Methods for Separating Temporally Overlapping Sources of Neuroelectric Data

A. Achim and F. Richer
Département de Psychologie, Université du Québec à Montréal, Service de Neurologie, Hôpital Notre-Dame
J. M. Saint-Hilaire
Service de Neurologie, Hôpital Notre-Dame, Université de Montréal

Keywords: Brain activity mapping; Spatio-temporal source modeling; Component overlap; Dipole localization methods; Principal component analysis; Potential topography

Summary: The localization of intracranial sources of EEG or MEG signals can be misled by the combined effect of several sources, as illustrated by simulated MEG data in which two of the three dipolar sources have slightly out of phase activity and partly complementary scalp topographies. These data were analysed by three different source localization methods. Fitting a single source to each sequential topography worked perfectly when only one source was active; this could also account for as much as 95% of the spatial variance of topographies resulting from two overlapping sources, although the solution was then far from any source. A principal component analysis approach followed by an oblique rotation (fitting one source to the spatial aspect of each component) correctly localized two of the sources but severely mislocated the source that was never active alone. Spatio-temporal source modeling (simultaneously fitting a set of sources to all consecutive topographies) correctly localized all three sources, provided that the parameter optimization method could escape sub-optimal local minima of the error function. Temporally overlapping sources can thus be separated and correctly identified if the mathematical model is adequate and the optimization procedure is well adapted.

Introduction

Efficient localization of the neuroelectric generators of signals recorded at the scalp requires adequate knowledge of biophysical principles, of electrophysiology and of brain anatomy (Gloor 1985). Quantitative source localization methods can contribute increased precision by extracting detailed information from the data.

When multiple sources are concurrently active, their detection, separation and localization constitute a difficult task for eye-ball analysis and also for the quantitative localization methods that are restricted to individual scalp topographies. More recent localization methods have been designed to differentiate multiple sources that overlap in time. These methods rest heavily on the spatio-temporal relationships in the data. Their object is to model the combined effect of several sources in both space and time simultaneously.

In order to identify a source localization method that can adequately deal with concurrently active sources, we applied three different approaches to a difficult problem of simulated MEG activity and compared their results to the known sources used in generating the simulated data.

In comparing methods for solving the specific problem of temporally overlapping sources, the otherwise important physical issues of source geometry and of signal propagation in a non-homogeneous volume conductor are secondary. In the present study, we chose MEG signals, a perfect spherical volume and current dipole sources for their computational simplicity. Because the problem of separating temporally overlapping sources is strictly that of identifying their respective surface topographies, the characteristics of the methods being compared would remain the same if more complex physical situations were adequately modeled by more complex equations.

In this context, a source could be any collection of contiguous neuroelectric generators that share a common activity pattern and that can be described by a restricted set of parameters from which the associated scalp topography can be appropriately computed.

Accepted for Publication: May 5, 1988.
Supported by grants from the Medical Research Council of Canada and from the Université du Québec à Montréal..
Correspondence and reprint requests should be made to Dr. Andre Achim, Service de Neurologie, Hospital Notre-Dame, 1560 Sherbrooke, est, Montreal, H2L 4M1, Canada

Methods

Instantaneous state models

Dipole localization methods, as reviewed by Wood (1982), typically account for the instantaneous spatial variation in neuroelectric data at a fixed time. This involves the use of a physical model of signal propagation to compute the expected surface topography associated with a source (a current dipole, in most cases) having arbitrary parameters. The position, orientation and intensity of each source are iteratively adjusted to maximally reproduce the target topography.

A given topography can be modeled with more than one active source. Usually, however, interpretation is restricted to latencies at which a single dipole-equivalent source accounts well for the data. This keeps the number of parameters small relative to the number of data values, which is an essential prerequisite for reliable estimates in the presence of recording noise. Each source usually requires six parameters in EEG (three for position, two for orientation and one for intensity) and five in MEG (no radial component to source orientation).

When a source becomes activated while a previous source is still active, instantaneous one-dipole solutions often describe virtual sources remote from both actual sources. Solutions at successive sampling times then suggest a relatively slow migration of the underlying localized neuroelectric excitation. If the adequacy of analytical models is indexed by their physiological plausibility, the description resulting from successive one-dipole solutions does not fare well. As a safeguard, the stability of scalp topography over an interval of time has been advocated as a prerequisite to source identification (Wood and Wolpaw 1982). Without assurance of stability, a one-dipole model is not acceptable.

