

ON BIOELECTRIC POTENTIALS IN AN INHOMOGENEOUS VOLUME CONDUCTOR

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ABSTRACT Green's theorem is used to derive two sets of expressions for the quasi-static potential distribution in an inhomogeneous volume conductor. The current density in passive regions is assumed to be linearly related instantaneously to the electric field. Two equations are derived relating potentials to an arbitrary distribution of impressed currents. In one, surfaces of discontinuity in electrical conductivity are replaced by double layers and in the other, by surface charges. A multipole equivalent generator is defined and related both to the potential distribution on the outer surface of the volume conductor and to the current sources. An alternative result involves the electric field at the outer surface rather than the potential. Finally, the impressed currents are related to electrical activity at the membranes of active cells. The normal component of membrane current density is assumed to be equal at both membrane surfaces. One expression is obtained involving the potentials at the inner and outer surfaces of the membrane. A second expression involves the transmembrane potential and the normal component of membrane current.

INTRODUCTION

Developments in the physics of electricity, including experiment, theory, and instrumentation, have been closely associated with investigations in bioelectricity. Of particular interest has been the study of the spread of electric currents, arising from sources in muscle and nerve, through surrounding tissue masses and fluids.

Helmholtz (1853) provided theoretical foundations for this study in a paper of considerable significance. Subsequently many theoretical papers have appeared in the electrocardiographic literature. (Much of the work is discussed or referred to in Hecht, 1957.) They have been concerned with potential distributions in conductors of various shapes containing various sources, with techniques for handling this type of problem including use of the reciprocity principle introduced by Helmholtz, and with the inverse problem of determining a source (equivalent generator) which could have given rise to potentials observed on the surface of a conductor. Results have been obtained analytically, numerically, and with the use of models for a rather large number of configurations including the human torso. One might mention in particular the attempt by Wilson et al. (1933) to relate external potentials

to time-varying distributions of current sources chosen to represent the spread of activation in the heart.

In neurophysiology the volume conductor problem has been of importance in connection with the interpretation of potentials recorded by extracellular electrodes. Lorente de N6 (1947) derived an expression for the potentials outside a long cylindrical axon based on the results of Helmholtz. More recently Plonsey (1965) and Stevens (1966), using Green's theorem, have given expressions which relate extracellular potentials to currents and potentials at the inner and outer surfaces of the cell membrane. One purpose of this paper is to point out that an alternative expression directly involving the transmembrane potential can be derived from Green's theorem. In addition, the two expressions are generalized to include the case of an inhomogeneous bounded conductor, and an equivalent source distribution is defined and related to the membrane potentials and currents and to the inhomogeneities.

ASSUMPTIONS

The biological volume conductor problem is somewhat unusual in the sense that the sources are contained in the conductor and do not result from induction. Several important conclusions relevant to the analysis of the problem can be drawn from studies of the electrical properties of body tissues. While the emphasis in the following discussion is on electrocardiographic potentials, the results should be applicable to potentials arising from nervous activity except when anisotropy cannot be ignored.

First we note that the current density, \mathbf{J} , in regions beyond the site of an action potential is linearly related to the electric field intensity, \mathbf{E} (Schwan and Kay, 1956). Furthermore, the capacitive component of tissue impedance is negligible at frequencies below several kilo Hz of interest to electrocardiography (Schwan and Kay, 1957), and in addition there is evidence that pulses with rise times of the order of a microsecond suffer only minor distortion through the thorax (Briller et al., 1966). Therefore, to a good approximation a region containing no bioelectric sources can be assigned a uniform bulk conductivity σ so that

$$\mathbf{J} = \sigma \mathbf{E}. \quad (1)$$

A second important point is that electromagnetic wave effects can be neglected (Geselowitz, 1963). Hence, at each instant the electric field can be obtained from the gradient of an electric scalar potential, V .

