Regional Head Tissue Conductivity Estimation for Improved EEG Analysis

T. C. Ferree*, K. J. Eriksen, and D. M. Tucker

Abstract—We develop a method for estimating regional head tissue conductivities in vivo, by injecting small (1–10 μA) electric currents into the scalp, and measuring the potentials at the remaining electrodes of a dense-array electroencephalography net. We first derive analytic expressions for the potentials generated by scalp current injection in a four-sphere model of the human head. We then use a multistart downhill simplex algorithm to find regional tissue conductivities which minimize the error between measured and computed scalp potentials. Two error functions are studied, with similar results. The results show that, despite the low skull conductivity and expected shunting by the scalp, all four regional conductivities can be determined to within a few percent error. The method is robust to the noise levels expected in practice. To obtain accurate results the cerebrospinal fluid must be included in the forward solution, but may be treated as a known parameter in the inverse solution.

Index Terms—Conductivity, electrical impedance tomography, electroencephalography.

I. INTRODUCTION

It is well established that three-dimensional (3-D) spatial analysis of electroencephalography (EEG) data requires accurate knowledge of the electrical properties of head tissues [1], [11], [20], [4]–[24]. In the strictest sense, this means knowing the geometry and impedance of each of the head tissues, including inhomogeneities and anisotropies. In simplified models, which represent the head with just four homogeneous, isotropic layers, one needs to know only the average regional conductivities of the brain, cerebrospinal fluid (CSF), skull and scalp. Although each of these has been measured experimentally [9], [16], [2], the limited number of measurements and the large variability in the data for all tissues except perhaps the CSF make it desirable to measure regional head tissue conductivities in vivo for individual subjects.

In a method suggested previously by [5], a dense-array EEG electrode net is placed on the scalp and small (1–10 μA) sinusoidal currents are injected into the head volume through selected pairs of electrodes. Because injection and measurement electrodes are distinct, this arrangement is effectively a 3-D extension of the four-electrode method using commonly for impedance measurements of biological tissues [12]. The injected current generates scalp potentials which depend upon the conductivities of the intervening head tissues. By measuring the potential at the remaining scalp electrodes, and by defining an error function based on the difference between these measured potentials and the computed potentials of an electric head model, the conductivities of the four head tissues can be estimated using inverse methods.

It is well known that the skull has a much lower conductivity than the other head tissues [9], [16]. When current is injected into the head through scalp electrodes, one expects that much of the current will be shunted through the scalp, leaving little to pass through the inner tissues, especially the brain and CSF. This raises a reasonable question as to whether the scalp potentials are sensitive enough to the inner tissue conductivities to allow their accurate retrieval by noninvasive methods. The main purpose of this paper is to demonstrate numerically that, despite the low skull conductivity, the scalp potentials are indeed sensitive to these inner tissue conductivities, and that all four regional head tissue conductivities can be retrieved accurately by the methods developed here. To demonstrate the basic feasibility of the approach, we kept the problem simple by using a four-sphere model of the head and assuming uniform and isotropic conductivities. By including the CSF in the model, the resulting equations are an extension of those in [23], and those used previously by [5].

We reviewed the experimental literature on the conductivities of head tissues, and estimated the mean, standard deviation, and minimum and maximum plausible values for each tissue. To demonstrate the retrieval process as it would be applied to real data, we first generated mock scalp data using our spherical head model and the mean conductivity values. We then perturbed these potentials with spatially uncorrelated Gaussian noise, with levels like those expected in modern EEG systems. We used a multistart version of the downhill simplex algorithm of [18] to minimize the error function. We compared two error functions and obtained similar results. Initial attempts, in which tissue conductivities were started far from the global minimum and totally unconstrained during the search, yielded limited success. In a more adapted approach, the conductivities were constrained to fall within the plausible ranges implied by the experimental literature. These ranges were actually quite broad, so this method had the desired effect of guiding the search based on prior experimental knowledge, without overly constraining it so as to render the inverse solutions predetermined and artificial.
We emphasize that this method is neither conventional electrical impedance tomography (EIT) nor electrical impedance plethysmography (EIP). While it has been argued that the spatial resolution of conventional EIT is limited in the head due to the low skull conductivity [14], regional head tissue conductivity estimation is a simpler problem, because we assume the head geometry is known and represent the volume with a small number of conductivity parameters. The approach used here is more like that of [6], in that they also solved for regional tissue conductivities using surface current injection and surface potential measurement. It is also like that of [4], who termed a similar approach parametric EIT. Yet neither group considered the obstacle of low skull conductivity. Furthermore, [6] assumed that the surface potential could be represented as a linear function of the regional tissue resistivities. No such assumption is made here, hence, we expect more accurate estimates, despite the less direct nature of the nonlinear inverse problem. Preliminary results based on the present approach are described briefly in [7].

II. METHODS

This section describes the analytic and numerical methods used in the forward and inverse solutions.

