Brain stimulation using electromagnetic sources: theoretical aspects

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ABSTRACT We prove that, at the frequencies generally proposed for extracranial stimulation of the brain, it is not possible, using any superposition of external current sources, to produce a three-dimensional local maximum of the electric field strength inside the brain. The maximum always occurs on a boundary where the conductivity jumps in value. Nevertheless, it may be possible to achieve greater two-dimensional focusing and shaping of the electric field than is currently available. Towards this goal we have used the reciprocity theorem to present a uniform treatment of the electric field inside a conducting medium produced by a variety of sources: an external magnetic dipole (current loop), an external electric dipole (linear antenna), and surface and depth electrodes. This formulation makes use of the lead fields from magneto- and electroencephalography. For the special case of a system with spherically symmetric conductivity, we derive a simple analytic formula for the electric field due to an external magnetic dipole. This formula is independent of the conductivity profile and therefore embraces spherical models with any number of shells. This explains the "insensitivity" to the skull's conductivity that has been described in numerical studies. We also present analytic formulas for the electric field due to an electric dipole, and also surface and depth electrodes, for the case of a sphere of constant conductivity.

INTRODUCTION

During the past decade there has been increasing interest in the possibility of stimulating the brain using extracranial current sources (see, e.g., Cohen and Cuffin, 1991). Stimulation is an important new method for exploring brain function and could lead to the development of neuroprosthetic devices. Relatively little is known about how neurons respond to an electric field nearby, however. For example, it is not clear what feature of this field is most important when trying to stimulate the neuron. Is it the strength of the field, its component parallel with or transverse to the neuronal surface, the parallel component of the gradient of the latter, or some other quantity?

To facilitate the study of these questions, it is valuable to be able to calculate the electric field distribution inside a conducting medium produced by various external sources. Numerical calculations have already been made using magnetic stimulators in special geometries (Ueno et al., 1988, 1990; Cohen and Cuffin, 1991; Roth et al., 1991; Yunokuchi and Cohen, 1991). In this paper we consider that particular problem as well as related ones involving electric stimulators. Because the spatial variations of the electric fields from the various sources are different, they may all be useful, separately or in combination, for stimulating different regions of the brain.

There is an intimate connection between the electric field inside a conductor produced by an external source and the field outside that is produced by an internal source of current; this is a direct result of the reciprocity theorem. Because the internal source problem has been studied in cardiography and encephalography, we shall make use of the same mathematics. The essential ingredient is the function (lead field), depending only on the head model, that relates the electric potential to the primary current.

After justifying in Section II that the quasistatic approximation is valid, we prove that, at the frequencies generally considered for brain excitation, it is not possible, using any set of external current sources whatsoever, to produce a three-dimensional local maximum of the electric field strength inside any region of constant conductivity.

In Section III we present an analytic formula for the electric field inside any spherically symmetric conductor, due to an external current loop (magnetic dipole). In Section IV we discuss the electric field inside a conductor produced by an external linear antenna (electric dipole). The mathematics is formulated for a general head model, and an explicit formula is given for a sphere with constant conductivity. In Section V we show that for stimulation using either surface or depth electrodes, the formula is similar to that for an electric dipole. In all cases we show the simple averaging of the point source formula that is needed if the size of the source is not negligibly small.

Some qualitative features of these various electric fields are discussed in Section VI, which also provides a summary of the paper. The application of the reciprocity theorem to a magnetic dipole source and to an electric dipole source is presented in Appendix A. Some of the mathematics needed for analyzing a layered head model, namely, one in which the conductivity is a different constant in different regions, is summarized in Appendix B. Explicit formulas are given there for a uniform sphere and also for three concentric spherical shells.

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II. LOW FREQUENCY (QUASISTATIC) APPROXIMATION

An approximate treatment of Maxwell's equations at low frequencies is presented in Plonsey (1969), in terms of the scalar and vector potentials; here we do it directly in terms of the electric field. There are two related points that govern the solution of these equations. The first is the fact that at low frequency they contain two small parameters (Plonsey, 1969); and the second is that the equations depend upon the frequency in an *analytic* manner. As a consequence, expansion of the field in powers of the frequency converges rapidly, and the first nonvanishing term provides a good approximation.

The first small parameter follows from the conservation of electric charge,

$$\nabla \cdot \mathbf{J} + \frac{\partial \rho}{\partial t} = 0, \tag{2.1}$$

where $\mathbf{J}$ is the electric current density and ρ is the electric charge density. It is useful to decompose $\mathbf{J}$ into two parts,

$$\mathbf{J} = \mathbf{J}^p + \sigma \mathbf{E}, \tag{2.2}$$

where $\mathbf{J}^p$ is referred to as the *primary* current and $\sigma\mathbf{E}$ is the conduction or *return* current; σ is the electrical conductivity. For a dielectric material there is also a polarization current, which is generally negligible relative to $\sigma\mathbf{E}$. In encephalography $\mathbf{J}^p$ is the current inside the neurons, whereas in the stimulation problem it is the current in the stimulating device; in both problems $\sigma\mathbf{E}$ is the current that flows in the conducting material of the brain, skull, and scalp. $\mathbf{J}^p$ can therefore be thought of as the driving current in both problems.

When Eqs. 2.1 and 2.2, including the polarization current, are combined with Gauss's law it is seen that inside any region of constant conductivity the charge density must fall off with time like $\exp(-\omega_0 t)$ at all points where $\nabla \cdot \mathbf{J}^p = 0$ (Nunez, 1981). Thus, it is only at the surfaces where σ jumps in value that charge can appear. The characteristic frequency ω_0 is given by

$$\omega_0 \equiv \frac{\sigma}{\epsilon}, \tag{2.3}$$

and the decay time is short even in the skull. We are not aware of a measurement of the dielectric constant $\epsilon = \kappa\epsilon_0$ for the skull; assuming $\kappa \approx 1$, we obtain from Nunez (1981)

$$\omega_0^{-1} \approx 1.8 \times 10^{-9}\ \mathrm{s}. \tag{2.4}$$

We shall only consider frequencies such that $\omega/\omega_0 \ll 1$.

