The practical approach to detection of evoked responses

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RESUME

Dans l'article on envisage une méthode de détection de perturbations dans un signal non stationnaire; comme example on a choisi les réponses evoquées. Le problème se pose dans le diagnostic medical basé sur l'annalyse des potentiels d'action électrique. On adopte l'hypothèse que les characteristiques statistiques du signal sont inconnues a priori et que la conversion est effectuée avec un petit nombre de données. Avec les valeurs du signal aux moments choisis, on forme le vecteur de discrimination qui constitue la solution du problème. L'article dècrit une méthode recursive qui rend le choix de moments et le calcul du vecteur de discrimination optimum. On présante aussi l'algorithme qui détermine les niveaux de détection; les résultats de l'annalyse d'un signal ECoG sont présantés.

SUMMARY

A method of detection of disturbances in nonstationary signal of finite time duration has been considered in the paper. The problem is very important in medical research; in the analysis of evoked potential signals. In order to formulate an useful method it is necessary to accept a difficult assumption that no statistical characteristics are known a priori and the amount of the processed data is relatively small. The concept of the solution of the problem lies in creating a discriminant vector using signal values at selected time instants. A special recursive routine was found for the points selection and discriminant vector evaluation. The routine, presented in the paper, is optimized for minimum calculation time. Additionally, a concept of the detection threshold evaluation is given. The method is illustrated with same results obtained from actual ECoG signal analysis.

1. Introduction and concept

Evoked responses investigation is well known technique of the nervous system research [2]. The evoked response is a electrophisiological registration of brain activity following to a specific stimulus, for example auditory or visual. The evoked signal is very small level compare to spontaneous activity, so repeated registration is performed. Useful information can be extracted from the set of data by applying statistical methods.

However, some of measured records contain high level disturbances (artefacts) resulting mainly from patient movement and these should be rejected. Thus, the primary procedure in the data set processing must be input data selection basing on artefacts detection.

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To apply classical methods of data classification to the digitized signal we should for each response x_i evaluate a number y_i which determines the quality of the response. The simplest transformation $x_i \rightarrow y_i$ can be defined as the inner product:

$$y_i = 1^T x_i \qquad (1.1)$$

where 1 is so called discriminant vector. The vector 1 should be chosen to maximize the discrimination index:

$$D^2 = E^2(y)/V(y) \qquad (1.2)$$

where $E^2(y)$ is the square of the mean value of y_i and $V(y)$ is the variance of y_i. We assume that mean value of artefacts is statistically equal to zero at each point of time and any correct response is a stochastic process of nonzero mean. Therefore, the quality of particular response may be valued by comparison the y_i value with two characteristic values, E(y) and zero. (for details see Section 3). If the basic statistical characteristics of input data, such as mean values vector and covariance matrix are known then the discriminant vector can be derived from the following expression [3]:

$$1 = C^{-1} m \qquad (1.3)$$

where: m – mean values vector of x ,

C – covariance matrix of x_i.

In practice, the problem is more complicated because neither m nor C are known a priori. These quantities depend on the conditions of the measurement and should be evaluated individually for each patient in each examination. It is possible to chose the discriminator relaying on reference measurement. However, the formal inversion of an estimated $\hat{C}$ matrix is possible only if the number of responses is not less then the number of samples in one response. Additionally, statistical significance of the discriminator 1 is small unless the first number is much greater the second one.

The main idea of the paper is to limit the number of samples of x_i taken to the discriminative analysis. Selection of the samples is performed with a step by step method. Let us assume that a set of p-1 samples at time instants $(t_1, t_2, \ldots t_{p-1})$ has been chosen. The set is then complemented with a sample t_p which maximizes the estimated index of discrimination:

$$\hat{D}^2_p = \frac{E^2(\hat{1}^T_p \hat{m}_p)}{V(\hat{1}^T_p \hat{m}_p)} = \hat{m}^T_p \hat{C}^{-1}_p \hat{m}_p = \hat{1}^T_p \hat{m}_p \qquad (1.4)$$

where $\hat{m}_p$ – vector of averaged values in the considered set of time points,

$\hat{C}_p$ – estimated covariance matrix of the set,

$\hat{1}_p$ – estimated discriminator.

The routine of selecting the successive samples will continue until the F-Snedocor statistics [3]:

$$F_p = \frac{(n-p)\ (\hat{D}^2_p - \hat{D}^2_{p-1})}{\frac{n-1}{n} + \hat{D}^2_{p-1}} \sim F(1, n-p) \qquad (1.5)$$

(n – number of responses)

shows that there is no sample which significantly increases $\hat{D}^2_p$.