Spatio-Temporal Source Modeling

Scherg pioneered an approach to source localization that accounts for the whole sequence of scalp topographies over some interval by a few dipole-equivalent sources having fixed position and orientation but a fluctuating intensity level over time (Scherg 1984; Scherg and Von Cramon 1985, 1986). In other words, the approach requires that the same set of sources account for all the sequential topographies, by changing only their intensity and polarity.

The sequence of sources obtained from static one-dipole solutions fits the above description if the source obtained at any latency is assigned null activity at any other latency. The spatio-temporal source modeling of Scherg differs from this in two important aspects. Conceptually, its global solution is both more economical in terms of the number of sources postulated and more physiologically plausible since it does not imply impulse-like activation patterns of the various sources. Computationally, the few sources are fitted simultaneously to all data across space and over time; this results in a higher ratio of constraints (i.e. data values) to free parameters and consequently, increased reliability. Multiple sources whose activity overlap in time produce unstable topographies; this appears as a problem in the instantaneous states approach but constitutes a source of information for spatio-temporal modeling.

In some of Scherg's applications, the fluctuating intensity level of the sources over time was modeled with spline functions using parameters specifying the inflexion points of the activity waveforms (Scherg 1984; Scherg and Von Cramon 1985). In a later application, the activity waveforms of the sources were simply derived from the data as the least-squares solution of an overdetermined system of linear equations describing the relationship between the topographies of the sources and the spatio-temporal data matrix (Scherg and Von Cramon, 1986). Thus, only the spatial parameters of each source needed to be optimized by iterative non-linear procedures.

Scherg and Von Cramon (1986) further excluded the orientation parameters from the non-linear procedures by modeling three orthogonal components at each source position. Because the model was restricted to the plane defined by the coronal row of recording sites, only two position parameters and two orthogonal components were required for each source. A separate activity waveform was obtained for each orthogonal component at each position; this operation implicitly assimilated the components to co-located sources having independent activity. Some appropriate orthogonal rotation then redistributed the activity of the co-located sources in a more physiologically acceptable manner. Very specific conditions are required to justify the assumption that each co-located orthogonal source has its own independent activity over time.

For testing the spatio-temporal source modeling approach, a synthesis of elements from Scherg's various implementations appeared preferable to any one implementation. In order to achieve maximum generalizability, we defined a form of spatio-temporal source modeling that (1) extracts the activity waveform of each source from the data and (2) considers a single source per location. Thus, no arbitrary assumption is required to restrict the activity pattern of each source, and conceptual economy is achieved, although at the expense of fitting orientation parameters. In the presence of co-located sources having independent activity, a model with a single source per location is expected to move two sources to the same location without the necessity to assume co-location. This general form of spatio-temporal source modeling requires an assumption about the number of sources, although a lower limit can be obtained from principal component analysis (Achim et al. 1988). This model also requires assumptions about the geometry of each source and of the volume conductor in order to derive a scalp topography from the parameters describing each source.

Oblique Rotation of Principal Components

Maier et al. (1987) described an approach based on principal component analysis (PCA) to explain spatio-temporal data as being produced by sources each having a fixed position and orientation and some pattern of activity over time. PCA identifies a minimal multi-dimensional sub-space that can adequately describe the data. The sub-space is then approximately delimited by oblique axes that correspond to the topographies of individual sources. This is achieved by fitting one dipole to the spatial aspect of each component. The topography of each fitted source becomes new oblique axis of the system. The associated activity waveforms are extracted from the data, as in Scherg and Von Cramon (1986).

We identify two restrictions in this approach. First, it requires the assumption that the dimensionality of the data correspond to the number of dipole equivalent sources. Bilaterally symmetrical sources synchronously activated by a bilateral stimulus would contribute a single principal component; that component could not be adequately accounted for by a single spatially restricted source (Achim et al., 1988). Even when one has reasons to believe that each dimension results from a single dipole-equivalent source, we doubt that the oblique rotation procedure described by Maier et al. is adequate. The goal of oblique rotation, here, is to define axes that are maximally accounted for by current dipoles (criterion 1) and that maximally account for the original PCA sub-space (criterion 2). Among the many solutions that perfectly satisfy criterion 1, the proposed oblique rotation selects the one that maximally correlates with the PCA components. This optimizes criterion 2 only for sub-spaces defined by a single PCA component. Generally, for multi-dimensional sub-spaces, the proposed oblique rotation will not optimize criterion 2.