The second small parameter in these problems is the ratio of the size of the conductor, D, to the skin depth, δ, of the medium, where

$$\frac{1}{\delta^2} \equiv \frac{1}{2}\mu_0\sigma\omega. \tag{2.5}$$

This follows from the equation satisfied by the electric field in any region where there is no electric charge density

$$\nabla^2\mathbf{E} = -(i\mu_0\sigma\omega + \mu_0\epsilon\omega^2)\mathbf{E}. \tag{2.6}$$

The most stringent requirement now comes from the brain region where $\sigma = 0.4/\Omega\text{-m}$ (Nunez, 1981), leading to

$$\delta^2 = \frac{2}{\mu_0\sigma\omega} = 4.0 \times 10^5\ \mathrm{cm}^2 \tag{2.7}$$

for $\omega = 10^5$ Hz; consequently, with $D = 20$ cm, $(D/\delta)^2 \ll 1$. Since the driving current $\mathbf{J}^p$ depends upon the frequency ω in an analytic way, the solution of Eq. 2.6 will also. We have now shown, therefore, that an expansion of $\mathbf{E}$ in powers of ω will converge rapidly to the actual solution. This is the essence of the quasistatic approximation.

Inserting this expansion of $\mathbf{E}$ into Eq. 2.6 and equating the two sides term by term establishes that

$$\nabla^2\mathbf{E} = 0 \tag{2.8}$$

to *first* order in the frequency. This follows from the fact that a static electric field cannot penetrate into a conductor.

Eq. 2.8 has important consequences for electromagnetic stimulation. It shows that to first order in the frequency no component of the electric field can have a three-dimensional local maximum inside any region of constant conductivity. The same is clearly true for a spatial derivative of any component and also for the magnitude of the electric field. Furthermore, because Eq. 2.8 is linear in $\mathbf{E}$, no superposition of external sources having different frequencies or different locations can alter the conclusion. The maxima for all such quantities must be found on a boundary where the conductivity jumps in value.

It may be possible, nevertheless, to achieve greater two-dimensional focusing and shaping of the electric field than is currently available. This is a necessary requirement if extracranial stimulation is to become useful for probing fine details of brain function. For stimulation of the cortex, for example, a major issue is how confined is the field in directions tangent to the surface and how rapidly does it fall off with depth. To provide the necessary tools for pursuing this matter, in the next three sections we will examine the electric field due to three different kinds of current sources.

III. MAGNETIC DIPOLE SOURCE

There is more than one way to solve for the electric field inside a conductor due to a prescribed current on the outside. One method makes use of a reciprocity theorem. An early application of this theorem is given in Rush and Driscoll (1969); but for our purpose the nicest statement of the theorem is given in Lorrain and Corson (1970) and Plonsey (1972), as a relation between the electric fields that are produced by two different currents of the same frequency. It is shown in Appendix A that, for the particular case in which $\mathbf{J}_1^p$ is a current dipole **p** at position $\mathbf{r}_1$ inside a conductor, and $\mathbf{J}_2^p$ is a small current loop having magnetic moment **m** located at position $\mathbf{r}_2$ outside the conductor, the reciprocity theorem leads to

$$\mathbf{p}\cdot\mathbf{E}(\mathbf{r}_1) = i\omega\mathbf{m}\cdot\mathbf{B}(\mathbf{r}_2). \tag{3.1}$$

Eq. 3.1 provides a simple, direct relation between the solutions to two different problems, one arising in magnetoencephalography and the other in electromagnetic stimulation of the brain. For the former problem one needs to calculate the magnetic field $\mathbf{B}(\mathbf{r}_2)$ outside a conductor, due to a current dipole **p** inside and its associated return current. If that problem has already been solved, then Eq. 3.1 determines the electric field $\mathbf{E}(\mathbf{r}_1)$ that results from a magnetic moment **m** at position $\mathbf{r}_2$. See Fig. 1. An oscillating magnetic moment will, of course, induce electric charge on the conductor, and the contribution to the field **E** from that charge is fully taken into account in Eq. 3.1.

Two important results follow from Eq. 3.1. Because **p** can be chosen to have any orientation, all components of **E** can be determined. Furthermore, to obtain **E** to *first* order in the frequency, it is sufficient to know **B** only to *zeroth* order. The static **B** is given by the Biot-Savart law,

$$\mathbf{B}(\mathbf{r}) = \frac{\mu_0}{4\pi}\int d^3r'\mathbf{J}(\mathbf{r}')\times\nabla'\frac{1}{|\mathbf{r}-\mathbf{r}'|}, \tag{3.2}$$

which can be further decomposed into primary and return current contributions using Eq. 2.2. For any head model in which the electric conductivity is a different constant in different regions, the contribution to **B** from the return current can be converted to a surface integral (Geselowitz, 1970), giving

$$\mathbf{B}(\mathbf{r}) = \frac{\mu_0}{4\pi}\left[\mathbf{p}\times\nabla_1\frac{1}{|\mathbf{r}-\mathbf{r}_1|} - \sum_j(\sigma_j^- + \sigma_j^+) \times\int dS'_j V(\mathbf{r}')\mathbf{n}(\mathbf{r}')\times\nabla'\frac{1}{|\mathbf{r}-\mathbf{r}'|}\right]. \tag{3.3}$$

In Eq. 3.3 $\sigma_j^-(\sigma_j^+)$ is the value of the conductivity just inside (outside) the jth surface, V is the electric potential on that surface, and the sum runs over all the surfaces of discontinuity of σ.

In Section IV we discuss the general procedure for obtaining V in such a head model, but here we take up the case in which the conductivity is any spherically symmetric function; that is, σ depends only on the distance from the origin. A clever solution for the magnetic field outside due to a static current dipole **p** inside is given by (Sarvas, 1987)

$$\mathbf{B}(\mathbf{r}_2) = \frac{\mu_0}{4\pi}\nabla_2\frac{\mathbf{p}\times\mathbf{r}_1\cdot\mathbf{r}_2}{F}$$
$$= \frac{\mu_0}{4\pi F^2}[F\mathbf{p}\times\mathbf{r}_1 - (\mathbf{p}\times\mathbf{r}_1\cdot\mathbf{r}_2)\nabla_2 F], \tag{3.4}$$

where the function F of the two independent variables $\mathbf{r}_1$ and $\mathbf{r}_2$ is defined as

$$F \equiv a(r_2 a + \mathbf{r}_2\cdot\mathbf{a}) \tag{3.5}$$

and

$$\mathbf{a} \equiv \mathbf{r}_2 - \mathbf{r}_1. \tag{3.6}$$

To obtain the formula for $\mathbf{E}(\mathbf{r}_1)$ from Eq. 3.1 one needs $\mathbf{m}\cdot\mathbf{B}$, and the first line of Eq. 3.4 gives it as

$$\mathbf{m}\cdot\mathbf{B}(\mathbf{r}_2) = \frac{\mu_0}{4\pi}(\mathbf{m}\cdot\nabla_2)\frac{\mathbf{p}\times\mathbf{r}_1\cdot\mathbf{r}_2}{F}$$
$$= \frac{\mu_0}{4\pi}\mathbf{p}\cdot(\mathbf{m}\cdot\nabla_2)\frac{\mathbf{r}_1\times\mathbf{r}_2}{F}. \tag{3.7}$$