A. Forward Solution

In our approach, a small (1–10 µA) sinusoidal current $I(t)$ is injected through the scalp surface into the head volume, and the resulting impressed potential $\Phi(r, t)$ is measured at the remaining electrodes of a dense-array EEG net. We assume that the frequency of $I(t)$ is low (<1 kHz), so that the amplitude of the resulting potentials may be computed at each time point as though $I(t)$ were static [21], [8]. Because the relative sign of the potential at each electrode is important, the phase must also be retained. Ignoring capacitive effects, the potentials will be in phase with the injected current. The induced potential $\Phi$ at any point $r$ obeys Laplace’s equation

$$\nabla^2 \Phi(r) = 0$$

(1)

which has a unique solution upon specifying appropriate boundary conditions [15].

To derive the solution for two injection electrodes at arbitrary locations on the scalp, we first solved (1) for a single electrode located at the top of the head where azimuthal symmetry simplifies the solution, then used coordinate rotation and linear superposition to generate the result for two electrodes. With the convention that positive current $I$ flows into the scalp through electrode A and out of the scalp through electrode B, the solution can be written

$$\Phi^{(\alpha)}(r) = \sum_{n=1}^{\infty} \left[ A_n^{(\alpha)} \left( \frac{r}{\alpha} \right)^n + B_n^{(\alpha)} \left( \frac{\alpha}{r} \right)^{n+1} \right]$$

$$\cdot \left[ P_n(\hat{r}_A \cdot \hat{r}_A) - P_n(\hat{r}_B \cdot \hat{r}_B) \right]$$

(2)

where $r = |r|; r_A$ and $r_B$ represent the locations of the injection electrodes A and B, respectively; $P_n$ is the Legendre polynomial of order $n$ [23]. The tissue layers are numbered starting with the brain and increasing outward. The constant $\alpha$, representing the outer radius of tissue layer $\alpha$, was introduced explicitly in (2) to prevent numerical overflows and underflows in the sum. Note that the $n = 0$ term does not appear in the sum, because $A_0 = 1$ and the currents at A and B are assumed to be equal and opposite in magnitude.

The constant coefficients $A_n^{(\alpha)}$ and $B_n^{(\alpha)}$ are determined by the boundary conditions. For the potential in the brain to be finite at $r = 0$, we must have $B_n^{(1)} = 0$. To determine the remaining coefficients, we require continuity of the potential $\Phi^{(\alpha)}$ and continuity of the normal current density $J^{(\alpha)}_{n+1} \equiv -\sigma_n \partial \Phi^{(\alpha)}/\partial r$ at each tissue interface. The final boundary condition must specify either the potential (Dirichlet), its normal derivative (Neumann), or a combination of both (mixed) on the outer surface [15]. Since the conductivity of air is effectively zero, the obvious choice at all locations except the injection electrodes is zero normal current density (Neumann). This is also valid at the measurement electrodes, since high input-impedance amplifiers ensure that the current flow across the scalp-electrode interface is small and does not significantly affect the potential or current distribution in the volume conductor.

For spatially extended injection electrodes, the scalp-electrode interface has constant potential and most of the current flows near the outer boundary of the electrode [26]. This would be correctly imposed as a Dirichlet boundary condition, but in the limit that the electrode diameter is small compared to the inter-electrode spacing, as is the case here, point electrodes are a reasonable approximation. To avoid solving a mixed boundary value problem, therefore, we use Neumann boundary conditions for the injection electrodes as well. When a positive current $I$ is injected into the scalp at a point $A$ on the surface, the normal current density can be written

$$J^{(4)}(\theta, \phi) = -\frac{1}{r^2} \delta'(\cos \theta - \cos \theta_A) \delta(\phi - \phi_A)$$

where $\delta$ is the Dirac delta function, and the factor $1/r^2$ arises from spherical geometry [15].

Equation (1) and the corresponding boundary conditions constitute seven equations for the seven unknown coefficients in (2). We solved these equations analytically and simplified the results using Mathematica [27] to obtain the expressions in the Appendix. To establish their accuracy we verified that they satisfy the appropriate reciprocity relation with the standard solution for a current dipole in a four-sphere head model [23].

B. Inverse Solution

Expression (2), along with the analytic expressions for the expansion coefficients $A_n^{(\alpha)}$ and $B_n^{(\alpha)}$ given in the Appendix, allow the calculation of scalp potentials for any particular set of conductivities $\{\sigma_\alpha\}$. This defines the forward problem for conductivity estimation. Given the algebraic complexity of the expressions in the Appendix, it is not possible to solve explicitly for the conductivities in terms of the measured scalp potentials. Instead we use nonlinear inverse methods. Note that this inverse problem does not suffer from nonuniqueness of solution of the sort which challenges dipole source localization, because the number and location of the sources is known. Instead, the ability to find the optimal conductivity values depends upon the definition of the error function and the signal-to-noise ratio (SNR).

