ELECTRIC AND MAGNETIC FIELD OF THE HEART 9021

DAVID B. GESELOWITZ
The Pennsylvania State University, University Park, Pennsylvania

INTRODUCTION

The potential of the interior of a muscle or nerve cell in the resting state is typically about 0.1 volt negative with respect to the extracellular potential, and the cell is said to be polarized. During activity, the transmembrane potential changes (depolarizes) and ions move across the membrane. Since the extracellular fluid and body tissues in general are electrical conductors, currents will spread through the surrounding media. Currents may penetrate adjacent areas of membranes of the same cell or nearby cells, leading to a spread of activation. If no insulating barrier is present, currents will spread through the entire body and may be detectable as a potential difference at the body surface, or as a magnetic field outside the body. Electrograms have provided important tools for physiology and for medical diagnosis. Examples include the electrocardiogram, electroencephalogram, electromyogram and electrooculogram. By contrast, the study of magnetograms is still in its infancy.

The beating heart (and on occasion the nonbeating heart) gives rise to potential differences of the order of a millivolt and magnetic fields of the order of a microgauss at the surface of the human body. Electric signals recorded from the skin provide much information to the clinician about the state of the heart. The technique is attractive because it is noninvasive, and with advances in technology has become a rather simple procedure, although further advances threaten to reintroduce much more complexity.

The greatest effort to relate surface recordings quantitatively to bioelectric sources has probably been in the context of the electrocardiogram. The theme of the present review is the relationship between external electric and magnetic fields and the cardiac sources that give rise to them. A number of articles, symposiums, and reviews emphasizing the biophysical aspects of electrocardiography have appeared in recent years (1–9), and overlap among them is unavoidable. Since each author tends to present things from his own perspective, the interested reader will do well to consult these works. We will here tend to follow an historical approach.

THE ELECTROCARDIOGRAM

Electrical activity in the heart may be conveniently divided into four phases: 1. depolarization of the atria; 2. repolarization of the atria; 3. depolarization of the ventricles; 4. repolarization of the ventricles. Three of these events are clearly dis-

cernible at the body surface. The depolarization of the atria gives rise to a *P*-wave, which is usually monophasic and of smaller amplitude than the other electrocardiographic waves. Ventricular depolarization appears as a QRS complex, which is often triphasic (hence QRS) but may be monophasic or biphasic or quite irregular, depending on the site of the electrodes and pathology of the heart. Repolarization of the ventricles gives rise to a *T*-wave, which is generally smooth and monophasic. The repolarization of the atria is seldom seen at the body surface since it is of much smaller amplitude and usually occurs during the inscription of QRS. The configuration of the magnetocardiographic waveform is much the same; no special nomenclature has been developed.

The electrocardiogram provides immediate evidence of the rhythm of the heart, including the basic heart rate and the independent rates of the atria and ventricles. Indeed, one of its greatest values to the clinician is in determining the nature of the heart rhythm. By observing intervals between the *P*-wave and the *R*-wave, between successive *P*-waves and successive *R*-waves, etc, electrocardiographers have deduced a number of facts about the sequence of excitation in the atria, ventricles, and atrioventricular (AV) node. More recently, investigators have been studying this behavior quite intensively in the region of the AV node and bundle of His. These microelectrode studies, especially when an array of electrodes are used simultaneously, have confirmed earlier deductions and are providing new insight into the basic mechanisms. Such studies, however, will not be included in this paper.

The electrocardiographer also gleans information from the configuration of the waveform as it appears at various recording sites. The pattern of the potentials recorded on the body surface is related to the spread of excitation and recovery in the myocardium and may provide information about diffuse or localized damage to the heart muscle, ischemia, enlargement, electrolyte abnormalities, abnormalities in conduction pathways in the heart, and changes in electrical properties of surrounding tissues.

Much of electrocardiographic diagnosis is empirical. Particular waveforms have been associated with particular pathologies on the basis of other clinical evidence and postmortem studies. In most cases a reasonable qualitative understanding exists of the observed correlation between waveform and pathology.

More recently, sophisticated techniques for processing the signals have been employed, especially for the electroencephalogram and electrocardiogram. Often moderate-scale digital computers are involved. For example, considerable progress is being made in the development of computer programs for classification of the electrocardiogram (10). Earlier programs mimicked a cardiologist. Later programs attempt to separate normals and various categories of abnormals based on the application of statistics to a large data base of records, each of which can be assigned with reasonable certainty to a particular category. Such studies, which emphasize the signal as a time function or use statistical techniques without regard to the biophysical basis of the signal, will be excluded from this review.

