the method. The convergence rate of the method is strongly dependent on the types of underlying signal, fast components, noise type, and the SNR. For the clean signals (high SNR) the number of zero crossings decreases and the number of local minima can increase, so the convergence can be very slow. Convergence can be forced by adding white noise to the signal during the estimation process.

REFERENCES

[1] R. K. Avent and J. D. Charlton, "A critical review of trend-detection methodologies for biomedical monitoring systems," *Crit. Rev. Biomed. Eng.*, vol. 17, pp. 621–659, 1990.

[2] C. R. Meyer and H. N. Keiser, "Electrocardiogram baseline estimation and removal using cubic splines and state-space computation techniques," *Comput. Biomed. Res.*, vol. 10, pp. 459–470, 1977.

[3] J. A. Van Alste and T. S. Schilder, "Removal of baseline wander and power-line interference from the ECG by an efficient FIR filter with a reduced number of taps," *IEEE Trans. Biomed. Eng.*, vol. BME-32, pp. 1052–1062, 1985.

[4] P. Hsia, J. M. Jenkins, Y. Shimoni, K. P. Gage, J. T. Santinga and B. Pitt, "An Automated system for ST segment and arrhythmia analysis in exercise radionuclide ventriculography," *IEEE Trans. Biomed. Eng.*, vol. BME-33, pp. 585–593, 1986.

[5] C. H. Chu and E. J. Delp, "Impulsive noise suppression and background normalization of electrocardiogram signals using morphological operators," *IEEE Trans. Biomed. Eng.*, vol. 36, pp. 262–273, 1989.

[6] M. Arzi and M. Magnin, "A fuzzy set theoretical approach to automatic analysis of nystagmic eye movements," *IEEE Trans. Biomed. Eng.*, vol. 36, pp. 954–963, 1989.

[7] S. A. Kassam and H. V. Poor, "Robust techniques for signal processing: A survey," *Proc. IEEE*, vol. 73, pp. 433–481, 1985.

[8] R. S. C. Cobbold, *Transducers for Biomedical Measurements: Principles and Applications*. New York: Wiley, 1974, pp. 435–436.

[9] W. H. Press, B. P. Flannery, S. A. Teukolsky, and W. T. Vetterling, *Numerical Recipes the Art of Scientific Computing*. London, U.K.: Cambridge Univ. Press, 1986.

[10] L. R. Rabiner and R. W. Schafer, *Digital Processing of Speech Signals.* Englewood Cliffs, NJ: Prentice-Hall, 1978, pp. 127–135.

[11] B. Kedem, *Binary Time Series*. New York: Marcel Dekker, 1979.

[12] J. Frong, V. F. Froelicher. and M. D. Olson, "Application and limitations of continue baseline estimation and removal using a cubic-spline technique during exercise ECG testing," in *Proc. Comput. Cardiol.*, 1987, pp. 537–540.

[13] G. M. Friesen, T. C. Jannett, M. A. Jadallah, S. L. Yates, S. R. Quint, and H. T. Nagle, "A comparison of the noise sensitivity of nine QRS detection algorithms," *IEEE Trans. Biomed. Eng.*, vol. 37, pp. 85–98, 1990.

[14] B. Widrow and M. A. Lehr, *30 Years of Adaptive Neural Networks: Perceptron, Madaline, and Backpropagation*. Piscataway, NJ: IEEE Press, 1992, pp. 27–54.

[15] M. Berger, *Computer Graphics with PASCAL*. Menlo Park, CA: Benjamin/Cummings, 1986.

The Electrical Conductivity of Human Cerebrospinal Fluid at Body Temperature

Stephen B. Baumann,* David R. Wozny, Shawn K. Kelly, and Frank M. Meno

***Abstract*— The electrical conductivity of human cerebrospinal fluid (CSF) from seven patients was measured at both room temperature (25 °C) and body temperature (37 °C). Across the frequency range of 10Hz–10 kHz, room temperature conductivity was 1.45 S/m, but body temperature conductivity was 1.79 S/m, approximately 23% higher. Modelers of electrical sources in the human brain have underestimated human CSF conductivity by as much as 44% for nearly two decades, and this should be corrected to increase the accuracy of source localization models.**

