LOCALIZATION OF MULTIPLE DIPOLE SOURCES OF HUMAN CEREBRAL POTENTIALS BASED ON SCD AND A MODEL SELECTION CRITERION

Wenyu Wang, Henri Begleiter and Bernice Porjesz
Wenyu Wang,SUNY HSC,Box 1203,450 Clarkson Ave.,Brooklyn,NY11203

Keywords: Laplacian; Multiple Sources Localization; Model Selecting Criterion; Consistency

1. Introduction.

The localization of sources of electrical activity generated in the human brain is a fundamental problem in topographic analysis. The localized sources can be used either to characterize brain functions in related experiments or to decompose and compress the recorded data. Almost all efforts have been directed at localization of dipole like analogous sources from potentials measured with electrodes on the scalp, as in EEG or event-related potential (ERP), or the external magnetic field measured in magnetoencephalography (MEG).

In the literature, the head is usually treated as a sphere or some simplistic shape, and the brain is assumed to be a homogeneous isotropic conductive media in the magnetic theory based methods, or is modelled as one, three, or more shells in the potential theory based methods. With the assumption that the exact number of dipoles k in an application is known, some methods have been proposed to solve dipole source localization problems such as the spatio-temporal source model (Scherg and Von Cramon 1985; Scherg 1990; Turetsky et al. 1990), non-linear least-square method and potential theory based methods (e.g. Sidman et al. 1978), non-linear least-square method and magnetic theory based methods (e.g. Ueno and Iramina 1990, Mosher et al. 1990), etc. Let $\{e_j, j = 1, 2, \ldots, w\}$ denote the locations of measuring sites, $\{t_u, u = 1, 2, \ldots, m\}$ denote the sampling times, and $\vartheta_k(t)$ denote a vector whose elements are possible locations and moments of k dipoles at time t. Then the methods in the literature use the following model

$$SP(e_j, t_u) = SP_k(e_j, t_u, \vartheta_k(t_u)) + \varepsilon_j(t_u),$$
$$j = 1, 2, \ldots, w; u = 1, 2, \ldots, m, \qquad (1.1)$$

and look for the optimal ϑ^* which minimize

$$\sum_{u=1}^{m}\sum_{j=1}^{w}(SP(e_j, t_u) - SP_k(e_j, t_u, \vartheta_k(t_u)))^2$$

with respect to $\vartheta_k(t_u)$, where $\varepsilon_j(t_u)$ denotes the noise, $SP(e_j, t_u)$ denotes observed scalp electric potential (SP) or magnetic field at the site e_j and time t_u, and $SP_k(e_j, t_u, \vartheta_k(t_u))$ denotes theoretical electric potential or magnetic field at the site e_j and time t_u created by k dipoles (or $\vartheta_k(t_u)$) in the brain through the physical model of the head. All aforementioned methods do not work if the possible number of dipoles in an application is unknown. In the literature, there does not exist a sufficient way to test the assumption of the a priori knowledge of the exact number of dipoles. For example, the reduced χ^2 statistic (see e.g. Bevington 1969), used for the determination of adequate underlying model order, is not the χ^2 statistic with mean one if the fitted model is not the actual underlying model or if the noise $\varepsilon_j(t_u)$ are not Gaussian. Even if $\varepsilon_j(t_u)$ are Gaussian, it fails to select a model if several fitted models are all significant under different model assumptions or at the same or different significant levels. If the values of the reduced χ^2 statistic under different models are used only, there is no unique way to set a critical value for selecting a model among all possible models.

It is well known that recorded voltages at electrode sites on the scalp are potential differences between the recorded sites and the reference electrode, while the observed potentials SP and the theoretical potentials SP_k in (1.1) are referenced to the infinite point. Denote the recorded potential difference at electrode e_j and time t_u as $SPD(e_j, t_u)$, then $SPD(e_j, t_u) = SP(e_j, t_u) - SPR(t_u)$, where $SPR(t_u)$ denotes the potential at the reference electrode and time t_u. Then, the average reference transformed potential $SPN(e_j, t_u)$ used in the literature has, from (1.1),

$$SPN(e_j, t_u) \overset{\text{def}}{=} SPD(e_j, t_u) - (1/w)\sum_{i=1}^{w} SPD(e_i, t_u)$$
$$= SP(e_j, t_u) - (1/w)\sum_{i=1}^{w} SP(e_i, t_u)$$
$$= SP_k(e_j, t_u, \vartheta_k(t_u)) - (1/w)\sum_{i=1}^{w} SP_k(e_i, t_u, \vartheta_k(t_u))$$
$$+ \varepsilon_j(t_u) - (1/w)\sum_{i=1}^{w} \varepsilon_i(t_u). \qquad (1.2)$$