We studied two error functions for their efficacy in solving this inverse problem. Let $\Phi(r)$ equal the potential at electrode...
\[ i, \quad \text{that is} \quad \phi_k^{(4)}(r_i), \quad \text{computed as a function of a putative set of tissue conductivities encountered during the inverse search. Let} \quad V_i \quad \text{equal the experimentally measured potential at electrode} \quad i. \quad \text{The first error function was defined by} \]

\[
E_{AB}^{(1)} = \left[ \sum_{i=1}^{N} (\phi_i - V_i)^2 (1 - \delta_{iA})(1 - \delta_{iB}) \right]^{1/2} \tag{3}
\]

where \( N \) is the total number of scalp electrodes. The Kronecker delta functions \( \delta_{ij} \) exclude the injection electrodes from the calculation of the error, because measuring the potential at the injection electrodes is inherently problematic [12], and because the potentials computed using (2) diverge at the injection electrodes in our point electrode approximation. The second error function we studied was defined by

\[
E_{AB}^{(2)} = \left[ \sum_{i=1}^{N} (\phi_i - V_i)^2 (1 - \delta_{iA})(1 - \delta_{iB}) \right]^{1/2} \tag{4}
\]

In contrast to (3), this error function is normalized to the root mean square (rms) of the measured potentials, as is sometimes done in dipole source localization [25]. The reason for considering this normalization in the present problem will be made clear below.

Intuition and lead field theory [23] suggest that different injection electrode positions will probe the various head tissues differently. If the injection electrodes are very close, for example, most of the current is shunted through the scalp. If the injection electrodes are in opposition, more current will pass through the brain and CSF. We investigated the effect of injection electrode separation on retrieval accuracy (Table II). Based upon these results and the work of [6], we defined an angle-average error function \( E_{AB}^{(k)} = (E_{AB}^{(k)}) \) where \( k = 1 \) or \( 2 \), and the average is taken over several injection pairs. In the spherical head model studied here, the angle \( \theta_{AB} \) between injection electrodes A and B completely specifies the current distribution in the head volume. We therefore computed the error with electrode A always on the positive \( z \) axis, and with electrode B ranging over several electrode positions having unique \( z \) coordinates.

To solve the inverse problem, we used the downhill simplex method of [18] as implemented by [22]. The initial simplex was constructed randomly based upon the values of \( \sigma \) and \( \delta \sigma \) in Table I. The search was stopped when one of two criteria were met. The first is when the decrease in the error function is fractionally smaller than some tolerance parameter. The second is when the number of steps of the simplex exceeds some maximum value. We varied these parameters, and settled on a tolerance equal to \( 10^{-4} \), and a maximum number of steps equal to 500. This gave a nice balance between accuracy and efficiency of the search. During the search, the conductivities were constrained to stay within their pre-defined plausible ranges \([\sigma_{\text{min}}, \sigma_{\text{min}}]\), listed in Table I. If the simplex attempted to step outside this range, then the offending conductivity was reset to the nearest allowed value. In practice, at the end of the search, only a small percentage of the inverse solutions had one or more of the conductivities at one of these limits. Our procedure had the desired effect of guiding the search based on prior knowledge, without overly constraining it so as to render the solutions predetermined and artificial. A small number of solution sets included conductivities which were well separated from the bulk of the distribution. These were rejected as outliers, and noted in the tables below.

In practice it is not possible to determine the induced potentials exactly. Background EEG, amplifier noise, and errors in electrode positions and head geometry all contribute. To challenge our retrieval process with a more realistic situation, we perturbed the mock scalp data with additive noise, i.e., we let \( V_i \rightarrow V_i + n_i \), where \( n_i \) was a zero-mean Gaussian random variable assumed to be uncorrelated across electrodes. The numerical results below are reported as a function of the noise level parameter \( \delta V \), the standard deviation of \( n_i \). The seed for the random number generator was reset at the beginning of each search, so that the noise and the starting simplex were different each time. Modern EEG amplifiers introduce random noise on the order of \( \delta V = 0.1 \mu V \) at each time step. We chose this as our primary test case, assuming that by averaging over enough cycles of the input, the background EEG can be removed completely. To test for robustness, we considered noise levels up to \( \delta V = 0.5 \mu V \).

### III. Results

This section describes numerical results for forward and inverse solutions.

#### A. Parameter Choices

We used \( r_1 = 8.0 \text{ cm}, r_2 = 8.2 \text{ cm}, r_3 = 8.7 \text{ cm}, \) and \( r_4 = 9.2 \text{ cm} \) for the outer radius of the brain, CSF, skull and scalp. In keeping with our sphericity assumption, we used a montage with 42 electrodes distributed uniformly over the scalp surface. According to UL544, the most stringent limitation on leakage current from electronic devices to human subjects is \( I \sim 20 \mu A \). We used \( I = 1 \mu A \) in the simulations below. Obviously, increasing \( I \) will increase the SNR and lead to better results.