***Index Terms*—Biological tissues, brain modeling, conductivity measurements, temperature.**

I. INTRODUCTION

The electrical conductivity of tissues within the head is an important parameter in mathematical models that are used to predict the location and strength of electrical generators in the brain [1] or models that are used to predict current densities within the head from exposure to external fields [2], [3]. The concentric-spheres model often includes four layers: scalp, skull, cerebrospinal fluid (CSF), and brain (e.g., [4], [5]). However, this model is inaccurate for many sources, particularly for deeper dipoles [6] or for dipoles located in the anterior portion of the brain or near the flat sides of the head [7]. More sophisticated methods rely upon realistic geometry obtained from magnetic resonance imaging (MRI) scans of subjects. Boundary element models extract the real boundaries between tissues and then assume a homogeneous and isotropic conductivity between the layers (e.g., [8], [9]). Finite element methods (FEM's) are capable of modeling nonhomogeneous and anisotropic conductivities within each tissue and therefore will be dependent upon accurate conductivity values for the whole head, but present FEM models are limited by the paucity of conductivity data [10].

Tissue boundaries with high conductivity gradients can cause field distortions and lead to localization errors, if the conductivities are not modeled accurately [11]. Within the head, the boundary with the greatest contrast in conductivity occurs between the bone and the CSF. The literature on electrical conductivity values for human tissues from the head is sparse. This is especially true of CSF. There is only one sketchy report (a conference abstract) of measurements taken on human CSF [12], apparently only a single sample. The measurement technique is not adequately described, the frequency range of 1–30 kHz is not within the bandwidth of most neuronal signals (1 Hz–1 kHz), and the measurements were performed at room temperature (24.5 °C), not the standard human body temperature of

Manuscript received December 27, 1995; revised October 17, 1996. This research was supported by The Copeland Foundation, Children's Hospital of Pittsburgh, and The Departments of Neurological Surgery and Biomedical Engineering at The University of Pittsburgh. *Asterisk indicates corresponding author*.

*S. B. Baumann is with the Department of Neurological Surgery, B-400, University of Pittsburgh Medical Center, The University of Pittsburgh, Pittsburgh, PA 15213 USA.

D. R. Wozny, S. K. Kelly, and F. M. Meno are with the Department of Neurological Surgery, University of Pittsburgh Medical Center, The University of Pittsburgh, Pittsburgh, PA 15213 USA.

Publisher Item Identifier S 0018-9294(97)01476-6.

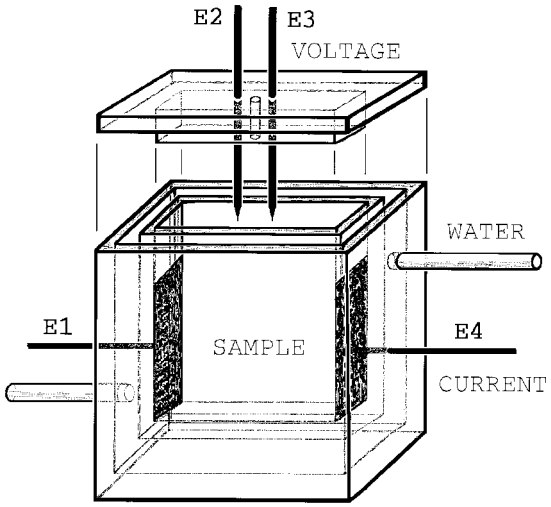

Fig. 1. The plexiglass cell for making measurements of CSF conductivity. Hollow walls allow for circulation of temperature-controlled water. Platinum electrodes are treated with an electrolytic deposition of colloidal platinum (platinum black). Current is delivered through $E1$ and $E4$, which are attached to 1-cm^2 platinum plates, and the potential difference across the sample is detected with platinum rods $E2$ and $E3$.

37 °C. Electrical conductivity is a temperature-dependent parameter for metals, decreasing as temperature is elevated, but conductivity in biological tissues increases with temperature as ionic motion and diffusion increase. Higher temperature has been shown to increase the conductivity of animal tissues such as muscle [13], fat [14], blood [24], and plasma [15], as well as standard KCl solutions [16]. Since CSF is mostly a weak solution of NaCl and protein [17], it is expected to be temperature dependent, also.

II. Methods

A 1-cm^3, plexiglass conductivity cell is used to make measurements with the four-electrode technique (Fig. 1). Current-injection electrodes are 1-cm^2 platinum plates at opposite ends of the cell, and voltage-sensing electrodes are two platinum rods 0.55 mm in diameter located approximately 2.5 mm apart in the removable top. The voltage-sensing electrodes project halfway into the cell (5 mm) and are insulated with varnish except at the tips. Both the current-injection and voltage-sensing electrodes are blackened using Kohlraush solution at a current density dependent upon electrode surface area [18].

