Statistical methods of magnetoencephalographic signals processing

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Human brain is one of the most complex structures scientists have ever studied. The amount of knowledge about brain functioning dramatically increases from year to year, but there are still many discoveries to be made in this field. This thesis gives a brief overview of several statistical approaches which were used to analyze magnetoenchephalographic (MEG) data. MEG is noninvasive functional neuroimaging technique which allows to record multichannel signals of brain's magnetic field variations near the head of person doing some experiment. MEG signals coupled with some auxiliary data (fMRI scans, actogramms, miograms, etc.) can be used not only in scientific domain (for neurophysiological hypothesis testing), but for medical applications as well (MEG is widely used for epileptic regions detection). More information about MEG can be found in Hamalainen [1] and Zakharova, Nikiforov, Goncharenko [2].

Typical MEG data analysis workflow can be divided in following steps:

- Preprocessing (noise cancellation, bad channels detection, MEG–MRI co–registration, etc.)
- Data transform (region of interest selection, time frequency transforms, signal segmentation with trials detection, etc.)
- Inverse problem solving (signal to source space transform)
- Statistical inference (condition contrasts, multi hypothesis testing with some correction procedure)

Next chapters of this paper describe how statistical techniques can help to enhance some of these steps.

Improved noise model. MEG sensors are very sensitive devices, so it is very important to clear the data from noisy components. MEG setup allows to record signals without the subject inside MEG–chamber (i. e. before the experiment start). These signals are called ”empty room” records and contain environmental noise of MEG device and surrounding. It is very important data for fitting noise distribution, which often assumed to be Multivariate Gaussian. Our experiments with real ”empty room” recordings showed that this assumption in general does not hold. Better model for this noise distribution is finite Gaussian mixture, see Fig. 1.

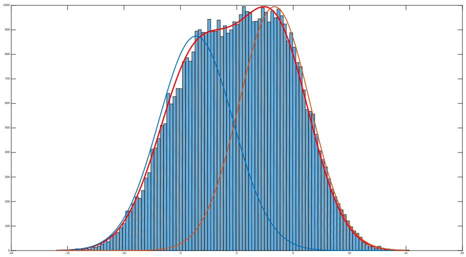

Figure 1: One channel of MEG–record fitted to Gaussian mixture

Such paradigm change in noise distribution allows building more flexible processing algorithms from one side (ordinary Gaussian noise will be one of the cases of such general model), but some essential properties of noise distribution might not held anymore, which could be critical for some applications.

It was established in Goncharenko and Zakharova [3] that some well–known properties of transformations of Gaussian mixtures have similarities with ordinal Gaussian distribution, see following sets of theorems.

Theorem 1. *If ξ has a Gaussian location scale mixture distribution with density*

$$p_\xi(x) = \int_0^\infty \int_{-\infty}^\infty \frac{1}{\sigma}\, \varphi\left(\frac{x-\mu}{\sigma}\right) \mathrm{Q}(d\sigma, d\mu), \quad x \in \mathbb{R},$$

then $\eta = \exp(\xi)$ is location scale log–Normal mixture with density

$$p_\eta(x) = \int_0^\infty \int_{-\infty}^\infty \frac{1}{x\sigma} \varphi\left(\frac{\ln x - \mu}{\sigma}\right) \mathrm{Q}(d\sigma, d\mu).$$

Opposite result is also true. If η has a location scale log–Normal mixture distribution, then $\xi = \ln \eta$ is a location scale Gaussian mixture with respect to same probability measure Q.

Theorem 2. *If ξ has a Gaussian scale mixture distribution, then ξ^2 is a Gamma scale mixture distribution with respect to same probability measure* Q*. Density of ξ^2 is following*

$$p_{\xi^2}(x) = \int_0^\infty \frac{1}{\sigma\sqrt{x}}\, \varphi\left(\frac{\sqrt{x}}{\sigma}\right) \mathrm{Q}(d\sigma) = \int_0^\infty \frac{1}{\sigma\sqrt{2\pi x}}\, e^{-\frac{x}{2\,\sigma^2}}\, \mathrm{Q}(d\sigma).$$

But the next theorem shows important difference in behavior.