Table I summarizes the experimental literature on the conductivity of head tissues. The conductivity of brain has been measured for a wide range of animals and conditions [9]. The diversity of experimental conditions and intrinsic inhomogeneity and anisotropy of the tissue itself probably explain the large variability in these data. We selected only those data which were collected at low frequency and body temperature. The mean \( \bar{\sigma} \)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>( \bar{\sigma} )</th>
<th>( \delta \bar{\sigma} )</th>
<th>( \sigma_{\text{min}} )</th>
<th>( \sigma_{\text{max}} )</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>0.25</td>
<td>0.13</td>
<td>0.05</td>
<td>1.0</td>
<td>Geddes &amp; Baker (1967)</td>
</tr>
<tr>
<td>CSF</td>
<td>1.79</td>
<td>0.02</td>
<td>1.73</td>
<td>1.85</td>
<td>Baumann et al. (1997)</td>
</tr>
<tr>
<td>Skull</td>
<td>0.018</td>
<td>0.014</td>
<td>0.002</td>
<td>0.1</td>
<td>Law (1993)</td>
</tr>
<tr>
<td>Scalp</td>
<td>0.44</td>
<td>0.2</td>
<td>0.05</td>
<td>1.0</td>
<td>Burger and van Milaan (1943)</td>
</tr>
</tbody>
</table>

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and variance \( \sigma \) were thus computed, and the minimum \( \sigma_{min} \) and maximum \( \sigma_{max} \) values were set to encompass the entire data range. The conductivity of CSF has recently been measured systematically in humans, and was found to vary little across subjects [2]. The mean and variance were computed, and the minimum and maximum values were set equal to three standard deviations from the mean. Only one study was found measuring scalp conductivity [3]. In dipole source modeling, most authors have taken the scalp conductivity to be the average of skin and muscle [1], or the same as that of brain [24]. For our study, the mean was taken from [3]. The variance was set arbitrarily to a value slightly higher than that of brain, and the minimum and maximum values were set equal to those of brain. The skull conductivity has the most dramatic influence on the flow of current through the head. Since the study of [23], most researchers have assumed the skull conductivity to be 80 times lower than that of brain and scalp, despite the fact that the conductivity of skull has since been measured systematically for a human cadaver [16]. These data show large variability as a function of position, and are further confounded by the fact that the skull was initially dry and had to be resaturated prior to experiments. Nevertheless, we take these data to be the most accurate presently available for modeling. The mean and variance were computed directly from the data, and the minimum and maximum values were assigned to encompass the entire range of the data. In this study, therefore, the ratio of scalp to skull conductivity is approximately 24, although the allowed search range extends to a ratio of 220.

B. Convergence of the Forward Solution

In numerical calculations, the infinite sum in (2) must be approximated by a finite sum with \( N_{max} \) terms. The most obvious way to determine \( N_{max} \) is to continue adding terms until the potential (2) has converged to within some small tolerance [23]. This approach is inefficient, however, because as a function of \( N_{max} \), the sum oscillates indefinitely within a slowly decaying envelope. An alternative approach is suggested by noting that, although the sum oscillates as a function of \( N_{max} \), following a transient decay from \( N_{max} = 1 \) to \( N_{max} \approx 50 \) it oscillates about an average value very nearly equal to its apparent asymptote, defined by the limit \( N_{max} \to \infty \). To estimate the asymptote, therefore, we computed the sum \( (2) \) as a function of \( N_{max} \), then averaged these partial sums over a range of \( N_{max} \). By including many oscillations in the average, this approximation is not overly sensitive to the endpoints of the averaging interval. To test for convergence, we compared the scalp potentials when the partial sums were averaged over the range \( N_{max} = 100–150 \) to those averaged over \( N_{max} = 100–250 \). The differences at the measurement electrodes were typically less than 0.01 \( \mu V \) and always less than 0.03 \( \mu V \). This is small compared to the rms potentials on the scalp, which range from 5–10 \( \mu V \) depending upon \( \theta_{AB} \), the angle between the injection electrodes. On a 300-MHz Macintosh G3, our implementation in ANSI C required approximately 0.6 s to compute the potentials for the 42-electrode montage.

C. Behavior of the Error Functions

The error functions \( E_{AB}^{(1)} \) and \( E_{AB}^{(2)} \) have different normalizations and different behaviors as functions of conductivity. While it is not possible to visualize them in the four-dimensional (4-D) parameter space in which the simplex searches, visualizing them along each axis illustrates their differences and aids intuition about why this approach to conductivity estimation is successful. For this discussion, no measurement noise was added to the mock potentials. The addition of noise undoubtedly destroys the smoothness of both error functions, but does not invalidate the general points made here.