Despite this a priori analysis, the procedure of Maier et al. (1987) was included, along with the instantaneous states approach and the general form of spatio-temporal source modeling, in our sample of candidate source localization procedures. If the sub-optimal nature of the solution of Maier et al. had turned out to be of trivial consequence, this approach would have been a good choice as it requires considerably less computing resources than spatio-temporal source modeling.

Our test problem was deliberately constructed to be misleading for eye-ball and instantaneous states analyses, in that the topographies of two sources interacted so as to suggest a single incorrect source. Only the spatio-temporal source modeling was expected to be flexible enough to successfully retrieve the original sources, provided that the associated iterative non-linear optimization procedure could escape the influence of the initial approximation of the parameters.

Simulated Data

The above three approaches were applied to simulated MEG data having the following properties: (1) there are three dipole-equivalent sources that partially overlap in time and are not all mutually orthogonal in their spatial and temporal manifestations, (2) one of the sources is never active alone (i.e., its interval of activity is completely covered by those of the other two sources combined), (3) there is no noise added to the data so that any erroneous localization of a source can only be attributed to the source localization method, not to spurious noise features, and (4) the topographies of two of the sources are such that, when their intensities are comparable, the resulting topography could be mistakenly interpreted as produced by a single dipole-equivalent source. This was achieved with two sources having slightly out of phase activity and positioned such that the outward (+) maximum of one source spatially coincided with the inward (-) maximum of the other source.

The radial MEG component of each dipolar source was computed for 75 recording sites over the top half of an homogeneous sphere, using the Biot-Savart law. The resulting topographies, their associated activity waveshapes, and their respective cross-correlations are presented in Figure 1. The spatio-temporal effect of a source was obtained by weighting, at each sampling time, its topography (calculated for a unit activity level), by its activity level. The matrix of simulated data was the sum of the spatio-temporal effects of the three sources.

Localization Procedures

For the instantaneous state dipole localization approach, a single dipole was fitted to each non-null topography using the Gauss-Newton partial derivative method of least-squares parameter optimization, as implemented in the ASYST software package for IBM PC microcomputers. Only four parameters were optimized non-linearly (the x, y and z coordinates and the tangential orientation); throughout the procedure, source intensity was always optimally set by linear projection of the observed topography on the modeled topography. In fitting a single source to a single topography, where a good initial approximation is easy to supply, iterative optimization methods differ mostly on their rate of convergence to a local minimum of the error function (sum of squared differences between modeled and observed values), and the choice of a specific method is not critical.

The procedure of Maier et al. (1987) was implemented by extracting the successive principal components by the

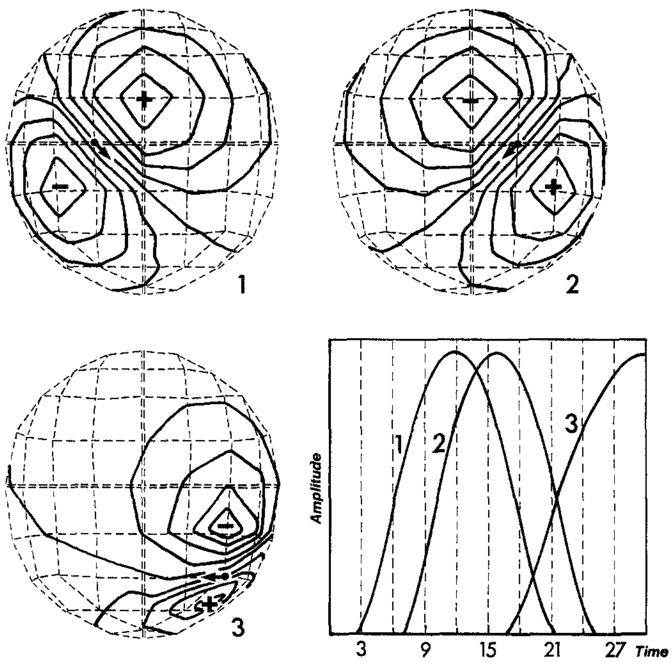

Figure 1. Topographies and waveshapes of the three dipolar sources used to produce simulated MEG test data. In each topography, the arrow is a projection of the source to the surface; plus and minus signs represent outward and inward fields respectively. Correlations between the topographies (over the 75 recording sites) are: $r_{12} = -.275$, $r_{13} = -.384$, and $r_{23} = .006$. Correlations between the waveforms (over the 30 time points) are: $r_{12} = .781$, $r_{13} = .014$, and $r_{23} = .153$.