A battery-operated circuit, modeled after Ackmann's [19], is used to make the measurements (Fig. 2). $V_{\rm in}$ is a sinusoid generated by a Wavetek model 182A function generator. A voltage follower $A1$ provides a low impedance output at $V1$, so that $V_{\rm in}/R_{\rm in}$ sets the level of $I_{\rm in}$ [approximately 10-μA root mean square (rms)] generated across the current-injection electrodes ($E1$ and $E4$). Dual diodes from $V2$ to ground help protect op-amp $A2$ by providing a current path to ground when the cell is empty, and resistor R_f (1 kΩ) limits the current to a safe level. When fluid is in the cell, $V2$ is a virtual ground and the diodes are turned off with negligible current leakage to ground. The voltage-sensing electrodes ($E2$ and $E3$) are used to measure the resulting potential drop across the tissue. The outputs from voltage followers $A3$ and $A4$ are connected to the inner shields of triaxial cables that have driven shields to decrease capacitive leakage currents. The outer shields are grounded. All op-amps are Burr–Brown OPA628 with <5-pA biasing current. The outputs from the followers $A3$ and $A4$ are fed into $A5$, a high input impedance (100-MΩ) differential amplifier (EG&G Princeton Applied Research Model 113 preamp, Princeton, NJ) with a gain of 100 and the low-frequency roll-off set at 0.03 Hz and the high-frequency roll-off at 100 kHz. The single-ended output from the preamp is displayed on a Keithley 197A Digital Multimeter for precise rms voltages as well as on a Tektronix oscilloscope to confirm that the output is not severely distorted or contaminated by noise.

Clear CSF was collected under sterile conditions in the operating room from seven neurosurgical patients (three males and four females), ranging in age from 4.5 mo. to 70 yr. (mean = 26.6 yr). Two or three cc's were withdrawn either by syringe or from CSF drains implanted in the ventricles. If the presence of blood was noted, the specimen was rejected. Each specimen was collected in a sterile vial, stored in a sealed plastic bag, and refrigerated until use at a later date, usually within one to four weeks.

On the day conductivity measurements were made, the specimen was taken out of the refrigerator and allowed to warm to room temperature. Then, the CSF was poured into the conductivity cell, and the top was taped on after assuring that no air bubbles were present in the cell. Measurements were made first at either room or body temperature. Average room temperature was 25 °C (range 22–27 °C), and body temperature was more precisely controlled at 37 °C (range 36.2–37.5 °C).

Hollow walls within the conductivity cell allow for temperature-controlled water to circulate around the specimen. A thermocouple in the circulating water at the exit from the cell wall was used to monitor the temperature continuously. Calibration studies with an additional thermocouple in the cell at the same time indicated a lag of 15–20 min before the temperature in the center of the cell stabilized at a new set point, either room temperature or body temperature. Therefore, voltage measurements were not made until at least 20–30 min after the thermocouple in the circulating water indicated the new set point had been reached.

Once temperature stability was achieved, voltage measurements were made at 10 Hz, 20 Hz, 33 Hz, 50 Hz, 100 Hz, 200 Hz, 333 Hz, 500 Hz 1 kHz, 3.33 kHz, and 10 kHz. Then the temperature was changed and stabilized at the second temperature and voltage measurements were repeated at the same frequencies. For calibration, a solution of 0.1 m KCl was tested at room and body temperature on the same day a specimen of CSF was tested. The calibration solution was carefully prepared in the laboratory using ultrapure water and high-grade KC1. Results were consistent with those obtained using a weaker conductivity standard (0.01 m KC1) obtained commercially (Lab Chem Inc., Pittsburgh, PA).

III. Results

Conductivity was calculated from the following equation [16]:

$$\sigma = (I_{\rm in}/V_{\rm out}) * K_{\rm cell}$$

where the cell constant $K_{\rm cell} = L/A$, L is the separation between voltage sensing electrodes, and A is the cross-sectional area of the CSF, which is essentially the same as the surface area of the current-emitting electrodes. Rather than use a calculated cell-constant based on imprecise measurements of separation between voltage sensing electrodes, (0.25 cm) and surface area of the current-emitting electrodes ($\sim$1 cm^2), $K_{\rm cell}$ was determined daily by calibration with a standard solution of 0.1 m KCl. The results were compared to the published values [16], which were linearly fit with a polynomial regression ($R^2 = 1$) and interpolated to obtain a conductivity value at 37 °C. This allowed the calculation of a cell constant each day at each frequency for both room and body temperature.