Fig. 1 shows \( E_{AB}^{(1)} \) as a function of each \( \sigma \) over its allowed range. Each of the curves were computed based upon the mock data described above, while the remaining parameters were held fixed to their average values \( \sigma \). The different curves represent different values of \( \sigma_{AB} \). With the exception of \( \sigma_{4} \) (scalp), each curve shows a single global minimum. Overall, the error depends most sensitively on \( \sigma_{3} \) (skull), and least sensitively on \( \sigma_{2} \) (CSF), although the dependence on \( \sigma_{3} \) (skull) is not unlike that of \( \sigma_{1} \) (brain) and \( \sigma_{4} \) (scalp), for increases in \( \sigma_{3} \). The error increases very rapidly as \( \sigma_{3} \) is decreased. A defining characteristic of the error function \( E_{AB}^{(1)} \) is that, as \( \theta_{AB} \) is decreased, the error becomes less sensitive to all tissue conductivities. For inner tissues (brain and CSF) this is intuitive, because shunting through the scalp results in less current flow. For the remaining tissues (skull and scalp), especially the scalp, this result is less intuitive. Indeed, as \( \theta_{AB} \) is decreased, one expects that shunting through the scalp will increase the sensitivity to \( \sigma_{1} \). This behavior of \( E_{AB}^{(1)} \) is likely due to the fact that, generally speaking, for smaller \( \theta_{AB} \), the induced potentials are smaller (in a rms sense) over the entire scalp surface, and the error \( E_{AB}^{(1)} \) scales linearly in this regard since it has units of \( \mu V \).

Fig. 2 shows \( E_{AB}^{(2)} \) in the same style as Fig. 1, but expressed in percentages since this definition of error is unitless. The general behavior of \( E_{AB}^{(2)} \) is similar to that of \( E_{AB}^{(1)} \) with the marked difference that \( E_{AB}^{(2)} \) behaves more intuitively as a function of the separation angle \( \theta_{AB} \). For smaller angles \( \theta_{AB} \), the error is more sensitive to the conductivities of the outer tissues (skull and scalp). Overall the dependence of \( E_{AB}^{(2)} \) on \( \theta_{AB} \) is somewhat weaker than that of \( E_{AB}^{(1)} \).

D. Accuracy of the Inverse Solution

Noise added to the mock data creates local minima in the error function. Though the simplex algorithm is deterministic, the point to which the simplex converges varies because it is initialized randomly. In each case below, we ran the simplex algorithm 100 times. Since the distributions of retrieved conductivities were approximately Gaussian, results are given for the mean and standard deviation.

Table II shows the percent error in retrieved conductivities for the error function \( E_{AB}^{(1)} \), assuming \( I = 1 \mu A \) and \( \delta V = 0.1 \mu V \). The first column lists all of the injection electrode separation angles \( \theta_{AB} \) available in the 42-electrode montage. The second column shows the number of outliers, \( N_{out} \), rejected on the grounds described in Section II-B. The third column shows the mean number of error function evaluations, \( N_{eval} \), made by the simplex before converging. The remaining columns show the means and widths of the distributions of retrieved conductivities, expressed as percent error relative to \( \sigma \), the values in Table I used to generate the mock data. With the sole exception...
Fig. 1. The error $E_{\text{cm}}^{(1)}$ as a function of individual tissue conductivities $\sigma$. Data are shown for injection electrode separations $\theta_{\text{AB}}$ equal to 180 (solid), 90 (dashed) and 32 (dot-dashed) degrees, over the ranges $[\sigma_{\text{min}}, \sigma_{\text{max}}]$, listed in Table I.

of the CSF, each distribution falls well within its search range $[\sigma_{\text{min}}, \sigma_{\text{max}}]$. The CSF distribution nears the edges of its range, but is nevertheless peaked about $\bar{\sigma}$. The means of these distributions provide estimates of the conductivities with errors on the order of 1% for brain, skull and scalp, and 0.1% for CSF. With the exception of $\theta_{\text{AB}} = 180^\circ$, the widths of the error distributions are on the order of 5% for brain and skull, 1% for CSF, and 10% for scalp.

Table III shows the distribution of retrieved conductivities for the angle-averaged error function $E_{\text{cm}}^{(1)}$ as a function of noise level $\delta V$. The first data row, for which $\delta V = 0 \mu V$, is unphysical, but is included for comparison. Comparing the means and widths in Table III to those in Table II shows that averaging over angles significantly increases retrieval accuracy for the brain, skull and scalp. The means of the error distributions imply retrieval accuracy on the order of 0.1% for each of these tissues, and the widths are smaller by about a factor of four. The remaining rows show the effect of increasing the noise level $\delta V$. For the CSF, the mean and width of the retrieval error distribution are unaffected by the noise level. For the remaining tissues, although the means and widths do increase, the increase is approximately linear in $\delta V$. Even for $\delta V = 0.5 \mu V$, the mean error is on the order of 2% for brain, skull and scalp. This graceful degradation with increasing noise level is a highly sought-after feature of practical inverse methods.

Table IV shows the distribution of retrieved conductivities for the angle-averaged error function $E_{\text{cm}}^{(2)}$, expressed as a function of noise level $\delta V$. The results are very similar to those for $E_{\text{cm}}^{(1)}$, with the exception that $E_{\text{cm}}^{(2)}$ degrades somewhat less gracefully as a function of the noise level $\delta V$. This is possibly due to the fact that $E_{\text{cm}}^{(2)}$ is a somewhat less sensitive function of $\theta_{\text{AB}}$. It seems intuitive that an error function with greater dependence on angle might perform better.

