r \leq r_1$$

Here r_1 is the radius of the innermost sphere. In each of the other spherical shells, $s = 2, 3...n$, the potential u^s can be expressed as

$$u^s = \tag{5}$$

$$\frac{Id}{4\pi\sigma_1 r_z^2} \sum_{n=1}^{\infty} \left[A_n^s \left(\frac{r}{r_s}\right)^n + B_n^s \left(\frac{r_s}{r}\right)^{n+1} \right] n P_n(\cos\theta);$$

$$r_{s-1} < r \leq r_s$$

The unknown coefficients in each spherical shell are determined from boundary conditions of continuous potentials

$$u^{s-1}|_{r=r_s} = u^s|_{r=r_s} \tag{6}$$

and continuous radial current density

$$\sigma_{s-1} \frac{\partial u^{s-1}}{\partial r}\Big|_{r=r_s} = \sigma_s \frac{\partial u^s}{\partial r}\Big|_{r=r_s} \tag{7}$$

at the $s-1$ interfaces between s spheres. At the outermost shell $s=n$ of an n-sphere model, the surrounding medium (air) has a conductivity of zero, so that radial current density at the outer surface must be zero:

$$\sigma_n \frac{\partial u^n}{\partial r}\bigg|_{r=r_n} = 0 \tag{8}$$

This leads to $2s-1$ equations that are solved for an equal number of unknown coefficients [1].

Since it is not possible to solve the Laplace's and Poisson's equations analytically for arbitrary geometry or dipole position and orientation, numerical methods must be used instead. There are many different numerical methods for solving partial differential equations, however, most widely used are finite difference and finite elements methods. Regardless of the numerical method, the space must be first divided into discrete subspaces or points for which the equation should be solved. The consequence of space discretization is transformation of differential equations into difference equations [3, 4].

3 Identification of EM-field sources in the head

In order to identify the sources of activity in the head, two-step procedure must be used. Since there is not enough information available from the potentials on the scalp, to uniquely identify the position, orientation and strength of the dipole, the identification method uses optimisation procedure that compares calculated potentials on the scalp for arbitrary dipole coordinates with measured values. Thus, the procedure requires the forward problem to be solved first. Since the position and dipole orientation can be arbitrary, numerical solution of the Poisson and Laplace equation must be calculated [1, 5, 6].

3.1 Finite Difference Method

The simplest method for numerical solving of partial difference equations is finite difference method [3]. However, it works well only for square-shaped volumes. Nevertheless, it is a good illustration of the problem to be solved. The corresponding finite difference equation for the Laplace's equation is:

$$\begin{aligned} u(x+h,y,z)+u(x,y+h,z)+u(x,y,z+h)+\\ u(x-h,y,z)+u(x,y-h,z)+u(x,y,z-h)-\\ 6u(x,y,z)=0 \end{aligned} \tag{9}$$

where h is called the mesh size.

And the coefficients scheme for this equation looks like:

$$\left\{ \begin{array}{ccc} & 1 & \\ & 1 & \\ 1 & -6 & 1 \\ & 1 & \\ & 1 & \end{array} \right\} \tag{10}$$

For square-shaped geometries, such as cubes, it is fairly easy to find a equidistant mesh grid and to define the neighbor mesh points $(x+h,y,z),(x-h,y,z)$.... Furthermore, in the case of square-shaped geometries, it is always possible to define a grid such that grid points are placed on body borders. This is important for calculation of boundary conditions. It is difficult achieve this for other geometries, such as spheres. For spheres it would be necessary to define a very narrow grid which would lead to high effort when solving the equations. Hence the finite difference method is not appropriate for geometries as can be found in the head.