Reprinted from the 1994 Proceedings of the Biopharmaceutical Section of the American Statistical Association

Denote

$$\varepsilon_j^*(t_u) = \varepsilon_j(t_u) - (1/w)\sum_{i=1}^{w} \varepsilon_i(t_u),$$
$$SP_k^*(e_j, t_u, \vartheta_k(t_u)) = SP_k(e_j, t_u, \vartheta_k(t_u)) - (1/w)\sum_{i=1}^{w} SP_k(e_i, t_u, \vartheta_k(t_u))$$

and $\vartheta_k(t_u) = (\alpha_k(t_u), \beta_k(t_u))$, where the elements of $\alpha_k(t_u)$ are locations of k dipoles and the elements of $\beta_k(t_u)$ are moments of k dipoles at time t_u. Then, we can write $SP_k^*(e_j, t_u, \vartheta_k(t_u)) = C_k(e_j, \alpha_k(t_u))^\tau M_k(\vartheta_k(t_u))$. When the locations of dipoles are assumed fixed in time, $C_k(e_j, \alpha_k)$ is not a function of time and plays the rule of the average reference transformed theoretical data in the literature (see e.g. Scherg 1990). It is clear that the produced noise $\varepsilon_j^*(\cdot), j = 1, \ldots, w$ are no longer independent, and hence it in turn will make diffcult in statistical inference for a model fitting procedure. Note that $C_k(e_j, \alpha_k(t_u))$ variates in time if the locations of dipoles are assumed changed in time.

Since each dipole possesses six parameters (three for position and the others for moments) that need to be estimated and the number of measuring sites w is usually small (e.g. in EEG or ERP, the number of electrode sites is usually 16, 31, 64), the upper bound of possible number of dipoles k is restricted by the number of measuring sites w multiplied by the number of time samples in a least-square principle based method. Therefore, other assumptions such as that locations and orientations of dipoles are not changed in time, magnitude of dipoles are non-parametric or some parametric functions of time, etc., are added in these methods in order to handle multiple dipole source cases. Again, the literature does not provide sufficient means to test the assumptions or to select the forms of the functions.

Moreover, even if the exact number of dipoles may be known in an application, the estimators of locations and moments of the underlying dipoles may be only a local optimal solution which are dependent on selection of the initial values in a non-linear iterated algorithm. In general, there is no fully effective way to select the initial values of the locations and moments. Therefore, there remain problems to use (1.1) for localization of dipole like analogous sources.

In reality, the possible number of the underlying dipoles, their locations and moments all are unknown and need to be estimated. It is clear that determining the possible number of dipoles and their locations of the underlying model are more important than their moments since if the number of the underlying dipoles and their locations are given, then their moments can be immediately derived by linear least-square method. The physical models are quite difficult to improve due to the architectural and functional complexity of the brain, and the inhomogeneity of the conductive media which surround it. We also adopt the aforementioned three-shell model. However, we show that we can solve the localization problem without having the reference dependency problem and a priori knowledge of the exact number of the underlying dipoles.

In this paper, we use a rectangular coordinate system with the origin at the center of the sphere, the x-axis passing through the inion, the y-axis passing through the right ear, and the z-axis going through the vertex. We propose the following model.