E. Effect of the CSF

In dipole source modeling, both three- and four-shell head models are in common use. Since existing papers discuss the role of the CSF only in the context of dipole source localization, it is worthwhile to determine the importance of the CSF in the present context. Because the error function $E_{\text{cm}}^{(1)}$ performed slightly better than $E_{\text{cm}}^{(2)}$, we conducted this study only for the former. A simple way to quantify the effect of the CSF is to compare the scalp potentials in three- and four-sphere head models. For $I = 1 \mu A$ and $\theta_{\text{AB}} = 180^\circ$, the rms difference in scalp potentials was 1.6 $\mu V$, and the maximum difference was 3.5 $\mu V$. For $\theta_{\text{AB}} = 32^\circ$, the differences were approximately half as large. Fig. 1 predicts that such errors in the potential will result in significant errors in retrieved conductivities for the brain, skull and scalp.

To make a more practical assessment, we attempted to use a three-sphere head model to estimate the conductivity of the brain, skull and scalp in a four-sphere head model. At low noise levels this resulted in errors in the mean of approximately 15%
for the brain and skull, and 5% for the scalp. We conclude that it is necessary to include the CSF when estimating the conductivity of the remaining tissues. Since human CSF conductivity is known experimentally and varies little, however, it seems reasonable to treat it as a known parameter in forward and inverse solutions.

F. Effect of the Skull

The simulations above assumed the skull conductivity to be a factor of 24 lower than that of the scalp [16]. Since many researchers currently assume a factor of 80 [23], we performed simulations analogous to those in Table III for this case. First, the number of outliers increased to typically 20%. Retrieval accuracy for the scalp was unaffected. Retrieval accuracy for the skull was reduced when expressed as percent error, but was similar when expressed as absolute conductivity. Retrieval accuracy for the CSF was reduced slightly, but this is of little concern since its conductivity is well constrained experimentally. Retrieval accuracy for the brain was reduced significantly, as expected. The width of the distributions of retrieved conductivities increased as much as ten fold, but the error of the mean increased only slightly, remaining below 3% for $\delta V = 0.5 \mu V$. Hence, despite decreased accuracy for inner tissues, this method is feasible even for lower values of skull conductivity.

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**TABLE II**

PERCENT ERROR IN RETRIEVED CONDUCTIVITIES FOR THE ERROR FUNCTION $E^{(1)}_{AB}$ AS A FUNCTION OF INJECTION ELECTRODE SEPARATION ANGLE $\theta_{AB}$, ASSUMING $\delta V = 0.1 \mu V$

<table>
<thead>
<tr>
<th>$\delta V (\mu V)$</th>
<th>$N_{out}$</th>
<th>$(N_{red})$</th>
<th>$\Delta \sigma_1 (%)$</th>
<th>$\Delta \sigma_2 (%)$</th>
<th>$\Delta \sigma_3 (%)$</th>
<th>$\Delta \sigma_4 (%)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>4</td>
<td>429</td>
<td>0.0 ± 0.3</td>
<td>0.2 ± 1.3</td>
<td>0.0 ± 0.2</td>
<td>0.0 ± 0.1</td>
</tr>
<tr>
<td>0.1</td>
<td>1</td>
<td>125</td>
<td>-0.2 ± 3.0</td>
<td>0.0 ± 1.4</td>
<td>0.4 ± 3.6</td>
<td>-0.8 ± 6.6</td>
</tr>
<tr>
<td>0.3</td>
<td>1</td>
<td>116</td>
<td>1.2 ± 5.7</td>
<td>-0.4 ± 1.5</td>
<td>0.1 ± 9.2</td>
<td>-1.7 ± 18.5</td>
</tr>
<tr>
<td>0.5</td>
<td>9</td>
<td>103</td>
<td>3.8 ± 11.9</td>
<td>0.1 ± 1.5</td>
<td>-1.7 ± 11.6</td>
<td>-1.4 ± 24.5</td>
</tr>
</tbody>
</table>

**TABLE III**

PERCENT ERROR IN RETRIEVED CONDUCTIVITIES FOR THE ANGLE-AVERAGED ERROR FUNCTION $E^{(2)}_{AB}$ AS A FUNCTION OF NOISE LEVEL $\delta V$

<table>
<thead>
<tr>
<th>$\delta V (\mu V)$</th>
<th>$N_{out}$</th>
<th>$(N_{red})$</th>
<th>$\Delta \sigma_1 (%)$</th>
<th>$\Delta \sigma_2 (%)$</th>
<th>$\Delta \sigma_3 (%)$</th>
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<td>0.0 ± 0.1</td>
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<tr>
<td>0.1</td>
<td>1</td>
<td>125</td>
<td>-0.2 ± 3.0</td>
<td>0.0 ± 1.4</td>
<td>0.4 ± 3.6</td>
<td>-0.8 ± 6.6</td>
</tr>
<tr>
<td>0.3</td>
<td>1</td>
<td>116</td>
<td>1.2 ± 5.7</td>
<td>-0.4 ± 1.5</td>
<td>0.1 ± 9.2</td>
<td>-1.7 ± 18.5</td>
</tr>
<tr>
<td>0.5</td>
<td>9</td>
<td>103</td>
<td>3.8 ± 11.9</td>
<td>0.1 ± 1.5</td>
<td>-1.7 ± 11.6</td>
<td>-1.4 ± 24.5</td>
</tr>
</tbody>
</table>