In the section 2 a dedicated, fast algorithm has been developed for the computation of

$$\Delta\hat{D}^2_p = \hat{D}^2_p - \hat{D}^2_{p-1}. \qquad (1.6)$$

The algorithm does not required the inversion of $\hat{C}_p$ to be carried out.

The time instants $t_1, \ldots, t_p$ mark a set of characteristic points in the evoked potential signal (see Fig. 1). Present experiments show that the points estimated in such way include ones being used in traditional diagnostics.

2. Numerical tools

Let us designate a symbol of x_{it} to the t-th sample in i-th epoch. The aim of the processing considered in this section is to select from the original data a subset of samples most representative for detection purposes. The subset $(x_{it_1}, x_{it_2}, \ldots, x_{it_p})$ consists of samples at time points $t_1, \ldots t_p$ in every response $i = 1, \ldots, n$. It is characterized with the following statistical parameters:

- the averaged values vector:

$$\hat{m}^T_p = [\hat{m}_1, \hat{m}_2, \ldots, \hat{m}_p] \qquad (2.1a)$$

$$\hat{m}_k = \frac{1}{n}\sum_{i=1}^{n} x_{it_k} \qquad (2.1b)$$

- the estimated covariance matrix:

$$\hat{C}_p = [\hat{c}_{kl}] \qquad (2.2a)$$

$$\hat{c}_{kl} = \frac{1}{n}\sum_{i=1}^{n} x_{it_k} x_{it_l} - \hat{m}_k \hat{m}_l \qquad (2.2b)$$

The scheme of evaluation the $\hat{1}^T_p$ and $\Delta\hat{D}^2_p$ proposed in this paper has a recursive form. To perform the p-th iteration we need the following data resulting from the previous iteration: vectors $\hat{m}^T_{p-1}$, $\hat{1}^T_{p-1}$, described above, and the matrix P_{p-1} being the inversion of the $\hat{C}_{p-1}$ matrix.

Now, we should decide how to complement the subset obtained from previous iteration. It needs to evaluating the increment $\Delta\hat{D}^2_{pt}$ for every time instant t except that selected before. The value of t, when $\Delta\hat{D}^2_{pt}$ reaches the global maximum, indicates the best sample to complement the subset. The computation for any particular t contain many steps. We should estimate the averaged value $\hat{m}_t$ at this time point and the covariance vector $\hat{c}_{p-1t}$ of the t-th samples with the rest of the subset:

$$\hat{c}_{p-1t} = [\hat{c}_{1t}, \hat{c}_{2t}, \ldots \hat{c}_{p-1t}] \qquad (2.3a)$$

$$\hat{c}_{kt} = \frac{1}{n} \sum_{i=1}^{n} x_{it_k} x_{it} - \hat{m}_k \hat{m}_t \qquad (2.3b)$$

and the corresponding variance:

$$\hat{c}_{tt} = \frac{1}{n} \sum_{i=1}^{n} x_{it}^2 - \hat{m}_t^2 \qquad (2.3c)$$

On the basis of these estimates we can compute the following intermediate data, known from the problem of inversion of symmetric matrix [1]:

$$w_{p-1t} = -P_{p-1}\hat{c}_{p-1t} \qquad (2.4)$$

$$\alpha_{pt} = \hat{c}^T_{p-1t} w_{p-1t} + \hat{c}_{tt} \qquad (2.5)$$

$$\beta_{pt} = \hat{m}^T_{p-1} w_{p-1t} + \hat{m}_t \qquad (2.6)$$

$$k_{pt} = \frac{\beta_{pt}}{\alpha_{pt}} \qquad (2.7)$$

$$\Delta l_{p-1t} = k_{pt} w_{p-1t}, \quad l_{pt} = k_{pt} \qquad (2.8)$$

$$\Delta\hat{D}^2_{pt} = \hat{m}^T_{p-1} \Delta l_{p-1t} + \hat{m}_t l_{pt} \qquad (2.9)$$