Our basic interest here is the relationship of external electromagnetic fields to bioelectric sources in a volume conductor. The problem may be divided as follows:

1. Characterization of the electrical properties of the volume conductor.
2. Description of the electrical sources as a function of space and time.

3. Relationship of the electrical sources to activity at the cellular and membrane levels.
4. Development of models for the spread of activation and recovery.
5. Calculation of external fields for a given source (forward problem).
6. Determination of sources from external fields (inverse problem).

Volume Conductor Problem

The measurement of bioelectric potentials has provided a tremendous challenge for more than two centuries, and attempts to obtain accurate records have had a profound effect on electric technology. Furthermore, problems posed by bioelectricity have also had a profound effect on the basic physics of electricity, transport, etc, and have led to the development of important principles and mathematical formulations. The reader is referred to several recent papers that have dealt with this fascinating history of the science and technology of electricity as it relates to biology (11, 12).

While we might begin with the experiments of Galvani and Volta, a more appropriate starting place is with the work of Helmholtz. Helmholtz realized that to understand and correctly interpret electrical measurements in physiological preparations one had to understand the nature of currents in a volume conductor. Accordingly, he addressed himself to this problem and in a monumental paper presented the basic physics of the volume conductor problem (13). This paper contains three important concepts which we will discuss.

First, Helmholtz pointed out that the principle of superposition could probably be applied to the bioelectric problem. Superposition is a characteristic of linear systems. The principle states that the electric field arising from several sources is the sum of the fields that would be present for each source acting separately.

Next we note the reciprocity theorem. Consider a current source I at point 1 and a sink of equal magnitude as point 2 in a volume conductor. This source will give rise to fields everywhere, and in particular to a potential difference V_{34} between a pair of points 3 and 4 on the surface of the conductor. Now let a current I' be injected at point 4 and removed at point 3. This current will lead to a potential difference V'_{12}. The reciprocity theorem states

$$-V_{34}I' = V'_{12}I \qquad 1.$$

If the points 1 and 2 are close together, then

$$-V'_{12} = \mathbf{E}' \cdot \mathbf{d} \qquad 2.$$

where $\mathbf{E}'$ is the (reciprocal) field between points 1 and 2 and $\mathbf{d}$ is the vector from point 2 to point 1. Therefore Equation 1 becomes

$$V_{34}I' = \mathbf{E}' \cdot \mathbf{p} \qquad 3.$$

where $\mathbf{p} = I\mathbf{d}$ is the dipole moment of the source. With the use of the superposition principle

$$V_{34} = \sum \frac{1}{I'} \mathbf{E}'_j \cdot \mathbf{p}_j + \int \frac{1}{I'} \mathbf{E}' \cdot \mathbf{J}^i \, dv + \int \frac{1}{I'} \mathbf{E}' \cdot \mu \, d\mathbf{S} \qquad 4.$$

The summation is for discrete sources and the integrals are for distributed sources, where $\mathbf{J}^i$ is the dipole moment per unit volume and μ is the dipole moment per unit area.

If we define

$$\mathbf{E}_L = \frac{1}{I'}\mathbf{E}' \tag{5.}$$

as the "lead field" associated with a particular pair of terminals, then the voltage appearing across these terminals is

$$V = \int \mathbf{E}_L \cdot \mathbf{J}^i \, dv + \int \mathbf{E}_L \cdot \mu \, d\mathbf{S} \tag{6.}$$

The lead field concept, which is a direct consequence of reciprocity and superposition, was introduced by McFee and Johnston (14, 15). The lead field is the electric field appearing throughout the volume conductor when unit current is injected at the "lead," i.e. the terminals where the particular ECG is recorded. Dimensions of the lead field are ohms per length.