Theorem 3. *Zero correlation of elements of vector distributed according to Multivariate Gaussian mixture does not imply independence of these elements.*

MEG–Inverse. In order to localize activity sources within the brain it is required to solve so-called MEG–Inverse problem. There are several different approaches for mathematical formalization of this task. All of them use quasi–static approximation of Maxwell equations introducing concept of "current dipole", which represent the source of electromagnetic activity. There are two main paradigms to formulate inverse problem: "distributive" and "parametric".

With distributive approach finding of inverse operator is equal to solving ill–posed system of linear equations.

$$Y = L\Theta + \mathcal{E},$$

where $Y \in \mathbb{R}^n$ — measured data, $L \in \mathbb{R}^{n\times k}$ — matrix of Biot–Savart–Laplace operator, $\Theta \in \mathbb{R}^k$ — unknown magnitudes of sources, $\mathcal{E} \in \mathbb{R}^n$ — noise, k — number of sources, n — number of MEG–sensors, $k \geq n$.

Many techniques were developed for solving such problems, one of the most popular is least squares approach (in MEG community it is often called minimum norm estimate (MNE), keeping L_2–norm in mind).

$$||\mathcal{E}||^2 = ||Y - L\Theta||^2 \to \min_{\Theta}.$$

Solution in general case provided by following formula for weighted least squares estimator (also called Eitken's estimator).

$$\hat{\Theta} = (L^\top C^{-1} L)^{-1} L^\top C^{-1} Y,$$

here C is covariance matrix for noise $\mathcal{E}$.

It is well–known that for Gaussian noise such general least squares estimate is valid and also is a best linear unbiased estimator. This result requires covariance matrix to be positively defined. Following theorem establishes the fact that for Gaussian mixtures this property is still valid.

Theorem 4. *Consider random variable $\mathcal{E}$ having Multivariate Compound Gaussian distribution with density*

$$h(\vec{x}) = \int\limits_{\mathbb{Y}} f_y(\vec{x}; \vec{\mu_y}, \Sigma_y)\mathrm{Q}(\mathrm{d}y),$$

where $f_y(\vec{x}; \vec{\mu_y}, \Sigma_y)$ — density of Multivariate Gaussian distribution with mean $\vec{\mu_y}$ and covariance matrix Σ_y.

Then covariance matrix of $\mathcal{E}$ is positively defined if any of covariance matrices Σ_y is positively defined.

Another formalization of the MEG–Inverse problem operates in terms of sources with unknown parameters.

$$Y_t = \sum_{i=1}^{N_d} L(R_t^i)Q_t^i + \varepsilon_t,$$

where R_t^i and Q_t^i — position and dipole moment of i-th source in time t. Here number of sources N_d considered unknown.

In such setup it is still ill–posed problem as was discovered by Helmholtz in 1853, so no closed form solution for general case exist. But there is a special case with single source where such solution can be derived. Such case can be considered as a model for epileptic brain activity. In most cases it is possible to treat epileptic source as the only activity source, because magnitude of other sources is much lower.

Let's consider spheroid head model. Solution for single source within such model was derived in Zakharova [4]. It lies in depth of r_Q between extremum points (corresponding to the maximum and minimum value of the radial component of the magnetic field B) on surface of sphere, and θ_m is an angle between source and main axis of sphere.

$$r_Q = r\frac{3 - \cos^2\theta_m - \sqrt{9 - 10\cos^2\theta_m + \cos^4\theta_m}}{2\cos\theta_m}.$$

The following theorem states that r_Q is actually biased estimator with respect to small deviations in θ_m.

Theorem 5. *If $\hat{\theta} = \theta_m + \varepsilon$, then estimator r_Q has bias $o(\mathbb{D}\varepsilon)$.*

Stability of such approach was tested in numerical simulation made in Karpov and Zakharova [5].

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