The average CSF data for the seven samples is listed in Table I. Intersubject variability, as reflected in the standard deviations, is comparable to that found in concentrations of the main ions in

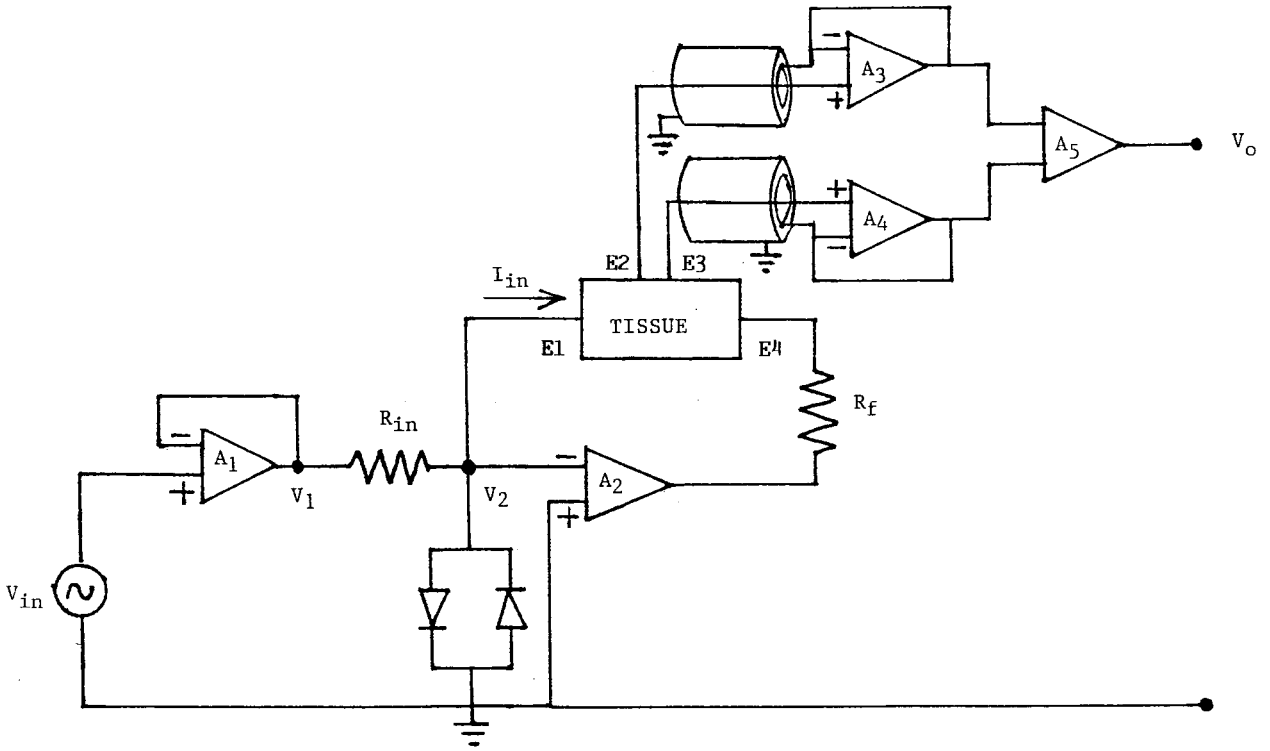

Fig. 2. The circuit for delivering current and measuring voltage across the conductivity cell. Constant current $I_{\rm in}$ is generated in the lower portion of the circuit and fed across outer electrodes $E1$ and $E4$ of the four electrode array. Inner electrodes $E2$ and $E3$ are used to measure the resulting voltage difference across the sample.

TABLE I
AVERAGE CONDUCTIVITY AND STANDARD DEVIATION (SD) OF SEVEN CSF SAMPLES ACROSS A RANGE OF FREQUENCIES AT ROOM TEMPERATURE AND BODY TEMPERATURE

