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TITLE: MONTE CARLO ANALYSIS OF LOCALIZATION ERRORS IN
MAGNETOENCEPHALOGRAPHY

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MONTE CARLO ANALYSIS OF LOCALIZATION ERRORS IN MAGNETOENCEPHALOGRAPHY

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INTRODUCTION

In magnetoencephalography (MEG), the magnetic fields created by electrical activity in the brain are measured on the surface of the skull. To determine the location of the activity, the measured field is fit to an assumed source generator model, such as a current dipole, by minimizing chi-square. For current dipoles and other nonlinear source models, the fit is performed by an iterative least squares procedure such as the Levenberg-Marquardt algorithm (Press 1986). Once the fit has been computed, analysis of the resulting value of chi-square can determine whether the assumed source model is adequate to account for the measurements. If the source model is adequate, then the effect of measurement error on the fitted model parameters must be analyzed.

Several computer modeling studies have explored the effects of measurement errors on fitting simulated MEG data to dipole models in conducting spheres. Cuffin (1985, 1986) analyzed the effects of additive error by computing individual parameter variances from 10-run Monte Carlo simulations. Two-parameter confidence regions were computed by Hari et al. (1988) by making a number of simplifying assumptions. Stok (1987) compared estimates of parameter variances computed via analytic model linearization with estimates computed by Monte Carlo simulations of 100 runs and found that the linearization approach could underestimate the variances by a factor of up to 25.

Although these kinds of simulation studies can provide a rough idea of the effect that measurement error can be expected to have on source localization, they cannot provide detailed enough information to determine the effects that the errors in a particular measurement situation will produce. In this work, we introduce and describe the use of Monte Carlo-based techniques to analyze model fitting errors for real data. Given the details of the measurement setup and a statistical description of the measurement errors, these techniques determine the effects the errors have on the fitted model parameters. The effects can then be summarized in various ways such as parameter variances/covariances or multidimensional confidence regions.

METHODS

The source generator model used to localize the underlying neural activity can be expressed as a parameterized function, $b_i = f(x_i, p)$, that specifies the neuromagnetic field b_i produced by the source as a function of the measurement location x_i . The function f represents the general form of the source model and the parameter set p represents the specific details of the source. In the case of a current dipole model, p corresponds to the location and orientation of the dipole. The model parameters are found by fitting the model to the measured data. Given N pairs of measurements and their corresponding measurement locations, denoted y_i and x_i , p is found by minimizing chi-square, $\chi^2 = \sum_{i=1}^N \left(\frac{y_i - f(x_i, p)}{\sigma_i} \right)^2$, where σ_i is the standard deviation of the error in the y_i measurement.

The effect of measurement error on fitted model parameters is usually analyzed statistically by computing covariances and/or multidimensional confidence regions of the parameters. These statistics can be computed by traditional analytic methods if the measurement errors are additive and normally distributed, and if the model is linear (Press et al. 1986). When these conditions do not hold, analytic computation requires either 1) a detailed analysis of the statistics for the particular case, or 2) approximation, such as model linearization.

Most MEG source models are nonlinear in some of their parameters. The current dipole model, for example, has a nonlinear dependence on its location parameters. MEG measurement errors contain both additive components, such as unrelated brain activity, intrinsic sensor noise, and environmental interference, and nonadditive components, such as sensor location errors. Furthermore, the distribution of some of these errors may not be normal. Because of these conditions, analytic approximations may provide incorrect results, as evidenced by Stok (1987) in the calculation of parameter variances.

To provide an alternative to the analytic-approximation approach, we have developed MEG localization error analysis techniques based on Monte Carlo simulation (Press et al. 1986). These techniques are not limited to computer simulation studies of the general effect of measurement errors. Instead, they are intended to provide an error analysis tool for real data, tailored to the specifics of the particular measurement situation. The basis of our approach is illustrated in Fig. 1. Fig. 1(a) illustrates the underlying statistical model of the measurement process. The measurements we use to compute the source model parameters correspond to one particular experimental realization. Because of the random nature of the measurement errors, repetition of the experiment would result in a slightly different set of measurements. Fitting the model to this different set of measurements would result in slightly different values for the model parameters. The most robust method of analyzing the effect of measurement errors on the fitted parameters is to repeat the experiment many times and fit the model to each set of the resulting measurements. This would provide a sample of the parameter population that could be directly analyzed.