$$\mathbf{E} = -\nabla V \quad (2)$$

As a consequence of these properties of body tissues, the currents at any instant depend only on the sources at that instant and obey the principle of superposition. Formally we can represent the sources by a distribution of impressed current dens-

ity or equivalently, by current dipole moment per unit volume, \mathbf{J}^i . According to this formalism, equation (1) is modified to include active regions as follows:

$$\mathbf{J} = \sigma \mathbf{E} + \mathbf{J}^i. \quad (3)$$

Later we shall attempt to relate \mathbf{J}^i to electrical activity associated with the plasma membranes of the active cells. For the present, however, the sources are taken into account by the addition of impressed currents to the appropriate conducting regions. Neglect of tissue capacitance implies that as the sources vary, charges on boundaries and interfaces redistribute themselves in a negligibly short time, or that equivalently

$$\nabla \cdot \mathbf{J} = 0 \quad (4)$$

which can be combined with equations (2) and (3) to give

$$\nabla \cdot \sigma \nabla V = \nabla \cdot \mathbf{J}^i. \quad (5)$$

Let the surface S_j separate regions of conductivity σ' and σ'' , and let $d\mathbf{S}_j$ be a differential element of area of this surface. Adopt the convention that $d\mathbf{S}_j$ is directed from the primed region to the double primed one. Since the current must be continuous across each boundary,

$$\sigma' \nabla V' \cdot d\mathbf{S}_j = \sigma'' \nabla V'' \cdot d\mathbf{S}_j. \quad (6)$$

Furthermore, the potential is also continuous at each boundary. Hence,

$$V'(S_j) = V''(S_j). \quad (7)$$

Let dv be an element of volume of a homogeneous region, v , and let ψ and ϕ be two functions which are well behaved in each region. Green's theorem (Smythe, 1960) then states that

$$\begin{aligned} \sum_j \int_{S_j} [\sigma'(\psi' \nabla \phi' - \phi' \nabla \psi') - \sigma''(\psi'' \nabla \phi'' - \phi'' \nabla \psi'')] \cdot d\mathbf{S}_j \\ = \sum_v \int_v [\psi \nabla \cdot \sigma \nabla \phi - \phi \nabla \cdot \sigma \nabla \psi] dv. \end{aligned} \quad (8)$$

Our problem is to determine V from a knowledge of \mathbf{J}^i using equations (5), (6), and (7). Several pertinent expressions can be obtained from equation (8) by appropriately identifying the functions ϕ and ψ .

Relation of Potentials to Impressed Currents. In equation (8) let

$$\psi = 1/r \quad (9)$$

where r is the distance from an arbitrary point to the element of volume or area. Then

$$\begin{aligned} \sum_j \int_{S_j} \left[(\sigma' \nabla \phi' - \sigma'' \nabla \phi'') \frac{1}{r} - (\sigma' \phi' - \sigma'' \phi'') \nabla \left(\frac{1}{r} \right) \right] \cdot d\mathbf{S}_j \\ = \sum \int_v \frac{1}{r} \nabla \cdot \sigma \nabla \phi \, dv + 4\pi \sigma \phi \end{aligned} \quad (10)$$

where σ and ϕ in the last term are evaluated at $r = 0$, i.e., the arbitrary point.

Two implicit expressions for the potential V can be obtained by letting

$$\phi = V \quad (\text{Case I})$$

or

$$\sigma \phi = V. \quad (\text{Case II})$$

In the first case, with the aid of equations (5), (6), and (7),

$$4\pi \sigma V = - \int \frac{1}{r} \nabla \cdot \mathbf{J}^i \, dv - \sum_j \int_{S_j} V(\sigma' - \sigma'') \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_j. \quad (11)$$

The first integral on the right may be transformed as follows:

$$\int \nabla \cdot (\mathbf{J}^i / r) \, dv = \int \mathbf{J}^i / r \cdot d\mathbf{S} = \int \left(\mathbf{J}^i \cdot \nabla \left(\frac{1}{r} \right) + \frac{1}{r} \nabla \cdot \mathbf{J}^i \right) dv.$$

If \mathbf{J}^i vanishes on S , the boundary of the region containing the sources, then

$$\int \frac{1}{r} \nabla \cdot \mathbf{J}^i \, dv = - \int \mathbf{J}^i \cdot \nabla \left(\frac{1}{r} \right) dv. \quad (12)$$

Furthermore, at the surface of the body, S_o , $\sigma'' = 0$, and equation (11) becomes

$$\begin{aligned} 4\pi \sigma V = \int \mathbf{J}^i \cdot \nabla \left(\frac{1}{r} \right) dv - \sum_j \int_{S_j} V(\sigma' - \sigma'') \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_j \\ - \int_{S_o} \sigma V \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_o \end{aligned} \quad (13)$$

where the summation is now over internal surfaces of discontinuity.