Comparison with Eq. 3.1 immediately yields the result for the electric field,

$$\mathbf{E}(\mathbf{r}_1) = i\omega\frac{\mu_0}{4\pi}(\mathbf{m}\cdot\nabla_2)\frac{\mathbf{r}_1\times\mathbf{r}_2}{F}$$
$$= i\omega\frac{\mu_0}{4\pi F^2}[F\mathbf{r}_1\times\mathbf{m} - (\mathbf{m}\cdot\nabla_2 F)\mathbf{r}_1\times\mathbf{r}_2]. \tag{3.8}$$

The gradient operator in these equations, ∇_2, is with respect to $\mathbf{r}_2$, and the explicit formula for $\nabla_2 F$ is (Sarvas, 1987)

$$\nabla_2 F = \left(\frac{a^2}{r_2} + 2a + 2r_2 + \frac{\mathbf{r}_2\cdot\mathbf{a}}{a}\right)\mathbf{r}_2 - \left(a + 2r_2 + \frac{\mathbf{r}_2\cdot\mathbf{a}}{a}\right)\mathbf{r}_1. \tag{3.9}$$

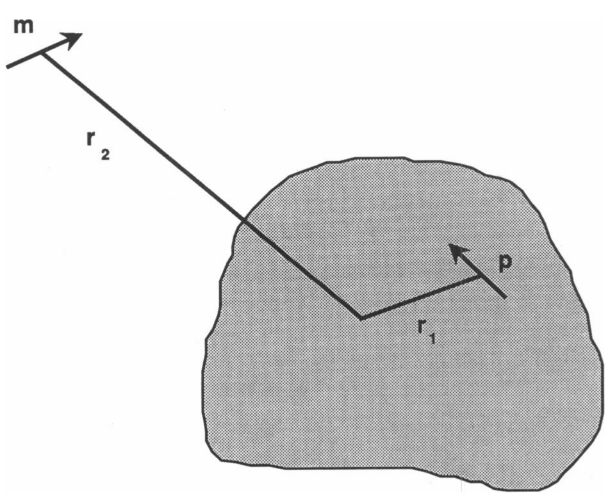

FIGURE 1 The geometry associated with Eq. 3.1. **p** is a current dipole at position $\mathbf{r}_1$ inside a conductor, and **m** is a magnetic dipole (current loop) at position $\mathbf{r}_2$ outside.

Eq. 3.8 is an explicit formula for the electric field, due to an external magnetic moment **m** of frequency ω, inside a conductor with any spherically symmetric conductivity profile. We have also verified this expression for **E** by solving the problem directly rather than by using the reciprocity theorem.

One of the consequences of Eq. 3.8 was already foreseen (Cohen and Cuffin, 1991) directly from the reciprocity theorem. Since it is known that a radially oriented current dipole in a spherically symmetric conductor produces no magnetic field outside, it must follow that no current loop on the outside can produce a radial component of electric field on the inside. This is confirmed here because the righthand side of Eq. 3.8 is orthogonal to $\mathbf{r}_1$. We note that this property of the electric field is not shared by an electric dipole source, to be discussed in the next section.

Branston and Tofts (1991) gave a direct proof that the vanishing of the radial component of **E** on the surface of a sphere of constant conductivity guarantees that it is zero throughout the volume. Their restriction to a special (linearly increasing) time course for the current in the coil is not necessary, however; we have seen that the result is valid to first order in the frequency. The proof provided by Saypol et al. (1991) is flawed, but can be easily corrected (B. J. Roth, personal communication).

Another special case of Eq. 3.8 is that in which **m** is in the direction $\mathbf{r}_2$, i.e., a radial magnetic dipole. Because the radial component of the magnetic field due to *any* current dipole is correctly given by just applying the Biot-Savart law to the current dipole itself, the expression for the electric field in this case becomes (after some algebra) correspondingly simple,

$$\mathbf{E}(\mathbf{r}_1) = i\omega \frac{\mu_0}{4\pi} \frac{\mathbf{a} \times \mathbf{m}}{a^3} \quad (\mathbf{m} \text{ radial}). \tag{3.10}$$

We emphasize the fact that Eq. 3.8 is completely independent of the conductivity profile, so long as it is spherically symmetric. This explains why a numerical solution of a three-shell model (Roth et al., 1991) finds the electric field to be "insensitive" to the skull conductivity; in fact, it is also independent of the brain and scalp conductivities, as well as of the radii of all the surfaces! The same conclusion was reached in Saypol et al. (1991) as a consequence of the vanishing of the radial component of **E** in any spherical shell having constant conductivity (but see the discussion above), and continuity of the tangential component of **E**.

It was shown in Section II that there is no maximum of the electric field strength inside any region of constant conductivity, for the frequencies under consideration; the maximum must occur on a boundary where the conductivity jumps in value. For a sphere of constant conductivity this is the surface of the sphere. With spherical symmetry the maximum will still occur there even if σ jumps in value at some interior radius, because the electric field is independent of the conductivity profile. One can also verify directly from Eq. 3.8 that $\nabla^2\mathbf{E}$ vanishes.

Finally, if the current loop is not sufficiently small that it can be treated as a point magnetic dipole, it is only necessary to average the expression for $\mathbf{E}(\mathbf{r}_1)$ given in Eq. 3.8 over $\mathbf{r}_2$ (the position of the source). This is a simple numerical integration, and is discussed further in Appendix A. Note that it is not necessary to solve Laplace's equation numerically. We performed this averaging over circular loops, and initial results have been presented (Heller et al., 1991). A paper is in preparation that examines the field resulting from a more general superposition of sources.

IV. AN ELECTRIC DIPOLE SOURCE

We now take up the problem of the electric field inside a conductor due to an external electric dipole; this is provided, for example, by a short, center-fed, linear antenna. Such a source has been used at higher frequencies to study energy deposition in the torso (Stuchly et al., 1986), but we are not aware of its use for brain stimulation. Because the electric field that it produces has a very different shape than that from a magnetic dipole, including a radial component, it may prove to be useful in the future.