Since repetition of the experiment is usually impractical, the approach of Monte Carlo error analysis is to simulate the measurements that would have been obtained if the experiment had been repeated. This is illustrated in Fig. 1(b). Using the parameters found by fitting the model to the real measurement data as surrogates for the unknown "true" parameters, multiple copies of the "ideal" field measurements produced by the model are generated. Each of these ideal fields is then perturbed by a different set of simulated errors. These sets of simulated errors are randomly generated on a computer with distributions that mimic those of the errors in the measuring process. The simulated errors can be used to perturb the ideal field additively, as when one simulates the error caused by noise sources, or nonadditively, as when one simulates the error (shift) caused by imprecise location of the sensors. The result is a number of simulated measurement sets. The source model is then fit to each measurement set, providing an ensemble of model parameters. This ensemble approximates the joint distribution of the parameters, and from it any statistics describing the parameter error can be directly estimated.

APPLICATION EXAMPLES

Monte Carlo simulations have been used to analyze parameter uncertainty in a variety of MEG experiments at Los Alamos. In a recent auditory attention study (Arthur et al. 1989), we used Monte Carlo error analyses to demonstrate that the closely spaced sources of the N1m and Ndm activity are spatially different and can be distinguished from one another. In a visual attention study (Aine et al. 1989), Monte Carlo analyses have indicated that, for the particular paradigm, the source locations of the attend and not-attend responses could not be distinguished. In another visual study (George et al. 1989), we employed Monte Carlo analyses to demonstrate distinct sources at differing latencies.

In this section we present two examples to illustrate the use of Monte Carlo error analysis. The data used in these examples are drawn from the third study cited above. For graphical clarity, the ensembles from 100 point Monte Carlo simulations are presented. Detailed statistical analyses will generally require larger ensembles. For these examples, we employed a simple five-parameter "dipole in a sphere" model. The forward field computations for this model took into account both the second-order gradiometer configuration and finite coil areas of the SQUID sensors.

Fig. 1 Monte Carlo approach to error analysis (Press et al. 1986) (a) Underlying statistical

In the first example, Monte Carlo analysis is used to compare dipolar fits of visually evoked fields at latencies of 90 and 110 ms. The evoked field was a response to a sinusoidal grating displayed in the lower right quadrant of the visual field. Field measurements were taken at 56 points on the head and each measurement is the average of 75 trials. This is an example of a relative analysis in which the objective is to determine if the sources of the two fields can be distinguished by the MEG measurements. Since the sensor location errors are the same for both fields, only measurement noise errors were incorporated into the analysis. For this example, the noise was assumed to be independent from channel-to-channel and normally distributed. A standard deviation of 21.1 fT for the noise was computed by averaging the standard deviations of the prestimulus intervals for the measurements at each location.

The parameter ensembles generated by a 100-point Monte Carlo analysis are shown in Fig. 2. The three frames show the ensemble dipoles from three orthogonal views, with the symbols marking the locations and the tails indicating the moment and orientation. The accompanying table lists the standard deviations of the dipole parameters for both cases. In this example, the sources for the two evoked fields are clearly distinguishable.

In the second example, Monte Carlo error analysis is used to examine absolute localization accuracy. The visually evoked field used in this example is a response at a latency of 90 ms to a sinusoidal grating in the central visual field. The evoked field was sampled at 42 points on the head and each field measurement is the average of 100 trials. Measurement errors caused by both additive noise and sensor location uncertainty were incorporated into this analysis. The noise was again assumed to be independent and normally distributed. Analysis of the prestimulus intervals for this data set yielded a noise standard deviation of 12.4 fT. Fig. 3(a) shows a 100-point Monte Carlo ensemble generated using only noise error.

The sensor location error was modeled by random shifts of the sensor locations along the surface of the measurement sphere. These shift errors are used to perturb the ideal field by using the field values at the actual or shifted sensor locations in place of the values at their nominal locations. In this example, the shift error was modeled by independent shift errors in the north-south and east-west directions. The shift errors were generated from a uniform distribution of ± 1 cm. Since our measurements were taken with a seven-sensor SQUID, the shift errors were not independent from channel-to-channel. To incorporate this into our error model, we randomly shifted the blocks of seven sensors rather than the individual sensors. Fig. 3(b) shows a 100-point Monte Carlo ensemble generated using location error only. Fig. 4 shows a 100-point Monte Carlo ensemble incorporating both noise and location error. In this particular example, it can be seen that the parameter uncertainty caused by sensor location error is significant and must be taken into account for a realistic error analysis.

Our experience with the use of Monte Carlo-based error analysis in these examples and many other similar cases has shown it to be a robust and flexible approach. If the distributions of the various sources of measurement error can be suitably characterized, then the Monte Carlo technique can determine their cumulative effect on the final fitted parameters.

Fig. 2. Monte Carlo-generated ensembles for visually evoked fields at 90 ms and 110 ms latencies.

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Fig. 3: Monte Carlo-generated ensembles for a visually evoked field at a 90 ms latency. (a) Additive noise error only, using a standard deviation of 12.4 fT. (b) Nonadditive location error only of ± 1 cm.