In the second case, where $\sigma \phi = V$, the result is

$$4\pi V = - \int \frac{1}{\sigma r} \nabla \cdot \mathbf{J}^i \, dv - \sum_j (E_n' - E_n'') \frac{1}{r} \cdot d\mathbf{S}_j \quad (14)$$

where E_n is the normal component of the electric field, i.e., the component in the direction of $d\mathbf{S}_j$. Define

$$E_j \equiv \frac{1}{2}(E_n' + E_n'') = \frac{1}{2}E_n'(1 + \sigma'/\sigma''). \quad (15)$$

Then

$$E_n' - E_n'' = E_n'(1 - \sigma'/\sigma'') = 2E_j \frac{\sigma'' - \sigma'}{\sigma'' + \sigma'} \quad (16)$$

and, with the use of equation (12), equation (14) becomes

$$4\pi V = \int \frac{1}{\sigma} \mathbf{J}^i \cdot \nabla \left(\frac{1}{r} \right) dv + \sum_j \int_{s_j} \frac{2E_j}{r} \frac{\sigma' - \sigma''}{\sigma' + \sigma''} d\mathbf{S}_j + \int_{s_o} \frac{2E_j}{r} d\mathbf{S}_o \quad (17)$$

where again the term involving the external boundary is given separately.

Relation to Equivalent Sources. When measurements can be made in regions containing sources, then in theory the source term can be evaluated using equation (5). Measurements would yield information about the divergence of \mathbf{J}^i which has the dimensions of current per unit volume. On the other hand when the active region is not accessible, the sources cannot be determined uniquely. In electrocardiography, for example, measurements are usually made at the body surface. Relations between these surface measurements and the source distribution on one hand or an equivalent generator on the other can be derived from equation (8) by letting $\nabla^2\psi = 0$, where ψ and its first derivative are continuous everywhere in the volume conductor. The result for Case I is

$$\int \mathbf{J}^i \cdot \nabla \psi dv = \sum_j \int_{s_j} V(\sigma' - \sigma'') \nabla \psi \cdot d\mathbf{S}_j + \int_{s_o} \sigma V \nabla \psi \cdot d\mathbf{S}_o. \quad (18)$$

Let \mathbf{P} be a fictitious volume distribution of sources in a homogeneous conductor, σ_o , chosen so that V on S_o is unchanged. Then

$$\int_{s_o} \sigma_o V \nabla \psi \cdot d\mathbf{S}_o = \int \mathbf{P} \cdot \nabla \psi dv. \quad (19)$$

Consider that the conductivity at the body surface is constant and let its value be σ_o . From equations (18) and (19)

$$\sigma_o \int_{s_o} V \nabla \psi d\mathbf{S}_o = \int \mathbf{P} \cdot \nabla \psi dv = \int \mathbf{J}^i \cdot \nabla \psi dv - \sum_j \int_{s_j} (\sigma' - \sigma'') V \nabla \psi \cdot d\mathbf{S}_j. \quad (20)$$

Equation (20) is valid for each choice of ψ satisfying the conditions specified above. Note that evaluation of the integral on the left requires knowledge of the potential distribution on the surface only. The fictitious, or equivalent, source

distribution, \mathbf{P} is not uniquely determined. Indeed there are an infinite number of choices of \mathbf{P} which will satisfy equation (19). The multipole expansion (Wilson et al., 1946; Geselowitz, 1960) provides a canonical description of \mathbf{P} in terms of singularities at a single point.