Let $\mathbf{S} = \{P_1, P_2, \ldots, P_n\}$ be a grid on the hemisphere, where n is dependent on the number of the electrode sites w. We assume that

$$SSCD(P_j, t_u) = SCD_k(P_j, t_u, \vartheta_k(t_u)) + \varepsilon_j(t_u), \quad j = 1, 2, \ldots, n; u = 1, 2, \ldots, m, \tag{1.3}$$

where $SSCD(P_j, t_u)$ denotes the value of empirical SCD field at the point P_j and time t_u (the empirical SCD field is obtained by first finding a smoothing spline on the sphere with the smallest bending energy and passing through the recorded potential differences at electrode sites on the scalp at sampling time t_u, and then taking the surface Laplacian for the spline), $SCD_k(P_j, t_u, \vartheta_k(t_u))$ denotes the value of theoretical SCD field at the point P_j and time t_u created by the k dipoles (or ϑ_k) in the brain (the theoretical SCD field is obtained by taking the surface Laplacian for $SP_k(\cdot, t_u, \vartheta_k(t_u))$), and $\varepsilon_j(\cdot), j = 1, 2, \ldots, n$, are independent white noise with mean zero and a common finite variance σ^2. Unlike the methods in the literature, we assume here that k is unknown and needs to be estimated.

In our model, the empirical SCD field (represented by SSCD values at all points of $\mathbf{S}$) is used instead of finite recorded scalp potentials. It is well known that recorded potential differences at electrode sites on the scalp are spatially smeared data due to the volume conductions of the different anatomical structures (brain, skull, scalp, etc.), record sites activity and reference site activity. In contrast, SCD acts as a spatial filter which provides an estimate of local skull current flow from the brain into the scalp and dramatic improvement in spatial resolution (Nunez et al. 1991) and is also free of the reference electrode. Therefore, the effect of smearing is reduced in our model since we use SCD and the reference dependency problem does not exist in our model. The methods in the literature tried to use the model (1.1) and the least-square method to find a dipole model whoes theoretical potentials at the finite electrode sites are close to the observed potentials at the same sites. There are no restrictions on the other points on the hemisphere. In contrast, our model (1.3) implies that we require not only that the theoretical potentials at the electrode sites calculated from the fitted dipole model are close to the observed potentials at the same sites, but also that the potential field on the hemisphere calculated from the fitted dipole model is close to the empirical potential field which has the smallest bending energy and passes through the observed potentials at the electrode sites. That is, our model requires more restrictions. This in turn implies, from a numerical point of view, that using our model will reduce the size of the solutions set in the backward solution problem more than using the model (1.1). Further, it is well known that the spline interpolated SP (hence SCD) field is a good approximation of the underlying SP (SCD) field if the number of recorded sites is large enough. Therefore, (1.3) is reasonable if the number of recording sites is large enough.

2. Model selection and dipole localization.

If we know the exact k in (1.3), the least-square estimator of ϑ_k may be obtained by chosing a suitable initial value of ϑ_k. But, if we know only a range of k, say $1 \leq k \leq B$, instead of the exact k, then the least-square method will lead to an optimal B dipoles model by the well known property of the least-square method; that is, the more the regressors are included in a regression equation, the smaller the residue is. Therefore, the least-square method is not suitable in this case. Here, we introduce the following model selection criterion (Wang 1989) to handle this case.

$$RCFC(m,k) = \sup_{\vartheta_k \in \Theta_k} \frac{1}{mn} \sum_{u=1}^{m} \sum_{i=1}^{n} f(P_i, t_u, \vartheta_k) - \frac{j(k,m)\log(nm)}{nm}, \qquad (2.1)$$

where

$$f(P_i, t_u, \vartheta_k) = -(SSCD(P_j, t_u) - SCD_k(P_j, t_u, \vartheta_k(t_u)))^2, \qquad (2.2)$$

Θ_k is the set consisting of all possible ϑ_k and $j(k,m)$ is a positive function related to the total number of parameters in ϑ_k. Here, we take $j(k,m) = 6km$ if assuming that moments and locations of k dipoles are changed across the sampling times; $j(k,m) = 6k$ if assuming that both the moments and locations are not changed across the sampling times; $j(k,m) = 3km + 3k$ if assuming that the moments are changed across the sampling times and locations are not; $j(k,m) = 3k+$ {total number of parameters in parametric functions for the moments } if assuming that the moments are the parametric functions of the sampling times and locations are not changed, etc. The model selecting is simply to choose a k^* dipoles model for which

$$RCFC(m,k^*) = max_{1 \leq k \leq B} RCFC(m,k). \qquad (2.3)$$

The corresponding estimator of ϑ_{k^*} can be obtained simultaneously from the k^* dipoles model.