Nevertheless, a cube can represent a rough approximation of the head and will be used as reference geometry to solve the equation numerically. The brain can be modelled as a cube surrounded by three concentric cubes. Each cube has a different conductivity ($s1$, $s2$ and $s3$). A dipole is located in the inner cube, with given orientation and strength. The dipole is not placed on the grid-point. The cubic grid is presented in Figure 3.1

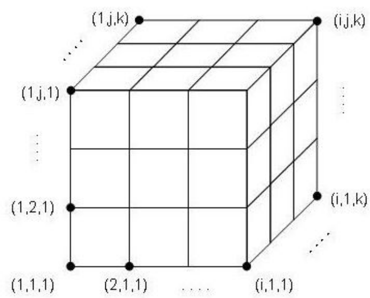


Fig. 1 Representation of cubic grid used for finite difference method

For the points on the borders of cubes the boundary condition from (6),(7) and (8) are used.
The Laplace equations for all the gridpoints can be written in the form:

$$\mathbf{A}\cdot\mathbf{u}=0, \tag{11}$$

where $\mathbf{A}$ is a $n\times n$ matrix of the coefficients schemes, $n = i\cdot j\cdot k$, and

$\mathbf{u} = (u(1,1,1), ..., u(i,j,k))$.

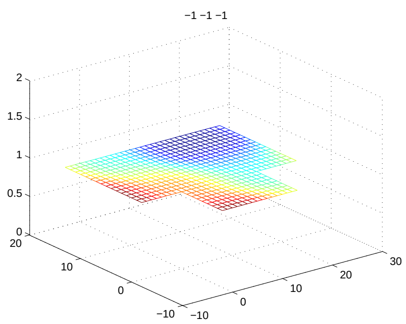
To solve the equation 11 the electrical potential for the eight neighbor-gridpoints of the dipole must be calculated. If we consider that those points are relatively far from the cube border, the potentials can be calculated with the formula

$$u(r) = \frac{1}{4\pi\epsilon_o r^2}(\mathbf{p}\cdot\hat{\mathbf{r}}), \qquad (12)$$

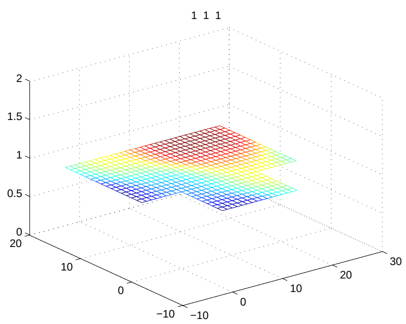
where $\mathbf{r}$ is the vector from the origin of coordinate system to the position of the dipole, r is the absolute value of $\mathbf{r}$: the distance from the dipole, $\hat{\mathbf{r}} = \mathbf{r}/r$ is the unit vector parallel to r $\mathbf{p}$ is the (vector) dipole moment.

With the electrical potential for the eight neighbor-gridpoints of the dipole as initial conditions, equation 11 can be solved as an equation system of $n-8$ equations with $n-8$ unknowns.

The potential at the surface of the cube is illustrated in Figure 2



a) Dipole orientation (1,1,1)



b) Dipole orientation (-1,-1,-1)

Fig. 2 Calculated potential on the cube surface of outer-most cube as a result of dipole, placed in the inner-most cube. Dark areas represent high positive or negative values of electric potential, light areas represent electric potential values of around 0

The surface in figure 2 represents the top of the outer-most cube, as well as upper parts of back, left and right sides of the cube, projected on the surface. Although, the calculation effort, necessary to solve the system is not very high, and the procedure could be used for identification of dipole source within the cube, the problem with selecting the appropriate grid for the arbitrary shape prevents the successful use of finite difference method for identification of dipole sources in the brain.

4 Inverse Solution Method RAP-MUSIC

There are many methods that are used for identification of sources of electric fields in the brain, and one of them is RAP-MUSIC [5]. The algorithm works as described below. Let $m(r)$ denote the electric potential on the scalp generated by a dipole with fixed orientation and moment q:

$$m = a(r, r_q, \Theta)q, \qquad (13)$$

where $a(r, r_q, \Theta)$ is the solution to the electric forward problem for a dipole with unit amplitude and orientation $\Theta = q/\|q\|$, $q \equiv \|q\|$ is the dipole magnitude. The potential is linear with respect to the dipole moment q and nonlinear with respect to the dipole location r_q.