The various terms of the multipole expansion can be obtained by letting

$$\psi_{nm} = (2 - \delta_m^0) \frac{(n - m)!}{(n + m)!} r^n P_n^m(\cos \theta) e^{im\phi} \quad (21)$$

where (r, θ, ϕ) are the coordinates of a point in space relative to the origin at the location of the multipoles, P_n^m is an associated Legendre polynomial, and δ_m^0 is the Kronecker delta which is unity for $m = 0$ and zero for other values of m . Both n and m are nonnegative integers, and m is less than or equal to n . Note that $\nabla^2 \psi_{nm} = 0$.

In particular, the multipole components a_{nm} and b_{nm} are given by (Brody, Bradshaw, and Evans, 1961).

$$a_{nm} + ib_{nm} = \int \mathbf{P} \cdot \nabla \psi_{nm} dv. \quad (22)$$

Therefore

$$\begin{aligned} a_{nm} + ib_{nm} &= \int \sigma_o V \nabla \psi_{nm} \cdot d\mathbf{S}_o \\ &= \int \mathbf{J}^i \cdot \nabla \psi_{nm} dv - \sum_j \int_{S_j} (\sigma' - \sigma'') V \nabla \psi_{nm} \cdot d\mathbf{S}_j. \end{aligned} \quad (23)$$

Thus the multipole components can be evaluated from a knowledge of the surface potential distribution and can be related to the actual source distribution, if known. The monopole term a_{00} vanishes. When n is 1, we have the dipole term for which

$$\begin{aligned} \psi_{10} &= r \cos \theta = z \\ \psi_{11} &= r \sin \theta e^{im\phi} = x + iy. \end{aligned}$$

If the dipole moment, \mathbf{p} , is defined as

$$\mathbf{p} \equiv ia_{11} + jb_{11} + ka_{10}, \quad (24)$$

then

$$\mathbf{p} = \int \sigma_o V d\mathbf{S}_o = \int \mathbf{J}^i dv - \sum_j \int_{S_j} (\sigma' - \sigma'') V d\mathbf{S}_j = \int \mathbf{P} dv. \quad (25)$$

The five components of the quadrupole are obtained by letting $n = 2$ and can be

evaluated in a similar fashion. Note that it is impossible from surface measurements to distinguish among source distributions whose multipole expansions are identical.

Analogous results can be obtained for Case II. Corresponding to equation (23) we have

$$\begin{aligned}
 -\int_{S_0} 2E_j \psi dS_0 &= \int \frac{1}{\sigma} \mathbf{J}^i \cdot \nabla \psi dv + \sum_j \int_{S_j} 2E_j \psi \frac{\sigma' - \sigma''}{\sigma' + \sigma''} dS_j \\
 &= \frac{1}{\sigma_0} \int \mathbf{P} \cdot \nabla \psi dv.
 \end{aligned} \tag{26}$$

The difficulty here is that the integral on the left requires a knowledge of the normal component of the electric field just outside the surface of the volume conductor. This measurement would be extremely difficult to make.

Relation to Membrane Activity. Active regions such as the myocardium have been represented above by a distribution of impressed current sources, \mathbf{J}^i , in a conductor. It is of interest to relate \mathbf{J}^i to electrical activity associated with cell membranes. We will assume that the interior of each cell is a passive conductor of conductivity σ_i , while the extracellular region (including neighboring glial cells in the case of a neuron) is a passive conductor of conductivity σ_e . The membranes are sites of complex electrical activity; they will be excluded when applying Green's theorem.

Again Cases I and II lead to separate formulations. In either case all regions of integration are now passive and the term involving \mathbf{J}^i disappears. Conversely, new terms appear which involve integrations over the internal surface, S_{mi} , and external surface, S_{me} , of each plasma membrane. The net result is thus to replace the volume integral involving \mathbf{J}^i with surface integrals over membranes. For Case I,

$$\begin{aligned}
 \int \mathbf{J}^i \cdot \nabla \left(\frac{1}{r} \right) dv &= \int_{S_{mi}} \sigma_i \left[\frac{1}{r_i} \nabla V_i - V_i \nabla \left(\frac{1}{r_i} \right) \right] \cdot dS_{mi} \\
 &\quad - \int_{S_{me}} \sigma_e \left[\frac{1}{r_e} \nabla V_e - V_e \nabla \left(\frac{1}{r_e} \right) \right] \cdot dS_{me}
 \end{aligned} \tag{27}$$

where r_i and r_e are distances from an arbitrary point to the elements of membrane area dS_{mi} and dS_{me} respectively, and V_i and V_e are the corresponding potentials.