**TABLE IV**

PERCENT ERROR IN RETRIEVED CONDUCTIVITIES FOR THE ANGLE-AVERAGED ERROR FUNCTION $E^{(2)}_{AB}$ AS A FUNCTION OF NOISE LEVEL $\delta V$

<table>
<thead>
<tr>
<th>$\delta V (\mu V)$</th>
<th>$N_{out}$</th>
<th>$(N_{red})$</th>
<th>$\Delta \sigma_1 (%)$</th>
<th>$\Delta \sigma_2 (%)$</th>
<th>$\Delta \sigma_3 (%)$</th>
<th>$\Delta \sigma_4 (%)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>4</td>
<td>429</td>
<td>0.0 ± 0.3</td>
<td>0.2 ± 1.3</td>
<td>0.0 ± 0.2</td>
<td>0.0 ± 0.1</td>
</tr>
<tr>
<td>0.1</td>
<td>1</td>
<td>125</td>
<td>-0.2 ± 3.0</td>
<td>0.0 ± 1.4</td>
<td>0.4 ± 3.6</td>
<td>-0.8 ± 6.6</td>
</tr>
<tr>
<td>0.3</td>
<td>1</td>
<td>116</td>
<td>1.2 ± 5.7</td>
<td>-0.4 ± 1.5</td>
<td>0.1 ± 9.2</td>
<td>-1.7 ± 18.5</td>
</tr>
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<td>0.5</td>
<td>9</td>
<td>103</td>
<td>3.8 ± 11.9</td>
<td>0.1 ± 1.5</td>
<td>-1.7 ± 11.6</td>
<td>-1.4 ± 24.5</td>
</tr>
</tbody>
</table>

Fig. 2. The error $E^{(2)}_{AB}$ as a function of individual tissue conductivities $\sigma$. Data are shown as in Fig. 1.
IV. DISCUSSION

We have developed a noninvasive method of estimating regional head tissue conductivities, which is robust to the noise levels expected in practice. This finding is significant, because conventional wisdom argues that the low skull conductivity causes too much of the current to be shunted through the scalp. Two related error functions were studied with similar results. Because the assumed current ($I = 1 \mu A$) was well within accepted safety limits and the number of scalp electrodes ($N = 40$) was relatively small, our conclusions should be viewed as conservative within the assumptions of the spherical head model. Using a larger current ($I \sim 10 \mu A$) will increase the signal to noise ratio and presumably improve the results. Increasing the number of scalp electrodes gives further improvements [7].

In retrospect, it is easy to understand why this method works. First, since the current source is known, this inverse problem does not suffer from nonuniqueness of solution of the sort that challenges dipole source localization. Second, both error functions show distinct global minima over the plausible ranges of the individual conductivities. Although these error functions cannot be visualized in four dimensions, the results presented here and the relatively simple physics of current flow in concentric tissue layers suggest that these error functions also behave simply in the 4-D parameter space. Noise added to the mock data produces local minima in the error functions, making perfect retrieval difficult or impossible. We found no significant correlation between the number of error function evaluations made during the search and the error for the final simplex, thus the distributions in retrieved conductivities were not simply due to letting the simplex search longer. Instead, retrieval accuracy depends on the starting simplex and how severely these local minima distort the shape, and especially the location of the center, of the global basin of attraction. For the parameter ranges and noise levels relevant to this problem, the general shape of the error function is apparently preserved. This allows a clustering of solutions in the vicinity of the correct answer, such that taking the average of an ensemble of solutions yields a highly accurate estimate.

The results throughout seem to suggest that the retrieval ability is best for the CSF, however, this view is too simplistic. For each tissue, an objective measure of retrieval ability should be based upon a comparison of initial and final conductivity distributions, to determine whether the simplex actually converged in that dimension. In the present context, the initial conductivity distributions are given by the initial simplexes, which were computed for each tissue using the mean $\bar{\sigma}$ and standard deviation $\sigma$ in Table I. The initial error, therefore, should be interpreted as the ratio $\Delta\sigma / \bar{\sigma}$. From the values in Table I, we have 52% for the brain, 1.1% for the CSF, 77.8% for the skull, and 45.4% for the scalp. Because the width of the results distribution for the CSF is consistently greater than 1.1%, we conclude that the simplex did not converge in this dimension, but rather wandered to a slightly broader distribution. This is in marked contrast to the brain, skull and scalp. Nevertheless, the final CSF errors are not flatly distributed throughout the allowed range, but are peaked about zero error, thus there is a clear tendency for $\sigma_4$ to maintain a tight distribution about the correct result. The slight broadening of the distribution for the CSF is probably more indicative of the tight experimental constraint used in generating the initial simplex than a failure of the method in this dimension.