In the expression of $RCFC(m,k)$, the first term (supremum of negative average of squared residuals) represents the gain by introducing k dipoles into the model and it will increase as k increases by the well known property of the least-square method, while the second term $-j(k,m)\log(nm)/nm$ represents the penalty which will decrease if the number of dipoles increases. The negative first term is also an estimator of the variance σ^2 of $\varepsilon_j(\cdot)$ in (1.3). In general, the more parameters added to a fitted model, the better the goodness-of-fit of the fitted model, but the greater the instability of the fitted model in prediction. Therefore, the selected k^* dipoles model by $RCFC$ is the best balanced model, balanced between the gain and the penalty among all possible one to B dipoles models.

Such kind of criteria are well-known in other fields. such as regression analysis and time series analysis (Akaike, 1974; Schwarz, 1978; Wang, 1989). The discussions regarding statistical properties of such criteria are beyond the scope of this article. It is suggested that interested readers read papers of Haughton (1988), Wang (1989) and Wei (1992). We only indicate that the order (with respect to the sample size) of the second term is determined by the results of the larger number theorem to assure that $RCFC$ will lead to select the true underlying dipole model consistently as the sample size mn tends to infinity.

The calculation of the first term in (2.2) is involved in non-linear optimization techniques. To avoid such difficulties, we introduce the following iterated procedure. Define, for each fixed α_k,

$$RCFCI(m,k,\alpha_k) = \sup_{\beta_k} \frac{1}{mn} \sum_{u=1}^{m} \sum_{i=1}^{n} f(P_i, t_u, \alpha_k, \beta_k)$$

$$- \frac{j(k,m)\log(nm)}{nm}. \quad (2.4)$$

(1) Define a global grid $\mathbf{D}$ in the brain (or some regions of the brain if one has some priori knowledge about the locations of the underlying dipoles) which represent all possible locations of the underlying dipoles. Then for any fixed $\alpha_k \in \mathbf{D}$, (2.1) is a linear regression model in which the moments are regression coefficients and the terms associated with α_k are regressors. Therefore, $RCFCI$ can be calculated by using linear regression techniques such as RSQUARE.

(2) Choose for example six models, which correspond to the six largest $RCFCI(m,k,\ \alpha_k)$'s among all possible $\alpha_k \in \mathbf{D}$ and $k \in [1, B]$, and then determine a further smaller region in the brain and a further smaller interval for k based on the six models. Use the obtained new interval for k and define a further denser grid in the obtained new region for possible locations of the underlying dipoles; then repeat the first step. Finally, stop this iterated procedure until the differences of dipole locations obtained from two adjacent iterated steps are less than the given error. The final model will give the estimated number of the underlying dipoles, their locations and moments simultaneously. If necessary, one can use the estimated number of dipoles in the final model, and treat the estimated positions and moments in the final model as initial values in a nonlinear optimal iterated algorithm to obtain a further solution.

There are some advantages to use this iterated procedure. The grid $\mathbf{D}$ is reflexible and can be defined in any region in the brain based on each application; Step (1) represents a global search which does not have the problem of initial values; for any fixed $\alpha_k \in \mathbf{D}$, the regressors associated with α_k in (2.1) do not change in the procedure and only need to be calculated and saved once for all later uses; all procedure are only involved in linear algebra and hence the computation is simple.