The last expression results from the following one:

$$D^2_{pt} = \hat{m}^T_{pt} \hat{l}_{pt} =$$

$$= \begin{bmatrix} \hat{m}_{p-1} \\ \hat{m}_t \end{bmatrix}^T \begin{bmatrix} \hat{l}_{p-1t} + \Delta l_{p-1t} \\ l_{pt} \end{bmatrix} = \qquad (2.10)$$

$$= \hat{m}^T_{p-1} \hat{l}_{p-1t} + \hat{m}^T_{p-1} \Delta l_{p-1t} + \hat{m}_t l_{pt} =$$

$$= \hat{D}^2_{p-1t} + \hat{m}^T_{p-1} \Delta l_{p-1t} + \hat{m}_t l_{pt}$$

The p-th iteration ends after choosing such $t_p = t$ that maximizes $\Delta\hat{D}_{pt}$. Then it is possible to update the P_p-matrix and the resulting vector $\hat{l}_p$ using the following formulas:

$$P_p = P_{p-1} + \alpha_p^{-1} \begin{bmatrix} w_{p-1} w^T_{p-1} & w_{p-1} \\ w^T_{p-1} & 1 \end{bmatrix} \qquad (2.11)$$

$$\hat{l}^T_p = [\, \hat{l}^T_{p-1} + \Delta l^T_{p-1t_p}, l_{pt_p} \,] \qquad (2.12)$$

where: $\alpha_p = \alpha_{pt_p}$, $w_{p-1} = w_{p-1t_p}$.

Notice that the most nested routine of computing $\Delta\hat{D}^2_{pt}$ avoid evaluating data from expressions (2.7-2.9) by using final combination

$$\Delta\hat{D}^2_{pt} = \beta^2_{pt}/\alpha_{pt} \qquad (2.13)$$

and then the number of multiplication is reduced to p^2-p+3 per one time instant t.

Ending this section let us make a remark that the number $\hat{D}^2_p$ required for F-statistics evaluation may be obtain by summing $\hat{D}^2_{p-1}$ from the previous iteration and the recent $\Delta\hat{D}^2_p$.

3. Detection thresholds

After having estimated discriminator it becomes possible to classify individual responses according to the corresponding y_i value. This number should be compared with some thresholds to decide if an individual response is correct or not. The thresholds evaluation depends on particular hypothesis concerning distributions of y_i obtained from both normal and disturbed responses. There is no doubt that distribution in the normal case may be approximated with gaussian function with nonzero mean value. Artefacts distribution is not such clearly determined. However, after examining a number of possibilities we decide to use for this purpose a gaussian distribution, this time with mean value equal to zero. This method proved the most effective in practical application.

The first operation in analysing the y_i sequence should be its normalization, in order to make the averaged value $\bar{y}_i$ equal to 1. The distribution of random variable y (with y_i being a sample of y) consists of two components:

- distribution of correct part of population

$$f_c(y) = \frac{1}{\sqrt{2\pi}\,\sigma_c} \exp\left[-\frac{(y-\bar{y}_c)^2}{2\sigma_c^2}\right] \qquad (3.1a)$$

- distribution of artefacts

$$f_a(y) = \frac{1}{\sqrt{2\pi}\,\sigma_a} \exp\left[-\frac{y^2}{2\sigma_a^2}\right] \qquad (3.1b)$$

where σ_c^2, σ_a^2 are corresponding variances,
$\bar{y}_c$ is the mean value of correct population, approximately equal to 1.

Let p_c denote the frequency of correct response appearance. The total observed distribution of y is given by:

$$f(y) = p_c f_c(y) + (1-p_c) f_a(y) \qquad (3.2)$$

To satisfy the normalization condition E(y) = 1 it is necessary to assume that:

$$\bar{y}_c = 1/p_c \qquad (3.3)$$

Eventually we have the distribution of y_i with unknown parameters σ_c, σ_a and p_c. One can estimate them using maximum likelihood method that is to maximize the following function:

$$\ln L(\sigma_c, \sigma_a, p_c) = \sum_{i=1}^{n} \ln [\, f(y_i) \,] \qquad (3.4)$$

The dedicated algorithm has been carried out for the solution of this problem, but its detailed description is out of the scope of this paper. After having estimated the above parameters it becomes possible to evaluate thresholds for artefacts detection. By comparing two components in (3.1) we obtain values of the same density of probability for both correct and disturbed distributions. It leads to the equation:

$$y^2\,(\sigma_a^{-2}-\sigma_c^{-2}) + 2\,y\,(\sigma_c^2 p_c)^{-1} = (\sigma_c p_c)^{-2} + 2\ln[\sigma_c\sigma_a^{-1}(p_c^{-1}-1)] \qquad (3.5)$$

The values of y satisfying the above equation can be accepted as the optimum threshold limits.