EEG measurements are made simultaneous at N different sensors, therefore m can be written as:

$$\mathbf{m} = \begin{bmatrix} m(r_1) \\ \vdots \\ m(r_N) \end{bmatrix} = \qquad (14)$$

$$= \begin{bmatrix} a(r_1, r_{q1}, \Theta_1) & \cdots & a(r_1, r_{qp}, \Theta_p) \\ \vdots & \ddots & \vdots \\ a(r_N, r_{q1}, \Theta_1) & \cdots & a(r_N, r_{qp}, \Theta_p) \end{bmatrix} \begin{bmatrix} q_1 \\ \vdots \\ q_p \end{bmatrix}$$

$$= \mathbf{A}(\{r_{qi}, \Theta_i\})\mathbf{S}^T,$$

where $\mathbf{A}(r_{qi}, \Theta_i)$ is the gain matrix relating the set of p dipoles to the set of N discrete locations, m is a generic set of N EEG measurements, and the matrix S is a generalized matrix of source amplitudes, defined below. Each column of $\mathbf{A}$ relates a dipole to the array of sensor measurements and is called the forward field, gain vector, or scalp topography, of the current dipole source sampled by the N discrete locations of the sensors.

Let

$$\mathbf{M} = \mathbf{U}\Sigma\mathbf{V}^T \qquad (15)$$

be the singular value decomposition (SVD) of $\mathbf{M}$. One can define a basis for the signal and noise subspaces from the column vectors of $\mathbf{U}$. The signal subspace is spanned by the p first left singular vectors in $\mathbf{U}$, denoted $\mathbf{U}_S$, while the noise subspace is spanned by the remaining left singular vectors. The best rank p approximation of $\mathbf{M}$ is given by

$$\mathbf{M}_S = (\mathbf{U}_S\mathbf{U}_S^T)\mathbf{M} \qquad (16)$$

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and

$$\mathbf{P}_S^{\perp} = \mathbf{I} - (\mathbf{U}_S \mathbf{U}_S^T) \tag{17}$$

is the orthogonal projector onto the noise subspace. The MUSIC cost function is defined as:

$$J(r, \Theta) = \frac{\left\| \mathbf{P}_S^{\perp} a(r, \Theta) \right\|_2^2}{\left\| a(r, \Theta) \right\|_2^2}, \tag{18}$$

which is zero when $a(r, \Theta)$ corresponds to one of the true source locations and orientations, $r = r_{qi}$ and $\Theta = \Theta_i$, $i = 1, ..., p$.

5 Brain Storm

BrainStorm is a free open source software suite dedicated to the forward and inverse problems in MEG and EEG. It also features 2D and 3D visualization tools, with emphasis on the appraisal of the source temporal dynamics. It is developed under Matlab [7], for faster development and implementation of emerging signal and image processing techniques applied to MEG and EEG signals [8].

For source localization in EEG data, BrainStorm uses RAP-MUSIC algorithm and requires a file with EEG data in "raw" format and additional a text file with the coordinates of the electrodes as well as the coordinates of anatomical landmarks (nose, ears, etc.). For recording of EEG data the Standard International 10-20 System can be used with possibility of adding several additional electrodes. If there is no anatomical information, such as MRI data, BrainStorm provides generic Phantom anatomy templates, which can be used instead. BrainStorm provides spherical, as well as generic head models, which are more accurate, for the forward modelling.

Once data is loaded into BrainStorm, it can be visualized, as can be seen in Figure 3. After

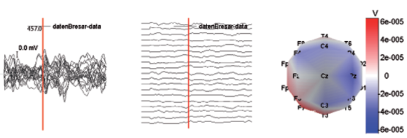

Fig. 3 Data time series and electrode positions in Brainstorm

performing Boundary Element Method for forward modeling and RAP MUSIC as inverse approach, the source location is represented on the MRI volume (Figure 4). The estimated EEG dipoles are visualized on the MRI volume. In the MRI viewer three MRI pictures are shown, the coronal, sagittal and axial view of the subjects head and located dipole is presented with white dot. Additionally, the estimated dipoles are illustrated in the Topography figure. Here the dipole strength and orientation can be seen. (see figure 6). Furthermore time-variabilities for all estimated dipoles are plotted over the selected time period (see figure 4).