The multistart method employed here was demonstrated to be highly accurate, even if not particularly efficient. It is likely that global optimization methods, such as simulated annealing or genetic algorithms, could find the global minimum more efficiently. To demonstrate the feasibility of the overall method, however, the multistart simplex method has two advantages. First, it is simple to implement, and has only two user-defined parameters. Second, the distributions of retrieved conductivities provide global information about the range of obtainable solutions, which could not be inferred from a single result of a global optimization method. Now that the feasibility of the approach has been established, global optimization methods should be investigated to improve search efficiency.

The most obvious limitation in applying this method to real data is the assumption that spherical geometry and four scalar parameters adequately describe the conductive properties of the head. Work is currently underway to extend this method to realistic head geometries using boundary element (BE) and finite element (FE) models. While BE and FE models account for departures from spherical head geometry, the question of how many conductivity parameters to include is more challenging. The results of [16] suggest that transverse skull resistivity may vary linearly with thickness for noncancellous tissue, but may be significantly lower for cancellous tissue, e.g., in the temporal plates. In this case, it may be desirable to assign a different conductivity to each skull plate. To avoid searching on a huge number of conductivity parameters, it may be desirable to parameterize the skull conductivity as a function of skull thickness, and search on the corresponding set of phenomenological parameters. In addition, the lead field theory derived for electrical impedance plethysmography [10], [17] may allow the determination of optimal electrode lead configurations which are maximally sensitive to local tissue conductivity. If this approach were effective only for the skull, that would be significant, because the skull is the most important tissue in determining the spread of current due to dipolar brain sources.

APPENDIX

The coefficients appearing in (2) are as follows:

\[
A^{(1)}_n = \frac{I}{2\pi r_4 \sigma_4 (1+2n)^4} \left[ K_{12} \left\{ K_{23} \left[ \left( 1+n \right) \frac{r_2}{r_3} + \frac{2n+1}{r_4} \right] \lambda_{34} + \kappa_{34} \lambda_{23} \right\} \right. \\
\left. - \left( 1+n \right) \frac{r_2}{r_3} + \frac{2n+1}{r_4} \lambda_{23} \right] \\
+ \left( 1+n \right) \frac{r_1}{r_2} + \frac{2n+1}{r_4} \lambda_{12} \right]
\]

\[
\left( n \left( 1+n \right) \lambda_{32} \lambda_{34} \frac{r_2}{r_3} \left( \frac{\sigma_3}{\sigma_4} \kappa_{32} \lambda_{34} \lambda_{32} \lambda_{34} \right) \right)^4
\]

(A1)
\[ A_n^{(2)} = \frac{A_1^{(1)}}{(2n+1)} \left( \frac{r_2}{r_1} \right)^n \kappa_{12} \]  
\[ B_n^{(2)} = \frac{A_1^{(1)}}{(2n+1)} \left( \frac{r_1}{r_2} \right)^{n+1} n \lambda_{12} \]  
\[ A_n^{(3)} = \frac{A_1^{(1)}}{(2n+1)^2} \left( \frac{r_3}{r_1} \right)^n \left( n(n+1) \left( \frac{r_1}{r_2} \right)^{2n+1} \lambda_{12} + \kappa_{12} \right) + n(n+1) \left( \frac{r_1}{r_2} \right)^{2n+1} \lambda_{12} \]  
\[ B_n^{(3)} = \frac{A_1^{(1)}}{(2n+1)^3} \left( \frac{r_1}{r_2} \right)^{n+1} n \lambda_{12} \]  
\[ A_n^{(4)} = \frac{A_1^{(1)}}{(2n+1)^3} \left( \frac{r_3}{r_1} \right)^n \left( \kappa_{12} + n(n+1) \right) + n(n+1) \left( \frac{r_1}{r_2} \right)^{2n+1} \lambda_{12} + \kappa_{12} \right) \]  
\[ B_n^{(4)} = \frac{A_1^{(1)}}{(2n+1)^3} \left( \frac{r_3}{r_1} \right)^n \left( \kappa_{12} + n(n+1) \right) + n(n+1) \left( \frac{r_1}{r_2} \right)^{2n+1} \lambda_{12} + \kappa_{12} \right) \]  
\[ \left( \frac{r_1}{r_2} \right)^{2n+1} \lambda_{12} + \kappa_{12} \right) \]  

where \( \kappa_{ij} \equiv (1 + n(1 + \sigma_i/\sigma_j)) \), and \( \lambda_{ij} \equiv (1 - \sigma_i/\sigma_j) \). Incidentally, in rederiving the three-sphere equations, we discovered a typographical error in the paper by [23, eq. (26)], \( (1 - \sigma_i/\sigma_j) \) should be replaced by \( (1 + \sigma_i/\sigma_j) \).

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REFERENCES


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