Although the electric field can be obtained directly, we again follow the procedure from Section III, using the reciprocity theorem as given in Appendix A. This time, however, we need the electric field outside a conductor due to a current dipole inside, rather than the magnetic field, because the integral on the right-hand side of Eq. A.3 runs over a line segment (the antenna), rather than a closed loop.

For a sufficiently short antenna at position $\mathbf{r}_2$ having an electric dipole moment **d**, it is shown in Appendix A that the reciprocity theorem becomes

$$\mathbf{p} \cdot \mathbf{E}_2(\mathbf{r}_1) = -i\omega\mathbf{d} \cdot \mathbf{E}_1(\mathbf{r}_2). \tag{4.1}$$

The factor $-i\omega\mathbf{d}$ is equal to the volume integral of the current in the antenna (see Eq. A.10), and **p** is again a current dipole at position $\mathbf{r}_1$ inside the conductor. It, together with its associated return current, produces the electric field $\mathbf{E}_1$. The antenna, together with the current it induces in the conductor, produces the electric field $\mathbf{E}_2$. Eq. 4.1 is the electric dipole analog of Eq. 3.1 for a magnetic dipole source, and, as in that problem, to obtain $\mathbf{E}_2$ to first order in the frequency it is sufficient to know $\mathbf{E}_1$ to zeroth order. We now show how to obtain $\mathbf{E}_1$.

For a static problem the electric field is determined by a scalar potential, $\mathbf{E}_1 = -\nabla V$, and when this is combined with Eqs. 2.1 and 2.2 it gives

$$\nabla \cdot (\sigma \nabla V) = \nabla \cdot \mathbf{J}^p. \tag{4.2}$$

Because Eq. 4.2 for V is linear, the solution must have the form

$$V(\mathbf{r}) = -\int d^3r' H(\mathbf{r}, \mathbf{r}')\nabla' \cdot \mathbf{J}^p(\mathbf{r}'), \tag{4.3}$$

where the lead field (Green's function) H depends on the head model, i.e., the geometry and the conductivity distribution, but not on the source function. After solving for the function H once, the potential produced by any assumed source can be found by just carrying out the integration in Eq. 4.3.

With $\mathbf{J}^p$ again specified to be a current dipole $\mathbf{p}$ at position $\mathbf{r}_1$, Eq. 4.3 becomes

$$V(\mathbf{r}) = \mathbf{p} \cdot \nabla_1 H(\mathbf{r}, \mathbf{r}_1). \tag{4.4}$$

Once the function H has been found for a given head model, the corresponding electric field is given by

$$\mathbf{E}_1(\mathbf{r}) = -(\mathbf{p} \cdot \nabla_1)\nabla H(\mathbf{r}, \mathbf{r}_1), \tag{4.5}$$

and inserting this into Eq. 4.1 yields the expression for the electric field at an interior point $\mathbf{r}_1$ due to an external electric dipole $\mathbf{d}$ at position $\mathbf{r}_2$,

$$\mathbf{E}(\mathbf{r}_1) = i\omega \nabla_1 (\mathbf{d} \cdot \nabla_2) H(\mathbf{r}_2, \mathbf{r}_1). \tag{4.6}$$

We have dropped the subscript 2 on $\mathbf{E}$ in Eq. 4.6 because it is no longer needed.

Eq. 4.6 for the electric field inside a conductor due to a linear antenna on the outside is valid for any conductor, provided one knows the function $H(\mathbf{r}_2, \mathbf{r}_1)$ for that conductor. For the special case of a sphere of constant conductivity, σ, it does not seem to be generally known that the answer can be written in closed form. It is shown in Appendix B that

$$H(\mathbf{r}_2, \mathbf{r}_1) = \frac{1}{4\pi\sigma}\left[\frac{2}{a} - \frac{1}{r_2} \ln \frac{\mathbf{r}_2 \cdot \mathbf{a} + r_2 a}{2r_2^2}\right], \tag{4.7}$$

where $\mathbf{a} = \mathbf{r}_2 - \mathbf{r}_1$. From this we find that

$$\nabla_1 H(\mathbf{r}_2, \mathbf{r}_1) = \frac{1}{4\pi\sigma}\left(2\frac{\mathbf{a}}{a^3} + \frac{\mathbf{b}}{F}\right), \tag{4.8}$$

where

$$\mathbf{b} \equiv \mathbf{a} + a\frac{\mathbf{r}_2}{r_2}, \tag{4.9}$$

and F is the function defined in Eq. 3.5.

The ∇_2 operation that is called for in Eq. 4.6 can be done analytically, giving

$$\mathbf{E}(\mathbf{r}_1) = i\omega \frac{1}{4\pi\sigma} \times \left[2\left(\frac{\mathbf{d}}{a^3} - \frac{3(\mathbf{d}\cdot\mathbf{a})\mathbf{a}}{a^5}\right) + \frac{1}{F}(\mathbf{d}\cdot\nabla_2)\mathbf{b} - \frac{\mathbf{d}\cdot\nabla_2 F}{F^2}\mathbf{b}\right] \tag{4.10}$$

where

$$(\mathbf{d}\cdot\nabla_2)\mathbf{b} = \left(1 + \frac{a}{r_2}\right)\mathbf{d} + \left(\frac{\mathbf{d}\cdot\mathbf{a}}{r_2 a} - \frac{a\mathbf{d}\cdot\mathbf{r}_2}{r_2^3}\right)\mathbf{r}_2, \tag{4.11}$$

and $\nabla_2 F$ is given in Eq. 3.9. Eq. 4.10 gives the electric field inside a sphere of constant conductivity σ due to an electric dipole $\mathbf{d}$ at position $\mathbf{r}_2$ outside the sphere. Note that this formula is independent of the radius of the sphere. It is not as general a result as Eq. 3.8, which gives the electric field due to a magnetic dipole; in that problem the electric field is completely independent of the conductivity profile in the spherically symmetric case. We have also verified Eq. 4.10 by solving the uniform sphere problem directly rather than going through the reciprocity theorem.

If the antenna is not sufficiently short that it can be treated as a point electric dipole, it is only necessary to average the expression for $\mathbf{E}(\mathbf{r}_1)$ given in Eq. 4.10 over the length of the antenna, as described in Appendix A.

V. SURFACE AND DEPTH ELECTRODES

We want to find the electric field inside a conductor when electrodes carrying a current are placed on the surface or inside the material. The difference between this problem and those studied in the previous sections is the following. Because the stimulating current is in actual contact with the conductor, there is an electric field inside the conductor even at zero frequency, so it is simpler to solve for $\mathbf{E}$ directly without going through the reciprocity theorem.