6 Results

The brainstorm software was used to analyze EEG data from three people during epileptic seizure. In Figures from 4 to 14 possible locations of epileptic seizures are presented. For calculations the following settings of the software was used. The three anatomical landmarks (nasion, left and right ear) were used to fit the actual positions for the electrodes. A rank of the covariance matrix of 4 and a correlation threshold for the result of 0.80 was used. As regularization method Tikhonov condition was used. Tikhonov regularization is the most commonly used method of regularization of ill-posed problems.

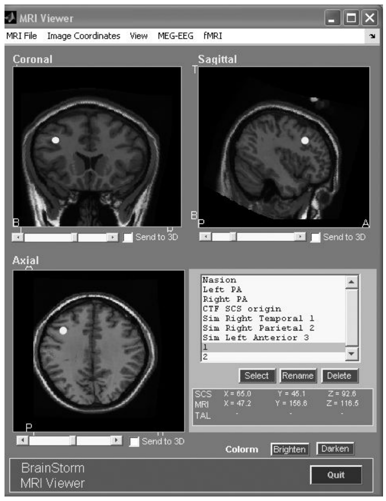

Fig. 4 Most probable position of dipole for the first person

7 Conclusions

Localization of electrical field sources in brain as an ill-posed problem, therefore, it cannot be solved directly. Although the algorithm for source calculation is generally simple, many additional conditions must be fullfiled in practice to obtain sustainable results. In this study, a simple systems of concentrically placed cubes as approximation for the head, was built first, understand the basic problems that can be encountered when solving such problems. Next, Brainstorm software was used to solve real source identification problem during epileptic seizures. Data from three persons was used in the