Assume that the transverse membrane current density, taken positive outward, is

$$-J_m = \sigma_i (\nabla V_i)_n = \sigma_e (\nabla V_e)_n. \tag{28}$$

Furthermore, if the membrane thickness is small compared with r_e and r_i and the radius of curvature of the membrane, then to first order approximation, $r_i \approx r_e =$

r , $dS_{mi} \approx dS_{me} = dS_m$, and

$$\int \mathbf{J}^i \cdot \nabla \left(\frac{1}{r} \right) dv = \int_{S_m} (-\sigma_i V_i + \sigma_e V_e) \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_m \quad (29)$$

$$= \int (-\sigma_i V_i + \sigma_e V_e) d\Omega$$

where $d\Omega$ is the solid angle subtended by dS_m . In the resting state, where V_e and V_i are constant over the closed surface formed by the membrane, the integral on the right vanishes for points outside the cell. From equation (13)

$$4\pi\sigma V = \int_{S_m} (-\sigma_i V_i + \sigma_e V_e) \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_m \quad (30)$$

$$- \sum_j \int_{S_j} V(\sigma' - \sigma'') \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_j - \int_{S_0} \sigma V \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_0.$$

Analogous results for Case II are

$$\int \frac{1}{\sigma} \mathbf{J}^i \cdot \nabla \left(\frac{1}{r} \right) dv = \int_{S_m} \left[\left(\frac{1}{\sigma_e} - \frac{1}{\sigma_i} \right) \frac{\mathbf{J}_m}{r} - (V_i - V_e) \nabla \left(\frac{1}{r} \right) \right] \cdot d\mathbf{S}_m \quad (31)$$

$$4\pi V = \int_{S_m} \left[\left(\frac{1}{\sigma_e} - \frac{1}{\sigma_i} \right) \frac{\mathbf{J}_m}{r} - (V_i - V_e) \nabla \left(\frac{1}{r} \right) \right] \cdot d\mathbf{S}_m + \sum_j \int_{S_j} \frac{2E_i}{r} \frac{\sigma' - \sigma''}{\sigma' + \sigma''} dS_j \quad (32)$$

$$+ \int_{S_0} \frac{2E_j}{r} dS_0.$$

Consider the extracellular potential of a single unit. If the potential falls off sufficiently rapidly so that effects of inhomogeneities in surrounding regions can be neglected, then from equations (30) and (32)

$$4\pi V = \int_{S_m} \left[\left(\frac{1}{\sigma_e} - \frac{1}{\sigma_i} \right) \frac{\mathbf{J}_m}{r} - (V_i - V_e) \nabla \left(\frac{1}{r} \right) \right] \cdot d\mathbf{S}_m \quad (33)$$

$$= \int_{S_m} \left(V_e - \frac{\sigma_i}{\sigma_e} V_i \right) \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_m.$$

Now make the additional assumption that the term involving V_e in each integral can be neglected in comparison with the term involving V_i . Then

$$4\pi V \approx \int_{S_m} \left[\left(\frac{1}{\sigma_e} - \frac{1}{\sigma_i} \right) \frac{\mathbf{J}_m}{r} - V_i \nabla \left(\frac{1}{r} \right) \right] \cdot d\mathbf{S}_m = -\frac{\sigma_i}{\sigma_e} \int_{S_m} V_i \nabla \left(\frac{1}{r} \right) \cdot d\mathbf{S}_m. \quad (34)$$

It follows from equating the two integrals, as well as from Green's theorem

applied to the interior of the cell (see Stevens, p. 168), that

$$\int \frac{\mathbf{J}_m}{r} dS_m = -\sigma_i \int V_i \nabla \left(\frac{1}{r} \right) \cdot dS_m. \quad (35)$$