power method applied to the variance-covariance matrix in the time domain and by fitting a single dipole on the factor scores of each principal component (i.e., on the spatial aspect of each component). When the topography of a principal component suggested two possible sources, the above dipole fitting procedure was applied twice, with initial values respectively approximating each candidate solution. The solution with least residual error was retained. The waveforms associated with the sources were least-squares estimated by solving the appropriate over-determined systems of linear equations (Appendix A).

Applying the general spatio-temporal source modeling is much like fitting multiple sources (in this case, three sources) to a single data topography where the intensity of each source is obtained by linear algebra (Appendix A). The essential difference is that the same set of sources must explain all successive topographies, so that the squared error between observed data and reproduced data is cumulative both across the recording sites and over the sampling interval.

The number of sources to include in the model was obtained from PCA (three components account for all the variance). In the present situation, it was not necessary to consider more complex situations in which a component would be due to a set of synchronous sources. As with the other approaches, the initial approximation of the source parameters were produced from inspection of the data, without reference to the generating model. For this approach, the best three sources from sequential instantaneous state analyses were used as most reasonable guesses for each of the three sources in the model. Since these consecutive analyses showed two intervals of identical solutions, each accounting for 100% of their target topography, the corresponding two sources were considered safely identified. In fitting a set of three sources to the data, these two sources were included with already fixed position and orientation; this left only four parameters to be subjected to non-linear iterative optimization.

The initial guess on the parameters of the remaining source was very reasonable from visual inspection of the data, but it unfortunately trapped various partial derivative methods (three such methods are available in ASYST) in a sub-optimal local minimum of the error criterion. From considerations on the general problem of error functions with sub-optimal minima (Appendix B), we decided to try a non-linear optimization procedure that is not as strictly minimizing as are the partial derivative methods. We used the simplex algorithm of Nelder and Mead (1965), which simultaneously maintains several sets of possible solutions for the parameters and iteratively substitutes a better set for the current set producing the most error, until all sets have converged together within very narrow limits. The same initialization as for the partial derivative method was used as one set of parameter values; other sets were derived from it by making substantial perturbations on each parameter in turn. This approach implements a broad exploration of the function space, while any set of values (including the original guess) is modified only when all remaining sets produce a lower sum of squared error.

Results

The instantaneous dipole solutions accounted for 100% of spatial variance when a single source was active, such that before latency 8, the exact position and orientation of source 1 was obtained and after latency 24, those of source 3 were found. The topographic distributions for latencies 10, 14 and 18 are presented in Figure 2, with the best-fitting one-dipole solution of each projected to the surface. In that latency range, the two extrema in the topographies belong respectively to sources 1 and 2, but are modeled as coming from a single incorrect source. The waveshapes at two symmetrical sites near the inward and outward magnetic field maxima are also

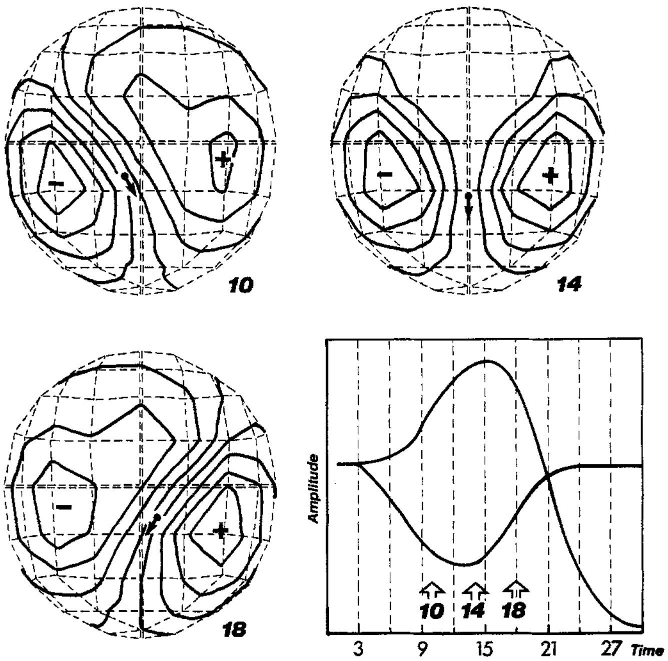

Figure 2. Amplitude distributions of the combined effect of the three sources at latencies 10, 14, and 18. The best-fitting one-dipole solutions are projected as arrows on the surface. These one-dipole solutions account for 93.7%, 95.1%, and 94.9% of the initial sum of squares respectively. Waveforms obtained near the maxima are shown at lower right. Notice the difference in the latency of their peaks.