	Room Temerature (25°C)		Body Temerature (37°C)	
Frequency (Hz)	Mean (S/m)	SD (S/m)	Mean (S/m)	SD (S/m)
10	1.451	0.019	1.789	0.018
20	1.451	0.019	1.793	0.015
33	1.452	0.019	1.789	0.021
50	1.453	0.020	1.791	0.017
100	1.454	0.020	1.794	0.018
200	1.456	0.020	1.796	0.019
333	1.457	0.022	1.799	0.016
500	1.456	0.022	1.792	0.024
1000	1.457	0.023	1.794	0.024
3333	1.455	0.024	1.789	0.024
10 000	1.456	0.024	1.802	0.022

normal CSF [17]. The differences between the average conductivities at room temperature and body temperature are highly significant ($p < .000\,01$) as determined by two-tailed T-tests. Radvan-Ziemnowicz [12] reported a conductivity of 1.557 S/m at 1 kHz and 24.5 °C, and our value at 1 kHz is slightly lower at 1.457 S/m, a 6% difference. More importantly, the conductivity at body temperature is 1.794 S/m, approximately 23% higher than the conductivity at room temperature.

Lissajou figures were used to make measurements of phase shift with a resolution of 2–3°. There was a measurable phase shift at the higher frequencies of 5–10 kHz, but this was present, also, when a resistor network was used in place of the conductivity cell, and so it was a product of the circuity. Consequently, in agreement with previous reports [12], [20], there was no significant reactive capacitance and, hence, no systematic difference in CSF conductivity across the frequency range of 10 Hz to 10 kHz.

IV. DISCUSSION

The conductivity of muscle tissue, sampled from a number of different animal species, increases in a curvilinear manner by twofold over the temperature range of 5–40 °C [13], while adipose tissue conductivity increases in a curvilinear manner by approximately a factor of 2.5 over the same temperature range [14], and bovine plasma conductivity increases by nearly 40%, from 1.11 S/m at 20 °C to 1.54 S/m at 40 °C [15].

In this study, the conductivity of human cerebrospinal fluid from seven patients was found to be 23% higher at body temperature (37 °C) than at room temperature (25 °C). This is in agreement with the temperature coefficient of approximately 2% per degree for 0.1 m KCl [16], which is similar in ionic concentration [17] and conductivity [16] to human CSF.

There is only one previous report of conductivity measurements on human CSF, and that was on one sample at room temperature [12]. A comparison with a sample of cat CSF at room temperature showed little difference. At least one body-temperature (39 °C) study was performed on animal (rabbit) CSF and reported an average conductivity of 1.79 S/m (range 1.64–1.94 S/m) at 1 kHz [20]. The study was listed in a widely quoted review of tissue resistivities [24] but, unfortunately, has been overlooked.

CSF conductivity can have a significant effect on source localization models [11]. A recent three-dimensional (3-D) finite element model of the head, using over 450 000 elements, shows that scalp electric and magnetic fields are very sensitive to CSF conductivity, in fact, about as sensitive as they are to brain and skull conductivities

[25], [26]. However, for nearly two decades modelers have used inaccurate values for CSF conductivity, in some cases [5], [21]–[23] values that are 44% lower (i.e., 1.0 S/m) than those reported here. Most often, researchers have simply used the same values for CSF conductivity that were used previously by other modelers or were reported in an early review article [24]. This has perpetuated an inaccuracy in the source-modeling literature. To decrease inaccuracies in models of source localization (or in models of bioeffects of external field exposure) for live human subjects, a body-temperature CSF conductivity of approximately 1.79 S/m should be used.

REFERENCES

[1] D. H. Fender, "Models of the human brain and the surrounding media: Their influence on the reliability of source localization," *J. Clin. Neurophysiol*., vol. 8, pp. 381–390, 1991.

[2] E. B. Lyskov, J. Juutilainen, V. Jousmaki, J. Partanen, S. Medvedev, and O. Hanninen, "Effects of 45-Hz magnetic fields on the functional state of the human brain," *Bioelectromagn.*, vol. 14, pp. 87–95, 1993.

[3] C. Polk and E. Postow, *Handbook of Biological Effects of Electromagnetic Fields*. Boca Raton, FL: CRC, 1986, P. 503.

[4] R. S. Hosek, A. Sances, Jr., R. W. Jodat, and S. J. Larson, "The contributions of intracerebral currents to the EEG and evoked potentials," *IEEE Trans. Biomed. Eng.*, vol. BME-25, pp. 405–413, 1978.

[5] H. Zhou and A. van Oosterom, "Computation of the potential distribution in a four-layer anisotropic concentric spherical volume conductor," *IEEE Trans. Biomed. Eng.*, vol. 39, pp. 154–158, 1992.

[6] E. Menninghaus, B. Lutkenhoner, and S. L. Gonzalez, "Localization of a dipolar source in a skull phantom: Realistic versus spherical model," *IEEE Trans. Biomed. Eng.*, vol. 41, pp. 986–989, 1994.