3. Simulation Results.

As we mentioned in Section **1**, determining the possible number of dipoles and their locations of the underlying model are more important than their moments since if the number of the underlying dipoles and their locations are given, then their moments can be immediately derived by linear least-square method. Therefore, we now use simulation method to only show how the proposed method improves the methods in the literature in determining the possible number of the dipoles and their locations of the underlying model. A grid on the hemisphere was chosen which consists of 775 points in the neighborhood of 31 electrode locations (25 points each). Simulations were performed for a total of 35 different dipole sources (five two-symmetric-dipole sources with seven different orientations which cover almost all possible kinds of orientations). All positions of dipoles here belong to a grid which consists of 186 points (dipole locations) in the hemisphere. For each source (two symmetric dipoles), we used the three-shell model to calculate potentials at 31 electrode locations, then modified the calculated potential (CP) at each electrode location by adding to it 5% of its value multiplied by $U[-1,1]$ (an uniformly distributed random variable ranging from -1 to 1) and treated these values as "empirical" potentials (EP) (i.e. $EP = CP{+}0.05{*}CP{*}U[-1,1]$). Then we performed Steps (1) in the iterated procedure of Section **2** to select six models which correspond to the six largest $RCFCI$'s among all possible one dipole to four dipole sources (all one to four combinations of the 186 dipole locations). Note that for each source the total number of models which have the same number of dipoles and locations as that of the source is equal to 49 ($= 7 \times 7$) since we treat each nonzero components combination of six moments of the two dipoles as a different model. Finally, we count the number of models which have the same number of dipoles and locations as that of the source in the six selected models. The larger the counted number, the better the localization ability (in determining the number of the underlying dipoles and their locations) of the proposed method. The counted number for each of the 35 dipole sources is shown at the corresponding row and column in Table **I**. To show the advantages by using SCD than by using SP, we also give in Table **I** the corresponding results by the proposed method with the SCD field replaced by the SP field (the values in the parentheses); and the corresponding results by the proposed method with the SCD field replaced by SP at 31 electrode sites only (the values in the square brackets). The first column in Table **I** shows, in the spherical coordinate system, nominal dipole locations (r_p, f_p, t_p) (we always take $r_p = 0.692$, so only (f_p, t_p) is shown in the column, where e.g. $(\frac{3}{8}\pi, \pm\frac{2}{7}\pi)$ denotes two symmetric dipole locations $(\frac{3}{8}\pi, +\frac{2}{7}\pi)$ and $(\frac{3}{8}\pi, -\frac{2}{7}\pi)$); the first row shows, in the spherical coordinate system, corresponding nominal dipole moments (r_m, f_m, t_m) (we always take $r_m = 0.5$, so only (f_m, t_m) is shown in the row, where e.g. $(\frac{1}{2}\pi, \pm\frac{1}{2}\pi)$ denotes two dipoles moments $(\frac{1}{2}\pi, +\frac{1}{2}\pi)$ and $(\frac{1}{2}\pi, -\frac{1}{2}\pi)$, and (f_p, t_p) means that $(f_m, t_m) = (f_p, t_p)$). Each of the 35 dipole sources is uniquely defined by the corresponding row and column. For each simulated underlying dipole source, our method selects a model which has the largest $RCFCI$ among all possible one dipole to four dipoles sources (all one to four combinations of the 186 dipole locations). To show the correctness of the proposed method in model selection, we count the number of times that the selected models have the same number of dipoles and locations as that of the corresponding 35 underlying dipole sources. The number is 33 out of 35 by the proposed method with the SCD field and is zero out of 35 by the proposed method with the SCD field replaced by the SP field or with the SCD field replaced by SP at 31 electrode sites only. From these results and Table **I**, we see that the correctness and the localization ability of the proposed method by using the SCD field is very good in itself and also much better than by using the SP field or by using SP at 31 electrode sites only. These also demonstrate that the proposed method by using the SCD field will reduce the size of the solutions set in the backward solution problem more than by using the SP field or by using SP at 31 electrode sites only, which we claimed in Section **1**.

We also did similar simulations by adding to the calculated potential 10% of its value multiplied by $U[-1,1]$. The corresponding results are showed in Table **II**, and the number of times, that the selected models (with the largest $RCFCI$) have the same number of dipoles and locations as that of the corresponding 35 underlying dipole sources, is 26 out of 35 by the proposed method with the SCD field and is zero out of 35 by the proposed method with the SCD field replaced by the SP field or with the SCD field replaced by SP at 31 electrode sites only. These results and Table **II** demonstrate further that our method is not only a good method in its correctness and localization ability, but also a stable method for noising data. The stable property can be thought due to both the filtering property of SCD and the consistency property of the criterion.

Simulations are also conducted for the 35 sources by using only the aforementioned empirical potentials at 31 electrode sites and fitting a model based on the residual only for $1 \leq k \leq 4$. In all 35 cases, the best fitted models are some four-dipole models which are not the corresponding underlying 35 models. Therefore, fitting a model based on the residual is poor if the exact number of dipoles is unknown or the possible number of dipoles is in an interval. This is not surprising as we mentioned early in Section **2**. Figure **3** shows the spherical-spline interpolated SP fields based on the calculated potentials at 31 electrode locations (the top left), the empirical potentials $EP = CP + 0.05 * CP * U[-1,1]$ (the middle left) and the empirical potentials $EP = CP + 0.1 * CP * U[-1,1]$ (the bottom left), and their corresponding SCD fields (the right column) created from two simulated symmetric dipoles with nominal position $(r_p, f_p, t_p) = (0.692, 0.25\pi, \pm\frac{1}{3}\pi)$ and nominal moment $(r_m, f_m, t_m) = (0.5, 0, 0)$.