The continuity condition in Eq. 4.2 and the expression of linearity in Eq. 4.3 are unchanged. With $\mathbf{J}^p$ consisting of current I entering the conductor at position $\mathbf{r}_i$, and exiting at position $\mathbf{r}_o$, Eq. 4.3 becomes

$$V(\mathbf{r}) = I[H(\mathbf{r}, \mathbf{r}_i) - H(\mathbf{r}, \mathbf{r}_o)]. \tag{5.1}$$

The function H is the same one that is discussed in Section IV and Appendix B, and for the present application $\mathbf{r}$ is assumed to be inside the volume.

The electric field is obtained from $\mathbf{E}(\mathbf{r}) = -\nabla V(\mathbf{r})$, but before taking the gradient we make use of the symmetry of H. It is shown in Appendix B that

$$H(\mathbf{r}, \mathbf{r}_i) = H(\mathbf{r}_i, \mathbf{r}) \tag{5.2}$$

for $\mathbf{r}$ and $\mathbf{r}_i$ inside or on the boundary, and it follows from Eqs. 5.1 and 5.2 that

$$\mathbf{E}(\mathbf{r}) = I[\nabla H(\mathbf{r}_o, \mathbf{r}) - \nabla H(\mathbf{r}_i, \mathbf{r})]. \tag{5.3}$$

Eq. 5.3 for the electric field due to a pair of electrodes is just a finite difference version of Eq. 4.6 for a short linear antenna. This connection is made explicit in Appendix A where the antenna is given a length that is not negligibly small.

For a uniform sphere, Eq. 4.8 can be used to evaluate the two gradients in Eq. 5.3 by making the appropriate substitutions. For example, $\nabla H(\mathbf{r}_o, \mathbf{r})$ can be obtained by making the replacements $\mathbf{r}_2 \rightarrow \mathbf{r}_o$ and $\mathbf{r}_1 \rightarrow \mathbf{r}$ in the definitions of $\mathbf{a}$, F, and $\mathbf{b}$, Eqs. 3.6, 3.5, and 4.9, respectively.

VI. DISCUSSION AND SUMMARY

We now want to discuss some qualitative features of the formulas that we have obtained for the electric field inside a conductor due to different kinds of stimulators. One important result is common to all the extracranial current sources considered, including any superposition of such sources. At the frequencies under consideration, it is not possible to produce a three-dimensional maximum of the magnitude of $\mathbf{E}$, nor of any component of $\mathbf{E}$, at any point where the conductivity is constant. This means that the maximum must occur on one of the boundaries where σ jumps in value. The exception in the case of depth electrodes results from the fact that they actually introduce electric charge inside the conductor, and it is precisely at the point where they do that the maximum occurs.

Furthermore, it was shown in Section III that for a magnetic dipole, i.e., current loop (or a superposition of loops) outside a spherically symmetric conductor, the maximum must occur on the outermost surface even if there are inner surfaces on which σ is discontinuous. It is likely that this result is more general; it probably applies to any head model and also to the electric dipole sources considered in Section IV. It is clearly true for surface electrodes.

For small distances away from any point current source, the strength of the electric field falls off with some power of the distance that is characteristic of that source. Examination of Eqs. 3.8, 4.10, and 5.3 shows that this power is two for a magnetic dipole and also for each individual electrode of an electrode pair, and it is three for an electric dipole, i.e., linear antenna. For either kind of dipole, however, using a superposition of sources or a single large source produces a major modification of the dependence on distance, so these simple power laws are not very informative.

For electrodes, the fact that they occur in pairs and, furthermore, are of opposite sign, leads to the same conclusion. The most prominent feature of the field due to electrodes is the obvious fact that there are singular points; this is one of the motivations for using extracranial current sources. Saypol et al. (1991) present a theoretical comparison of the electric fields produced by a current loop and by surface electrodes.

The fact that the electric field due to current loops outside a spherically symmetric conductor has no radial component follows immediately from the analytic formula presented in Eq. 3.8. This feature is not shared by the other current sources and suggests that different sources may be more suitable for exciting different neuronal populations.

It is also interesting to compare the overall strengths of the electric fields due to magnetic and electric dipoles. For this purpose we compare the point dipole formulas given in Eqs. 3.8 and 4.10. At a common distance (a) from two such sources the ratio of the strengths is of order

$$\frac{\omega\mu_0 m/a^2}{\frac{\omega}{\sigma}\,d/a^3} \approx (\mu_0\sigma\omega)Aa/L \approx \frac{La}{\delta^2}, \tag{6.1}$$

where we have expressed the magnetic moment m as the product of the current and the area A of the loop, and have used Eq. A.17, which gives the electric dipole moment d in terms of the length L of the antenna; we have assumed that the current strength is the same for the two sources. For the final version of Eq. 6.1 we have also assumed that the dimensions of the two sources are comparable and have made use of the definition of the skin depth δ from Eq. 2.7. For the conductivity of the brain, and with $L = 10$ cm, $a = 2$ cm, and $\omega = 10^4$ Hz, the ratio of the strengths of the two electric fields is $\approx 10^{-5}$. Alternatively, one can say that a linear antenna only needs 10^{-5} of the amount of current in a loop to produce the same electric field strength. A technical difficulty is that it requires a very large voltage to drive even this small current into a short antenna at these frequencies; this matter is being pursued further.

A summary of the main analytic formulas of the paper follows. We have obtained the electric field $\mathbf{E}(\mathbf{r})$ inside a conductor for three special cases: (i) a current loop outside a region with any spherically symmetric conductivity profile, Eq. 3.8; (ii) a linear antenna outside a sphere of constant conductivity, Eq. 4.10; and (iii) electrodes either on the surface or inside a sphere of constant conductivity, Eq. 5.3. These three formulas are valid for positions $\mathbf{r}$ such that the distance to the source is large compared to the size of the source. When this is not the case, to average over the size of the source only requires a simple numerical integration, as discussed in Appendix A.

For a more realistic head model, all the formalism of this paper can be used once the function H for that model has been obtained. If the conductivity is a different constant in different compartments of the head, then the procedure for obtaining $H(\mathbf{r}, \mathbf{r}_1)$, with $\mathbf{r}$ and $\mathbf{r}_1$ anywhere inside the head, is described in Appendix B.

We are now applying these results to various superpositions of current sources to see what can be achieved in the way of shaping and focusing the electric field. A paper on this work is in preparation.