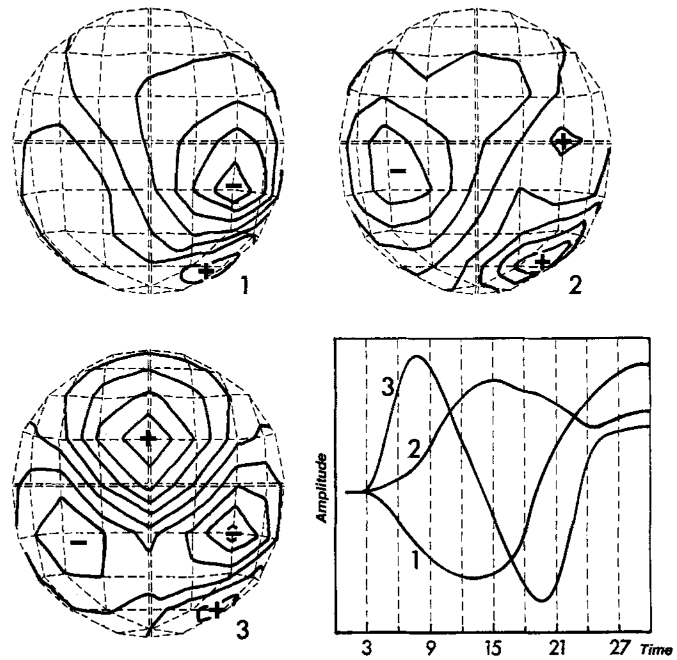

Figure 3. Principal components (lower right) and associated component scores (topographies) for the data generated with the model in Figure 1.

presented in Figure 2, to illustrate differences in peak latency between recording sites.

PCA, as expected, identified a three-dimensional subspace that accounts for 100% of the spatio-temporal variance. The three principal components (extracted in the time domain) respectively accounted for 57%, 36% and 7% of the data sum of squares. These components are presented in Figure 3, along with their associated topographies. The topographies of the dipoles best-fitting the spatial aspect of each principal component as well as the associated waveshapes are presented in Figure 4. This approximation of the principal components by dipoles introduced a residual error of 8.3%. Sources 1 and 3 of the generating model were correctly localized. Source 2, which in the model is never active alone, was severely mislocated, although its activity pattern was the only one approximately correct.

In the spatio-temporal source modeling approach, the modified simplex algorithm localized all three sources exactly as in the generating model of Figure 1, including the same associated waveshape. One hundred percent of the variance across space and time was accounted for.

Discussion

The key to efficient quantitative source localization is adequate mathematical modeling. When sources overlap in time, instantaneous states single source solutions are potentially misleading representations. With our test data, both the apparent source migration in time and the peak latency differences between plotted signals suggested inadequate mathematical representation for a range of latencies including at least points 10 to 18, despite about 95% of each topography accounted for and fair topographic stability over that interval. In this approach, the source that is never active alone was never correctly located. Difficulties of the PCA approach of Maier et al. (1987) have already been discussed. As expected, the proposed oblique rotation is less than optimal, since it severely mislocated one of the sources. Even if an optimal oblique rotation of PCA axes toward dipole topographies could be formulated, the axis rotation approach would be appropriate only in situations where each PCA dimension is due to a source that is spatially restricted. This restriction is absent from general spatio-temporal source modeling. In principle, spatially separate but synchronized sources and spatially extended sources, which both contribute a single principal component, can be modeled by a few dipoles sharing the same activity pattern and optimally located to account for the full extent of the source over all its activation interval.