There are 3 cases in which the method can indicate the absence of artefacts in the set of input data: the estimated p_c parameter appears to be equal to unity, the equation (3.5) has no solution or no value of y_i lies between the threshold limits. The method of such detection is then "careful" in response rejection. The author expects that further improvement in artefact rejection rate would be brought with new hypothesis on artefact distribution.

4. Exemplary results

The method described above has been tested using actual electrocochleographic signal as the input data. The responses from the cochlea were recorded after acoustic stimulation of the ear with 0.1 ms rectangular pulses of alternative polarity and 80dB peak sound pressure level.

Signal epochs of 19.2 ms time duration were sampled in 256 points using 13.3 kHz sampling frequency. There were 47 sweeps acquired and analysed.

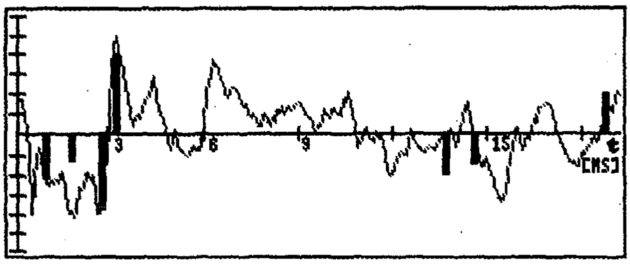

Fig.1. Actual averaged ECoG response with marked selected time instants and values of the discriminant vector.

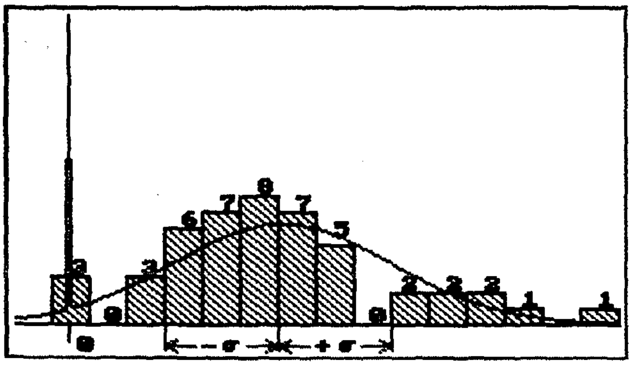

Fig. 2. Empirical and theoretical distributions of y random variable.

The averaged response of the set is shown in figure 1. The time instants with values of the discriminative vector are marked there. It was found that a set of 7 time instants is representative for discrimination purposes. In this example, the value of the D_p^2 index increases from 0.37 for one point to 3.47 for 7 point set, which shows the effect of the applied method.

Results of discrimination - the set of y_i values - has been collected using a histogram as shown in figure 2. A curve of total probability density of the y variable, fitted to the actual distribution, is also shown.

The figure 3 shows one response rejected as a result of the analysis. It does not fit to the rest of the set in terms of the assumed criterion.

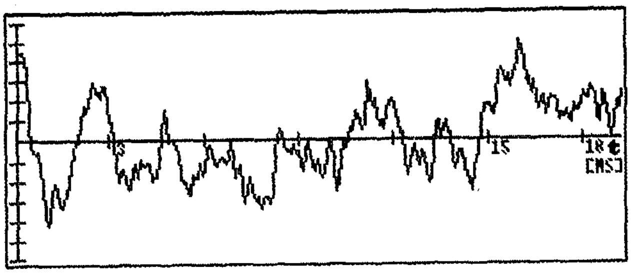

Fig. 3. The shape of one rejected response.

5. Conclusion

In the paper a problem of nonstationary signal discrimination was discussed. Generally, the covariance matrix of the signal is not known and it is hardly possible to access an amount of data sufficient to estimate an invertible form of this matrix. In the presented concept the discriminant vector was created from the signal values at selected time instants by optimizing the index $E^2(y)/V(y)$, where y is a random variable resulting from discriminative transformation.

The fast routine for this purpose is presented and the results are illustrated with the analysis of an actual ECoG signal.

These results shows that the set of representative time instants contains two classes of points: the first class is characterized by a large mean values and the second one with a relatively small mean values. The first class of points is quite consistent with that used in traditional diagnosis, where latency and level of peaks are used to determine the signal characteristics.

The subset of time instants characterized by small mean values is not visible in the averaged response. However, using our method becomes possible to detect them as being causally related with the main part of the signal.

References

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