APPENDIX A

THE RECIPROCITY THEOREM

This theorem relates the electric fields that are produced by two different current sources, of the same frequency, in the presence of the same set of conductors (Lorrain and Corson, 1970; Plonsey, 1972). With the current written as in Eq. 2.2 as the sum of a primary current $\mathbf{J}^p$ and the conduction current $\sigma\mathbf{E}$, the theorem states that

$$\int d^3r\,\mathbf{J}_1^p\cdot\mathbf{E}_2 = \int d^3r\,\mathbf{J}_2^p\cdot\mathbf{E}_1, \tag{A.1}$$

where the integrations run over all space. $\mathbf{E}_1$ is the total electric field that is produced by the current $\mathbf{J}_1^p$ together with the current that it induces in the conductor; $\mathbf{E}_2$ has the same significance for the current $\mathbf{J}_2^p$. Taking $\mathbf{J}_1^p$ to be a point current dipole $\mathbf{p}$ inside the conductor at position $\mathbf{r}_1$,

$$\mathbf{J}_1^p(\mathbf{r}) = \mathbf{p}\delta(\mathbf{r}-\mathbf{r}_1), \tag{A.2}$$

Eq. A.1 becomes

$$\mathbf{p}\cdot\mathbf{E}_2(\mathbf{r}_1) = \int d^3r\,\mathbf{J}_2^p\cdot\mathbf{E}_1. \tag{A.3}$$

1. A Current Loop (Magnetic Dipole)

Let us take $\mathbf{J}_2^p$ to be a current loop outside the conductor, carrying current I; then the righthand side of Eq. A.3 becomes a line integral around the loop, i.e.,

$$\mathbf{p}\cdot\mathbf{E}_2(\mathbf{r}_1) = I\int d\mathbf{l}\cdot\mathbf{E}_1. \tag{A.4}$$

By Faraday's law this line integral equals the negative time rate of change of the magnetic flux Φ linking the loop in the right-handed sense, i.e.,

$$\mathbf{p}\cdot\mathbf{E}(\mathbf{r}_1) = i\omega I\Phi, \tag{A.5}$$

where

$$\Phi = \int dS\mathbf{n}\cdot\mathbf{B}. \tag{A.6}$$

The integration in Eq. A.6 is over the area of any surface bounded by the loop, and $\mathbf{n}$ is the local normal to that surface. We have dropped the subscript on $\mathbf{E}$ in Eq. A.5 because it is no longer needed; the factor i appearing in this equation indicates that the electric field is out of phase with the current.

For a very small loop located at position $\mathbf{r}_2$, Φ is equal to its area A multiplied by the component of magnetic field that is normal to the loop, and using the definition of the magnetic moment, Eq. A.5 becomes

$$\mathbf{p}\cdot\mathbf{E}(\mathbf{r}_1) = i\omega\mathbf{m}\cdot\mathbf{B}(\mathbf{r}_2). \tag{A.7}$$

Note that, if the current loop is not sufficiently small that it can be treated as a point magnetic dipole, Eqs. A.5 and A.6 provide the needed generalization. If the loop lies in a single plane, which is the most common situation, then it is only necessary to average the expression for the electric field given in Eq. 3.8 over the source position $\mathbf{r}_2$, i.e.,

$$\mathbf{E}(\mathbf{r}_1) \rightarrow \frac{1}{A}\int dS_2\mathbf{E}(\mathbf{r}_1). \tag{A.8}$$

The integration in Eq. A.8 is over the loop of area A. The physical significance of Eq. A.8 is that a large loop of current can be thought of as being composed of many small loops, each carrying the full current and having, therefore, a magnetic moment per unit area equal to $\mathbf{m}/A$.

2. A Linear Antenna (Electric Dipole)

We now take the primary current $\mathbf{J}_2^p$ to be flowing inside a linear antenna. For a sufficiently short antenna at position r_2 outside the conductor, $\mathbf{E}_1$ on the right side of Eq. A.3 can be taken out of the integral, giving

$$\mathbf{p}\cdot\mathbf{E}_2(\mathbf{r}_1) = \mathbf{E}_1(\mathbf{r}_2)\cdot\int d^3r\,\mathbf{J}_2^p(\mathbf{r}). \tag{A.9}$$

Using current conservation as in Section 9.2 of Jackson (1975), the integral in Eq. A.9 is related to the electric dipole moment $\mathbf{d}$ of the source, according to

$$\int d^3r\,\mathbf{J}_2^p(\mathbf{r}) = -i\omega\mathbf{d} = -i\omega\int d^3r\,\mathbf{r}\rho(\mathbf{r}), \tag{A.10}$$

thereby giving

$$\mathbf{p}\cdot\mathbf{E}_2(\mathbf{r}_1) = -i\omega\mathbf{d}\cdot\mathbf{E}_1(\mathbf{r}_2). \tag{A.11}$$

For the short antenna considered above, it was not necessary to know the variation of the current density in the antenna, $\mathbf{J}_2^p$, along its length, because only its volume integral (see Eq. A.9) was needed. We now generalize the previous result when the length of the antenna is not negligibly small compared with the distance to be head. The way to do this is to think of the full antenna as being composed of many small antennas, each contributing an electric dipole moment per unit length proportional to the current strength at that point.

With the thickness of the antenna assumed to be much less than its length, only the total current $I(z)$ passing through any cross section of the antenna is relevant. Setting up a coordinate system as in Fig. 2, with the origin at the center of the antenna and the z-axis along its length, the proper way to average Eq. 4.6 is

$$\mathbf{E}(\mathbf{r}_1) \rightarrow \frac{1}{\int dzI(z)}\int dzI(z)\mathbf{E}(\mathbf{r}_1). \tag{A.12}$$

The total moment $\mathbf{d}$ is obtained from Eq. A.10 as

$$-i\omega\mathbf{d} = \hat{\mathbf{z}}\int dzI(z), \tag{A.13}$$

where $\hat{\mathbf{z}}$ is a unit vector in the direction of the antenna. Eqs. A.12 and A.13 are valid for any current distribution in the antenna.