Table I. The total number of models which have the same number of dipoles and locations as that of the underlying dipole source in the six selected models by the proposed method with the noise $0.05 * CP * U[-1,1]$.

	$(0,0)$	$(\frac{1}{2}\pi, \pm\frac{1}{2}\pi)$	$(\frac{1}{2}\pi, 0)$	$(\pi, 0)$	$(\frac{1}{2}\pi, \mp\frac{1}{2}\pi)$	$(\frac{1}{2}\pi, \pi)$	(f_p, t_p)
$(\frac{3}{8}\pi, \pm\frac{2}{7}\pi)$	0(0)[0]	3(0)[0]	4(0)[0]	0(0)[0]	3(0)[0]	4(0)[0]	6(0)[0]
$(\frac{3}{8}\pi, \pm\frac{3}{7}\pi)$	1(0)[0]	4(0)[0]	6(0)[0]	1(0)[0]	4(0)[0]	6(0)[0]	6(1)[1]
$(\frac{3}{8}\pi, \pm\frac{4}{7}\pi)$	4(0)[0]	5(0)[0]	6(0)[1]	4(0)[0]	5(0)[0]	6(0)[1]	6(1)[1]
$(\frac{1}{4}\pi, \pm\frac{1}{3}\pi)$	3(0)[0]	5(0)[0]	6(0)[0]	3(0)[0]	5(0)[0]	6(0)[0]	4(0)[0]
$(\frac{1}{4}\pi, \pm\frac{1}{2}\pi)$	3(0)[0]	3(0)[0]	2(1)[1]	3(0)[0]	3(0)[0]	2(1)[1]	2(0)[0]

(·): The corresponding results by the proposed method with the SCD field replaced by the SP field.

[·]: The corresponding results by the proposed method with the SCD field replaced by SP at 31 electrode sites only.

Table II. The total number of models which have the same number of dipoles and locations as that of the underlying dipole source in the six selected models by the proposed method with the noise $0.1 * CP * U[-1,1]$.

	$(0,0)$	$(\frac{1}{2}\pi, \pm\frac{1}{2}\pi)$	$(\frac{1}{2}\pi, 0)$	$(\pi, 0)$	$(\frac{1}{2}\pi, \mp\frac{1}{2}\pi)$	$(\frac{1}{2}\pi, \pi)$	(f_p, t_p)
$(\frac{3}{8}\pi, \pm\frac{2}{7}\pi)$	0(0)[0]	5(0)[0]	5(0)[0]	0(0)[0]	5(0)[0]	5(0)[0]	3(0)[0]
$(\frac{3}{8}\pi, \pm\frac{3}{7}\pi)$	2(0)[0]	4(0)[0]	4(0)[0]	2(0)[0]	4(0)[0]	4(0)[0]	5(1)[2]
$(\frac{3}{8}\pi, \pm\frac{4}{7}\pi)$	0(0)[0]	5(0)[0]	5(2)[1]	0(0)[0]	5(0)[0]	5(2)[1]	6(1)[1]
$(\frac{1}{4}\pi, \pm\frac{1}{3}\pi)$	4(0)[0]	6(0)[0]	4(0)[0]	4(0)[0]	6(0)[0]	4(0)[0]	5(0)[0]
$(\frac{1}{4}\pi, \pm\frac{1}{2}\pi)$	0(0)[0]	2(0)[0]	6(2)[1]	0(0)[0]	2(0)[0]	6(2)[1]	0(0)[0]

(·): The corresponding results by the proposed method with the SCD field replaced by the SP field.

[·]: The corresponding results by the proposed method with the SCD field replaced by SP at 31 electrode sites only.