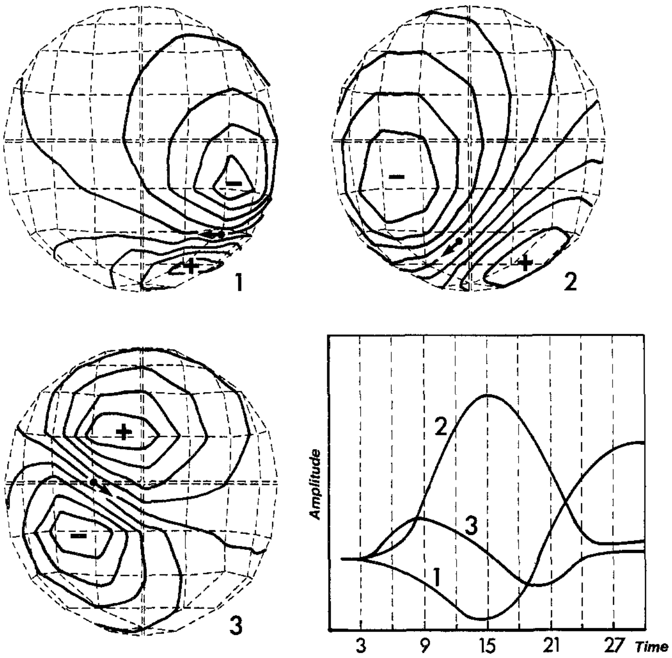

Figure 4. Source topographies, and associated waveshapes, resulting from fitting one dipole to the topography of each principal component of the simulated data.

Among the non-linear optimization procedures considered, only the simplex algorithm could obtain the correct solution in the general spatio-temporal model. This is partly due to the deliberately misleading nature of the problem, with two overlapping sources producing a very convincing dipole-like topography. When a procedure requires simultaneous initialization of several sources, the possibility of a similarly misleading interaction suggests a preference for algorithms that can escape sub-optimal local minima of the error criterion. The instantaneous states approach and the fitting of dipoles to PCA components did not require solving for several sources simultaneously; their failure with our test data could not be attributed to the specific optimization procedure used.

The flexibility of spatio-temporal source modeling calls for cautions. As Scherg has used it, a general hypothesis about the structure of the data is specified, the parameters involved are optimized, and the solution is always evaluated for anatomo-physiological plausibility and often contrasted to alternative hypotheses about the physiological generating processes.

For further security, we have developed a test of model adequacy (Achim et al. 1988), which attempts to falsify an apparently satisfactory explanation of averaged data. This test can reveal that some systematic part of the signal is not accounted for by the model, or that spurious parts of the data (e.g. residual noise) are described by the model. The former suggests that the model does not include enough sources while the latter suggests that too many sources are included.

Reviewing progress in biomagnetism, Cohen (1985) made the following comment about the inverse problem (inferring sources from surface manifestations), that "we have not learned how to connect the different instantaneous states, that is, we don't use data recorded at one instant to enhance the data recorded at the next instant. Yet the information is there; . . . what is needed in the case of the MEG is a large effort to perform iterative procedures."

This comment could apply to EEG analysis as well. General spatio-temporal source modeling, derived from Scherg's work, participates in the large effort called for. The result is a reduced risk of mislocation and should generally be worth the increased processing load. On advanced personal computers, this load remains within acceptable limits when dipole-equivalent sources are reasonable simplifications, allowing the association of scalp topographies to source parameters.

Appendix A

Extraction of the Activity Levels Associated with Given Scalp Topographies from the Matrix of Observed Data

Let t_i be the topography vector of source "i", (i.e., the set of expected amplitude values at each recording site per unit activity of the source). Let a_i be the activity vector of source "i" over the sampled time interval. When solving for individual topographies, a_i has a single element. Let T be a matrix formed of the t_i of each source, and A be the matrix formed by the a_i of the corresponding sources. The data matrix is first expressed as $D = T A^t$, (i.e., without residual noise, where A^t is the transpose of A). Essentially, this expresses that, at each time point, the topographies of all the sources are weighted by their activity level and added together.

If T is known, the corresponding A^t is obtained through the pseudo-inverse of T, by $A^t = T^t D = (T^t T)^{-1} T^t D$. If TT approximates T, then TT and the associated AA^t reproduce only an approximation of D, which can be written as $D = TT\ AA^t + E = TT\ (TT^t D) + E$, where E is the modeling error that is minimized by the pseudo-inverse procedure and is null when TT = T.