Hence, (see Stevens, 1966 and Plonsey, 1964)

$$4\pi V \approx -\frac{\sigma_i}{\sigma_e} \int_{S_m} V_i \nabla \left(\frac{1}{r} \right) \cdot dS_m = \frac{1}{\sigma_e} \int_{S_m} \frac{J_m}{r} dS_m. \quad (36)$$

With the same assumptions, the potential of an intracellular electrode is

$$4\pi V \approx - \int_{S_m} V_i \nabla \left(\frac{1}{r} \right) \cdot dS_m. \quad (37)$$

DISCUSSION

Equations (13) and (17) provide implicit expressions for the potential inside and on the surface of an inhomogeneous volume conductor containing a source distribution \mathbf{J}^i . In the first case, each surface separating regions of different conductivity is represented by a double layer whose magnitude at each point is proportional to the potential. In the second case, which has a more direct physical interpretation, surfaces of discontinuity bear a surface charge with a charge density proportional to the normal component of the local electric field. The volume integral involving J^i in each case is related to the potential that would exist if the sources were in an unbounded conductor.

Both equations can be solved on a digital computer using iterative techniques. Gelernter and Swihart (1964) originally reported a computer solution based on the second case, while more recently, Barr et al. (1966) have presented a technique utilizing the first case. The relation between these two computer approaches and equations (13) and (17) is discussed by Geselowitz (1966).¹

In electrocardiography the major discontinuities are those at the inner and outer surfaces of the heart, i.e., at the interface with the intracavitary blood mass and with the lungs. The changing impedance of the lungs during respiration probably contributes more to the respiratory variations observed in the electrocardiogram than does heart movement.

The equivalent cardiac generator in general and the manifest heart vector or dipole in particular (Einthoven, Fahr, and de Waart, 1913) have been the focus of much effort. The multipole expansion, of which the dipole is the first term, provides a complete description of the equivalent generator. Equations (22), (23), and (26) relate the multipolar components to information available at the body surface and

¹ GESELOWITZ, D. B. 1966. *IEEE Trans. Bio-Med. Eng.* In press.

to the current sources. From equation (25), in the special case of a homogeneous conductor the dipole term of the multipole expansion is simply the integral of the vector function \mathbf{J}' over the volume, or the resultant of the current source moments. For the particular definition of equivalent sources used here [see equation (22)] this simple result no longer holds when inhomogeneities are present. When defining an equivalent generator in the case of an inhomogeneous conductor, a choice has to be made between a simple relation to the impressed currents and a simple relation to the surface potentials.

Equation (30) is a generalization for an inhomogeneous conductor of the result obtained by Plonsey (1965) and Stevens (1966). This equation involves a separate knowledge of the potentials at the internal and external surfaces of the membrane. On the other hand, equation (32) involves the transmembrane potential directly and should be more useful when attempting to relate potentials in the volume conductor to current-voltage characteristics of the membrane.

It is important to realize that a particular redundancy is present in equations (30) and (32) as a consequence of the assumption of equation (28). V_i and V_e are not independent. Neither is $(V_i - V_e)$ independent of J_m . Since the interior of the cell has been assumed to be source-free, the potential on the boundary determines the potential everywhere in the interior including its normal derivative at the boundary. From equation (28) the normal derivative of the potential is now specified on the boundary of the region external to the cell, which is also source-free. Hence the potential is known everywhere outside the cell to within an arbitrary constant.

It follows that the constraints imposed by the laws of electricity and the geometry lead to an equation relating J_m to $(V_i - V_e)$ when either one is specified over the cell boundary. This relationship will, in other words, characterize the electrical load seen by the membrane. An example of such a result is the cable equation for a cylindrical axon surrounded by a thin conducting sheath. Equations (30) and (32) as they stand relate the potentials in the volume to the membrane potentials and currents at each instant of time. Addition of the current-voltage characteristics of the membrane would then complete the description of bioelectric potentials in a volume conductor at the level of Maxwell's equations and the constituent relations.

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