In Section 9.2 of Jackson (1975) a linear approximation is made to $I(z)$,

$$I(z) = I_0\left(1 - \frac{2|z|}{L}\right), \tag{A.14}$$

where I_0 is the total current fed into the antenna and L is its length; see Fig. 2. Substituting Eq. A.14 and the point dipole formula given in Eq. 4.6 into A.12, and integrating by parts, this approximation leads to

$$\mathbf{E}(r_1) = I_0\nabla_1[\langle H(-z,\mathbf{r}_1)\rangle - \langle H(+z,\mathbf{r}_1)\rangle], \tag{A.15}$$

where $\langle H\rangle$ is the simple average of H, computed separately in each half of the antenna, e.g.,

$$\langle H(+z,\mathbf{r}_1)\rangle \equiv \frac{2}{L}\int_0^{L/2} dzH(z,\mathbf{r}_1). \tag{A.16}$$

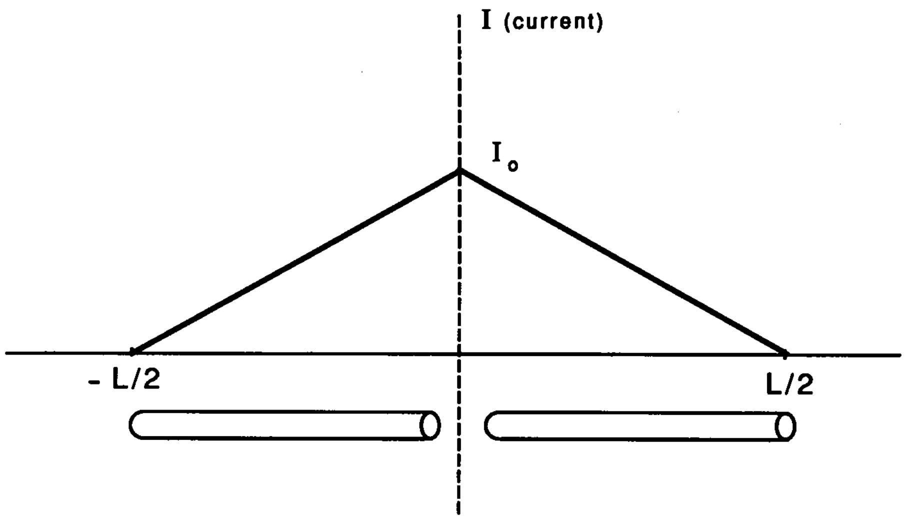

FIGURE 2 A center-fed linear antenna, showing the linear variation of current with distance given in Eq. A.14. The current flows in the same direction in both halves of the antenna.

Inserting the linear approximation to the current into Eq. A.13, the electric dipole moment becomes

$$i\omega \mathbf{d} = -I_0 \frac{L}{2} \hat{\mathbf{z}}. \tag{A.17}$$

For any other current distribution in the antenna, Eq. A.15 can still be used, but the formula for $\langle H \rangle$ in Eq. A.16 must be modified.

APPENDIX B

THE LAYERED HEAD MODEL

In Section IV the problem of finding the electric field inside a conductor at position $\mathbf{r}_1$ due to an electric dipole source outside at position $\mathbf{r}_2$, was reduced, by means of the reciprocity theorem, to solving for the lead field $H(\mathbf{r}_2, \mathbf{r}_1)$, a function that depends on the head model but not on the source. The starting point is the continuity equation (4.2) for the electric potential V due to a static, internal, primary current distribution $\mathbf{J}^p$. In any geometry, provided the conductivity σ is a different constant in different regions, Eq. 4.2 can be converted to an integral equation for V over all the surfaces at which σ jumps in value (Geselowitz, 1967). Using that equation we will first obtain $H(\mathbf{r}, \mathbf{r}_1)$ with $\mathbf{r}$ on the outermost surface and then use that to get $H(\mathbf{r}_2, \mathbf{r}_1)$ with $\mathbf{r}_2$ outside.

Substituting Eq. 4.4 into the integral equation for V (Geselowitz, 1967) leads to the equation that H must satisfy

$$\frac{\sigma_k^- + \sigma_k^+}{2} H(\mathbf{r}, \mathbf{r}_1) = \frac{1}{4\pi|\mathbf{r} - \mathbf{r}_1|} - \frac{1}{4\pi} \sum_j (\sigma_j^- - \sigma_j^+) \times \int dS'_j H(\mathbf{r}', \mathbf{r}_1) \mathbf{n}(\mathbf{r}') \cdot \nabla' \frac{1}{|\mathbf{r} - \mathbf{r}'|}. \quad (\mathbf{r} \text{ on the } k\text{th surface}) \tag{B.1}$$

Eq. B.1 is actually a set of n coupled integral equations; σ_j^- (σ_j^+) is the value of σ just inside (outside) the jth surface.

Once Eq. B.1 has been solved for all $\mathbf{r}$ on the surfaces where σ jumps in value, $H(\mathbf{r}, \mathbf{r}_1)$ can be obtained at any interior point where σ is constant by simply inserting that value of $\mathbf{r}$ on the righthand side of the equation, and replacing the left side by $\sigma H(\mathbf{r}, \mathbf{r}_1)$. Note that it may be necessary to add a function $f(\mathbf{r})$ that is independent of $\mathbf{r}_1$ to the righthand side of Eq. B.1. From Eq. 4.3 it is seen that such an addition has no effect on $V(\mathbf{r})$ provided no net primary current $\mathbf{J}^p$ flows into the conductor.

Eq. B.1 can be written in a more compact notation by defining

$$\lambda_j \equiv \frac{\sigma_j^- - \sigma_j^+}{\sigma_j^- + \sigma_j^+}, \tag{B.2}$$

and

$$K(\mathbf{r}, \mathbf{r}_1) \equiv \frac{\sigma_k^- + \sigma_k^+}{2} H(\mathbf{r}, \mathbf{r}_1), \tag{B.3}$$

for $\mathbf{r}$ a point on the kth surface; Eq. B.1 then becomes

$$K(\mathbf{r}, \mathbf{r}_1) = \frac{1}{4\pi|\mathbf{r} - \mathbf{r}_1|} - \frac{1}{2\pi} \sum_j \lambda_j \int dS'_j K(\mathbf{r}', \mathbf{r}_1) \mathbf{n}(\mathbf{r}') \cdot \nabla' \frac{1}{|\mathbf{r} - \mathbf{r}'|}. \tag{B.4}$$

For a general geometry, Eq. B.4 must be solved numerically. An important case that can be solved analytically is a sphere in which σ is a different constant in different concentric shells. It follows from rotational invariance that $K(\mathbf{r}, \mathbf{r}_1)$ can only depend on the magnitudes r and r_1, and the angle Θ between $\mathbf{r}$ and $\mathbf{r}_1$. For $\mathbf{r}$ on the kth surface one can expand K (or H) as

$$K(\mathbf{r}, \mathbf{r}_1) = \frac{1}{4\pi} \sum_{l=0}^{\infty} K_l^k P_l(\cos\Theta) = \sum_l \sum_{m=-l}^{l} \frac{1}{2l+1} K_l^k Y_{lm}(\theta, \phi) Y_{lm}^*(\theta_1, \phi_1), \tag{B.5}$$

where P_l is a Legendre polynomial and Y_{lm} is a spherical harmonic. If the function $f(\mathbf{r})$ referred to below Eq. B.1 is expanded in the same way, all the coefficients f_l^k vanish for l different from zero; for $l = 0$ the coefficients K_0^k are not determined, but such additions to K that are independent of $\mathbf{r}_1$ are irrelevant.