If D is more realistically expressed as $D = T A^t + R$, where R is residual noise, the pseudo-inverse procedure now minimizes E + R. Assuming statistical independence of E and R results in the property that the pseudo-inverse procedure actually minimizes E, the modeling error. It thus produces the best (in the least-squares sense) estimate of the amplitude of each source at each time point, given some hypothesis about the topographies of the sources. The total squared error, $|E + R|$, can be used to index the quality of the topography hypothesis TT, since E vanishes for TT = T. By adding sources to TT, however, the total error can be made arbitrarily small by modeling spurious features of the data. This can be detected, when the data are averages, by a test of model adequacy (Achim et al., 1988).

If D is a single topography, A^t is a vector containing the estimated intensity of each source. If D is a spatio-temporal matrix, A^t contains the estimated activity waveshape of each source (i.e., all consecutive data topographies are solved, for that set of source topographies, during the same matrix operation).

Appendix B

Non-Linear Parameter Optimization when the Error Function Has Sub-Optimal Local Minima

Partial derivative techniques of parameter optimization update a single set of parameter values at each iteration. They use the relative change in the criterion function brought about by small perturbations of each parameter in turn (i.e., the local slope of the error function landscape) to substitute a neighbouring set of values that improves the criterion (i.e., to make a step downward) if at all possible. They are thus strictly minimizing algorithms and because of this they can only accidentally escape a nearby sub-optimal local minimum of the error function.

The simplex algorithm (Nelder and Mead 1965) maintains several sets of parameter values (each is called a vertex and there are one more than the number of parameters to optimize) throughout the procedure. At each iteration, the vertex for which the error criterion is worst is replaced by a better one if one can be found by exploration rules based on the remaining sets of values, otherwise, all vertices are brought closer to each other. In other words, the procedure is a multipod on the error landscape, moving its highest foot down in a direction and by a step size suggested by the other feet. Iterations are stopped when all vertices have converged very closely. As only the least satisfying vertex is relocated at each iteration, an initial vertex near a local minimum is moved only after all others have reached more favorable positions. All good hypotheses are maintained long enough, in general, for other vertices to reach positions closer to the local minima, but the best sampled local minimum ends up attracting all vertices which yields a very good solution.

If the original set of vertices samples a wide area of the parameter space the initial explorations will also sample widely separated locations. Then, if the error function is somewhat fractal in nature (i.e., very low values are found within areas of low values which are found in regions of low values, etc.) the coarse space exploration performed when the vertices are wide apart will sample representative locations in distant regions and maintain good ones until all other locations represent better parameter values. Eventually the vertices get closer together and distant regions are not explored any further, but nearby areas are still explored for good local areas. The process thus narrows down on the best areas within the best areas, recursively.

References

Achim, A., Richer, F., Alain, C. and Saint-Hilaire, J.M. A test of model adequacy applied to the dimensionality of multichannel average auditory evoked potentials. In: D. Samson-Dollfus et al. (Eds.), Statistics and Topography In Quantitative EEG, Elsevier, Paris, 1988.

Cohen, D. Introduction: A 1984 perspective on biomagnetism. In: H. Weinberg, G. Stroink and T. Katila (Eds.), Biomagnetism: Applications & Theory. Pergamon Press, New York, 1985: 4-8.

Gloor, P. Neuronal generators and the problem of localization in electroencephalography: Application of volume conductor theory to electroencephalography. J. Clin. Neurophysiol., 1985, 2: 327-354.

Maier, J., Dagneli, G., Spekreijse, H. and van Dijk, B.W. Principal components analysis for source localization of VEPs in man. Vision Res., 1987, 27: 165-177.

Nelder, J.A. and Mead, R. A simplex method for function minimization. Computer J., 1965, 7: 308-313.

Scherg, M. Spatio-temporal modelling of early auditory evoked potentials. Rev. Laryng. (Bordeaux), 1985, 105: 163-170.

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.

Scherg, M. and Von Cramon, D. Evoked dipole source potentials of the human auditory cortex. Electroenceph. clin. Neurophysiol., 1986, 65: 344-360.

Wood, C.C. Application of dipole localization methods to source identification of human evoked potentials. Ann. N.Y. Acad. Sci., 1982, 388: 139-155.

Wood, C.C. and Wolpaw, J.R. Scalp distribution of human auditory evoked potentials. II Evidence for overlapping sources and involvement of auditory cortex. Electroenceph. clin. Neurophysiol., 1982, 54: 25-38.