4. Conclusions.

In this paper we have presented a novel model and a method for localization of the underlying dipole generators potentially involved in event-related potentials. This method is different from the current methods in the literature in that it does not require a priori knowledge of the exact number of dipoles; it uses the entire SCD field which possesses better properties than SP; it does not have the initial values problem; and it estimates the locations, orientations and the total number of the underlying dipoles simultaneously. While this approach may not provide us with a veridical reflection of the physical model of the brain due to the imperfact physical model assumption, the simplistic shape assumption of the head and finite number of recorded electrode sites, it nevertheless appears to possess advantages over currently available methods. Indeed, the dipole localization techniques currently available work if the exact number of the underlying dipoles is known in an application. In reality, the number of dipoles is unknown, and the number of electrodes imposes some undue restrictions on the potential number of equivalent dipoles to be identified. These serious limitations are likely to result in a gross distortion of the real number of brain generators responsible for the production of event-related potentials in the human brain.

Upon improving the physical model of the brain and the model of head, and increasing properly the number of recorded electrode sites, this method will work well and be worthy of further investigation.

References

[1] Akaike, H.. A new look at the statistical model identification. *IEEE Trans. autom. Control AC*, 1974, **19:** 716-723.

[2] Ary, J.P., Klein, S.A. and Fender, D.H.. Location of sources of evoked scalp potentials: corrections for skull and scalp thickness. *IEEE Trans. biomed. Engng, BME*, 1981, **28:** 447-452.

[3] Bevington, P.R. *Data Reduction and Error Analysis for the Physical Sciences.* 1969, New York: McGraw-Hill.

[4] Haughton, D.M.A.. On the choice of a model to fit data from an exponential family. *Ann. Statist.*, 1988, **16:** 342-355.

[5] Mosher, J.C., Lewis, P.S., Leahy, R. and Singh, M. Multiple dipole modeling of spatio-temporal MEG data. *Proceedings of the SPIE*, 1990, **1351:** 364-375.

[6] Nunez, P. and Pilgreen, K.L. The spline-Laplacian in clinical neurophysiology: a method to improve EEG spatial resolution. *J. Clin. Neurophysiol.* 1991, **8:** 397-413.

[7] Nunez, P., Pilgreen, K.L., Westdorp, A.F., Law, S.K. and Nelson, A.V.. A visual study of surface potentials and Laplacians due to distributed neocortical sources: computer simulations and evoked potentials. *Brain Topography.* 1991, **4:** 151-168.

[8] Perrin, F., Pernire, J., Bertrand, O. and Echallier, J.F.. Spherical splines for scalp potential and current density mapping. *Electroenceph. clin. Neurophysiol.* 1989, **72:** 184-187.

[9] Scherg, M. Fundamentals of dipole source potential analysis. In: Hoke, M., Grandori, F. and Romani, G.L. eds. *Auditory evoked magnetic fields and electric potentials. Advances in Audiology*, 1990, **6:** Basel: Karger.

[10] Scherg, M and Von Cramon, D. Two bilateral sources of the late AEP as identified by a spatio-temporal dipole model. *Electroenceph. clin. Neurophysiol.* 1985, **62:** 32-44.

[11] Schwarz, G.. Estimating the dimension of a model. *Ann. Statist.*, 1978, **6:** 461-464.

[12] Sidman, R.D., Giambalvo, V., Allison, T. and Bergey, T.. A method for localization of sources in human cerebral potentials evoked by sensory stimuli.*Sensory Processes*, 1978, **2:** 116-129.

[13] Turetsky, B., Raz, J. and Fein, G. Representation of multi-channel evoked potential data using a dipole component model of intracranial generators: application to the auditory P300. *Electroenceph. clin. Neurophysiol.* 1990, **76:** 540-556.

[14] Ueno, S. and Iramina, K.. Modeling and source localization of MEG activities. *Brain Topography.* 1990, **3:** 151-165.

[15] Wahba, G.. Spline interpolation and smoothing on the sphere. *SIAM J. Sci. Stat. Comput..* 1981, **2:** 5-16.

[16] Wang, Wenyu. Statistical inference on aggregated Markov processes. 1989, *Ph.D. Dissertation, Dept. of Math., Univ. of MD, USA.*

[17] Wang, Wenyu, Begleiter, H. and Porjesz, B. Surface energy, its density and distance: new measures with application to human cerebral potentials. 1993, *Brain Topography in press.*

[18] Wei, C.Z. On predictive least squares principle. 1992, *Ann. Statist.* **20**, 1-42.