Using the spherical harmonic expansions of the inhomogeneous term and the normal derivative in Eq. B.4, for each value of l one obtains a set of n coupled linear equations for the K_l^k. We now show these equations for $n = 1$, i.e., a single sphere of constant conductivity, and then state the result for $n = 3$.

1. A Uniform Sphere

For $n = 1$ there is only one surface with radius R, and λ for that surface is unity because the outside conductivity is zero. Setting $dS' = R^2 d\Omega'$, where $d\Omega'$ is the element of solid angle, leads to

$$K_l = \frac{r_1^l}{R^{l+1}} + \frac{1}{2l+1} K_l. \qquad \text{(B.6)}$$

As mentioned above, this relation is valid only for $l > 0$, K_0 being completely arbitrary. Solving Eq. B.6 for K_l and using B.3 gives

$$H_l = \frac{1}{\sigma} \frac{2l+1}{l} \frac{r_1^l}{R^{l+1}}, \qquad \text{(B.7)}$$

and summing over l as in Eq. B.5 leads to

$$H(\mathbf{r}, \mathbf{r}_1) = \frac{1}{4\pi\sigma} \sum_{l=1} \frac{2l+1}{l} \frac{r_1^l}{R^{l+1}} P_l(\cos\Theta), \qquad \text{(B.8)}$$

for $\mathbf{r}$ on the surface, i.e., $r = R$. To obtain H when $\mathbf{r}$ is *outside* the sphere, simply replace R in Eq. B.8 by r.

When the procedure described below Eq. B.1 is used to obtain $H(\mathbf{r}, \mathbf{r}_1)$ for $\mathbf{r}$ *inside* the sphere, the result is

$$H(\mathbf{r}, \mathbf{r}_1) = \frac{1}{\sigma} G^N(\mathbf{r}, \mathbf{r}_1; R) \quad (r \le R, r_1 \le R), \qquad \text{(B.9)}$$

where G^N is the Neumann Green's function for the inside of a sphere:

$$G^N(\mathbf{r}, \mathbf{r}_1; R) = \frac{1}{4\pi|\mathbf{r} - \mathbf{r}_1|} + \frac{1}{4\pi} \sum_{l=1} \frac{l+1}{l} \frac{(rr_1)^l}{R^{2l+1}} P_l(\cos\Theta). \qquad \text{(B.10)}$$

This function satisfies the boundary condition

$$\mathbf{n}(\mathbf{r}_1) \cdot \nabla_1 G^N(\mathbf{r}, \mathbf{r}_1; R) = -\frac{1}{A}, \qquad \text{(B.11)}$$

where $A = 4\pi R^2$ is the area of the surface.

The series in Eq. B.10 can be summed analytically (Aerts and Heller, 1981), giving

$$G^N(\mathbf{r}, \mathbf{r}_1; R) = \frac{1}{4\pi}\left[\frac{1}{|\mathbf{r} - \mathbf{r}_1|} + \frac{Rr}{|R^2\mathbf{r} - r^2\mathbf{r}_1|} - \frac{1}{R} \ln\left(\frac{R^2 - \mathbf{r}\cdot\mathbf{r}_1 + |R^2\mathbf{r} - r^2\mathbf{r}_1|/r}{2R^2}\right)\right]. \qquad \text{(B.12)}$$

It is clear from Eq. B.10 that G^N is symmetric under interchange of $\mathbf{r}$ and $\mathbf{r}_1$, and it is straightforward to show that the quantity $|R^2\mathbf{r} - r^2\mathbf{r}_1|/r$ is indeed symmetric. This leads to a symmetry property for H:

$$H(\mathbf{r}, \mathbf{r}_1) = H(\mathbf{r}_1, \mathbf{r}) \quad (r \le R, r_1 \le R). \qquad \text{(B.13)}$$

This relation can be derived more generally for an arbitrary conductor; it is a consequence of reciprocity. Eq. B.8 for $r \ge R$ can also be summed directly, or H can be obtained formally from B.9, B.10, and B.12 by putting $R = r$; the result is

$$H(\mathbf{r}, \mathbf{r}_1) = \frac{1}{4\pi\sigma}\left[\frac{2}{|\mathbf{r} - \mathbf{r}_1|} - \frac{1}{r} \ln \frac{\mathbf{r}\cdot(\mathbf{r} - \mathbf{r}_1) + r|\mathbf{r} - \mathbf{r}_1|}{2r^2}\right] \quad (r \ge R, r_1 \le R). \qquad \text{(B.14)}$$

2. Three Concentric Spherical Shells

With the function $H(\mathbf{r}, \mathbf{r}_1)$ expanded on each of the three spherical surfaces as in Eq. B.5, B.1 becomes a set of three simultaneous linear equations for the H_l^k for each value of the integer l, with $k = 1, 2$, or 3 designating the surface. These equations can be solved in terms of determinants of 3×3 matrices. The case of immediate interest is that in which one of the arguments ($\mathbf{r}_1$) of the function H is inside the brain, and the other ($\mathbf{r}$) is on the surface of the scalp. The reciprocal problem was studied by Rush and Driscoll (1969) in connection with stimulation by surface electrodes; matching the solutions of Laplace's equation at each of the boundaries leads to five equations in five unknowns. As a result of the symmetry of the function H our answer looks just like theirs with the roles of $\mathbf{r}$ and $\mathbf{r}_1$ interchanged,

$$H(\mathbf{r}, \mathbf{r}_1) = \frac{1}{2\pi\sigma_t} \sum_{l=1} A_l \frac{r_1^l}{c^{l+1}} P_l(\cos\Theta), \qquad \text{(B.15)}$$

where A_l is the quantity defined in Eq. 25 of their paper, σ_t is the conductivity of the scalp, and c is its outer radius. to find H when $\mathbf{r}$ is outside the head it is only necessary to replace c in Eq. B.15 by r.

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