[7] M. S. Hamalainen and J. Sarvas, "Realistic conductivity geometry model of the human head for interpretation of neuromagnetic data," *IEEE Trans. Biomed. Eng*., vol. 36, pp. 165–171, 1989.

[8] J. W. H. Meijs, O. W. Weier, M. J. Peters, and A. van Oosterom, "On the numerical accuracy of the boundary element method," *IEEE Trans. Biomed. Eng.*, vol. 36, pp. 1038–1049, 1989.

[9] R. Srebro, "Realistic modeling of VEP topography," *Vision Res*., vol. 30, pp. 1001–1009, 1990.

[10] J. Le and A. Gevins, "Method to reduce blur distortion from EEG's using a realistic head model," *IEEE Trans. Biomed. Eng.*, vol. 40, pp. 517–528, 1993.

[11] J. C. Huang, C. Nicholson, and Y. C. Okada, "Distortion of magnetic evoked fields and surface potentials by conductivity differences at boundaries in brain tissue," *Biophys. J*., vol. 57, pp. 1155–1166, 1990.

[12] S. A. Radvan-Ziemnowicz, J. C. McWilliams, and W. E. Kucharski, "Conductivity versus frequency in human and feline cerebrospinal fluid," in *Proc. 17th Ann. Conf. Eng. Med., Biol.*, 1964, vol. 6, p. 108.

[13] E. Zheng, S. Shao, and J. G. Webster, "Impedance of skeletal muscle from 1 Hz to 1 Mhz," *IEEE Trans. Biomed. Eng.*, vol. BME-31, pp. 477–481, 1984.

[14] H. J. Swatland, "Anisotropy and postmortem changes in the electrical resistivity and capacitance of skeletal muscle," *J. Animal Sci.*, vol. 50, pp. 67–74, 1980.

[15] H. C. Burger and R. van Dongen, "Specific electric resistance of body tissues," *Phys. Med., Biol.*, vol. 5, pp. 431–447, 1961.

[16] Y. C. Wu, W. F. Kock, and K. W. Pratt, "Proposed new electrolytic conductivity primary standards for KCL solutions," *J. Res. Nat. Inst. Stand., Technol.*, 1991, vol. 96, pp. 191–201.

[17] R. A. Fishman, *Cerebrospinal Fluid in Diseases of the Nervous System*, 2nd ed. Philadelphia, PA: Saunders, 1992.

[18] L. A. Geddes, *Electrodes and the Measurement of Bioelectric Events*. New York: Wiley, 1972, pp. 32–35.

[19] J. J. Ackmann, "Complex bioelectric impedance measurement system for the frequency range from 5 Hz to 1 Mhz," *Annl. Biomed. Eng.*, vol. 21, pp. 135–146, 1993.

[20] G. W. Crile, H. R. Hosmer, and A. F. Rowland, "The electrical conductivity of animal tissues under normal and pathological conditions," *Amer. J. Physiol*., vol. 60, pp. 59–106, 1922.

[21] B. N. Cuffin and D. Cohen, "Comparison of the magnetoencephalogram and electroencephalogram," *Electroenceph., Clin. Neurophysiol.*, vol. 47, pp. 132–146, 1979.

[22] C. J. Stok, "The influence of model parameters on EEG/MEG single dipole source estimation," *IEEE Trans. Biomed. Eng.*, vol. BME-34, pp. 289–296, 1987.

[23] P. Berg and M. Scherg, "A fast method for forward computation of multiple-shell spherical head models," *Electroenceph., Clin. Neurophysiol.*, vol. 90, pp. 58–64, 1994.

[24] L. A. Geddes and L. E. Baker, "The specific resistance of biological material—A compendium of data for the biomedical engineer and physiologist," *Med., Biol. Eng.*, vol. 5, pp. 271–293, 1967.

[25] J. Haueisen, C. Ramon, M. Eiselt, and H Nowak, "The influence of tissue resistivity changes on MEG and EEG," presented at *10th Int. Conf. Biomagnetism*, Santa Fe, NM, Feb. 1996.

[26] J. Haueisen, C. Ramon, M. Eiselt, H. Brauer, and H. Nowak, "Influence of tissue resistivities on neuromagnetic fields and potentials studied with a finite element and a boundary element model of the head," *IEEE Trans. Biomed. Eng.*, submitted for publication.