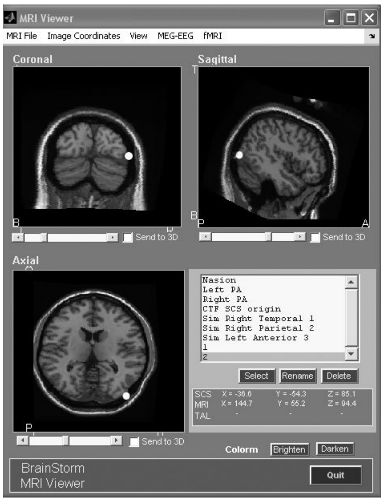

Fig. 5 Improbable position of dipole for the first person

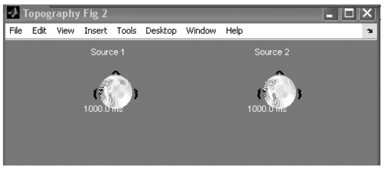

Fig. 6 Strength and orientation of both dipoles for the first person

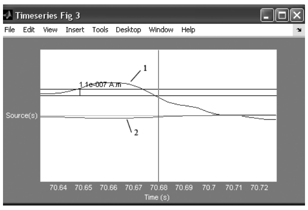

Fig. 7 Time-variability of both sources for the first person

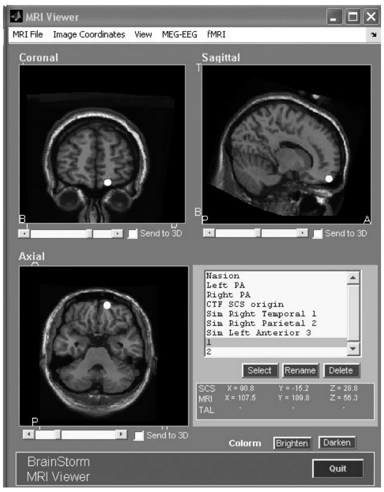

Fig. 8 Most probable position of dipole for the second person

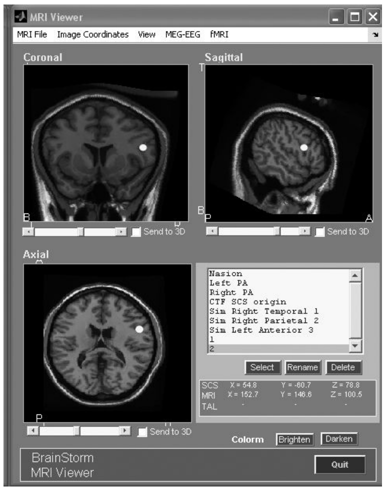

Fig. 9 Second most probable position of dipole for the second person

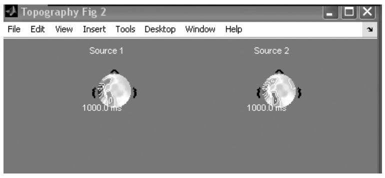

Fig. 10 Strength and orientation of both dipoles for the second person

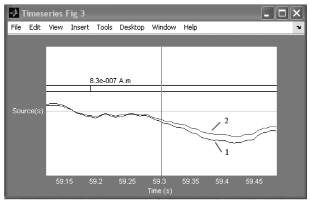

Fig. 11 Time-variability of both sources for the second person

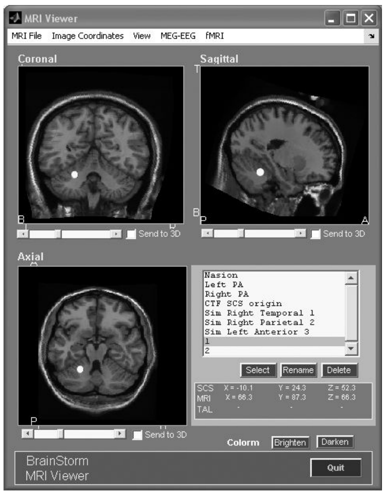

Fig. 12 Most probable position of dipole for the third person

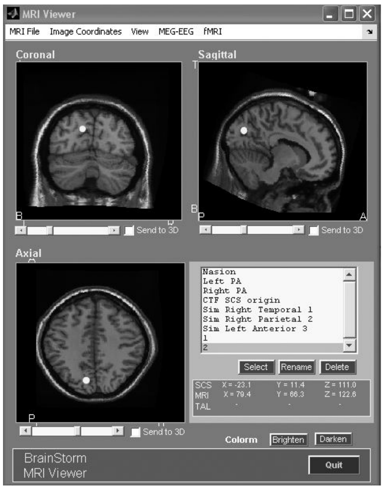

Fig. 13 Second most probable position of dipole for the third person

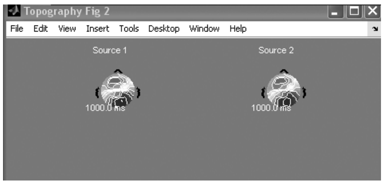

Fig. 14 Strength and orientation of both dipoles for the third person

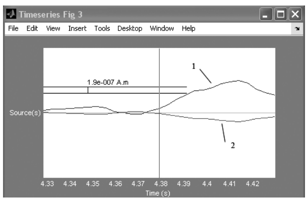

Fig. 15 Time-variability of both sources for the third person

study and the following can be concluded. Normally, more than one dipole is estimated by the software, and the selectivity can be controlled by the selection correlation threshold. The higher the rank of the covariance matrix and the lower the correlation threshold, the more dipoles are found. The rank of the covariance matrix can indicate two thins, either there is a lot of noise in the system, a large number of active dipoles or too few electrodes were used for EEG measurements to obtain reliable results. In the most cases not all estimated dipoles are realistic. Sometimes estimated dipoles are outside the brain, which is not sensible in reality (see figure 4). In spite of the fact, that concentric-spheres model was used and that only 32 electrodes were used for EEG measurements and that general electrode positions were used, the system provided very realistic results. Nevertheless, it can occur that real source location is not the most probable-one suggested by the program, therefore, only the specialist can decide at the end what is most probable location of the source. Brainstorm provides a relatively fast tool for identification of sources under Matlab environment.

8 References

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