In an unbounded conductor of conductivity σ the potential of a dipole is given by

$$V = \frac{1}{4\pi\sigma}\mathbf{p} \cdot \nabla\left(\frac{1}{r}\right) \tag{7.}$$

where r is the distance from the point where V is observed to the dipole. Similarly, for a double layer

$$V = \frac{1}{4\pi\sigma}\int \mu \nabla\left(\frac{1}{r}\right) \cdot d\mathbf{S} = \frac{1}{4\pi\sigma}\int \mu \, d\Omega \tag{8.}$$

where $d\Omega$ is the solid angle subtended by dS at the point where V is observed. For a uniform double layer

$$V = \frac{\mu\Omega}{4\pi\sigma} \tag{9.}$$

where Ω is the net solid angle subtended by the surface. If the surface is closed, $V = 0$ outside and $-\mu/\sigma$ inside the closed surface. In the general case the potential changes by μ/σ across the double layer, while there is no discontinuity in the normal component of the electric field (16). The fact that a double layer introduces a discontinuity in potential of $e = \mu/\sigma$ implies that if we have a surface on which a potential e appears (where e in general varies over the surface), then if a double layer $\mu = -\sigma e$ is placed on this surface the potential just outside the surface will be zero. This observation forms the basis of the final theorem of Helmholtz to be discussed.

Consider an inhomogeneous linear volume conductor containing electric sources. Take an arbitrary surface that encloses all the sources. Now remove all the conducting material outside this surface and measure the potential (open circuit voltage) on the surface. Place a double layer of moment equal to the open circuit voltage times the conductivity on the arbitrary surface, and set all the sources to zero. If the conducting material is now replaced, the fields outside the surface will be unchanged. Note that

the moment of the double layer is independent of the nature of the external conducting medium (as long as it is linear). The Helmholtz equivalent double layer is thus an equivalent generator which produces the same external electric field as the actual sources, regardless of the "load." The more familiar Thevenin's theorem in circuit theory is a special case of this theorem of Helmholtz. It follows from the theorem that it is impossible from measurements *outside* the source region to determine the sources uniquely.

Heart Vector

Voltages can be recorded from an indefinite number of electrode pairs on the body surface. A meaningful basis for handling these data is needed. The necessary concept was provided early in this century by Einthoven (17), who proposed that, to an approximation, the potentials on the body surface can be considered to arise from a fixed location dipole in the body. This construct has had a profound influence on all subsequent electrocardiography.

At the time of Einthoven's early work, just prior to the First World War, human electrocardiograms were recorded using electrodes attached to the left arm, right arm, and left leg. Three voltages can be recorded from these electrodes. As mentioned above, the term *lead* is used to indicate an electrode configuration, possibly including resistors, in which a potential difference is developed. The term *lead* is also used to indicate potential difference, i.e. electrogram recorded with this configuration.

A lead V, therefore, can be defined as

$$V = \sum a_i V_i \qquad 10.$$

where V_i is the potential appearing at the ith electrode with respect to an arbitrary reference. Since the potential difference V is independent of the reference,

$$\sum a_i = 0 \qquad 11.$$

The three voltages associated with the limb electrodes are designated Leads I, II, and III. Lead I is the potential difference from the left arm to the right arm, Lead II the potential difference from the left leg to the right arm, and Lead III the potential difference from the left leg to the left arm. Einthoven pointed out that these three voltages were not independent, but that Lead I plus Lead III equals Lead II. "Einthoven's law" is a consequence of Kirchoff's law for electric circuits, which states that the sum of the voltages around a loop must be zero.

Einthoven proposed that, to a good approximation, the voltages appearing in these three leads could be considered to be proportional to the voltages that would be recorded at the three vertices of an equilateral triangle (Einthoven triangle) in an unbounded conducting planar medium at whose center a dipole was placed. The variation of the voltages with time was accounted for by the rotation of the dipole and change of its moment.

The voltages at the vertices of this triangle depend only on the components of the dipole in the plane of the triangle and are independent of the dipole components perpendicular to the plane. This plane is designated the *frontal* plane. From this

model one can calculate the two components of the dipole in the frontal plane from the information contained in the three limb leads.

The equations relating the voltages in three leads can be cast in the following form, where the heart dipole moment is designated by **H**:

$$\begin{aligned} V_{\mathrm{I}} &= \mathbf{H} \cdot \mathbf{i} &&= \mathbf{H} \cdot \mathbf{c}_{\mathrm{I}} \\ V_{\mathrm{II}} &= \mathbf{H} \cdot (\mathbf{i} \cos 60^\circ + \mathbf{j} \sin 60^\circ) &&= \mathbf{H} \cdot \mathbf{c}_{\mathrm{II}} \\ V_{\mathrm{III}} &= \mathbf{H} \cdot (-\mathbf{i} \cos 60^\circ + \mathbf{j} \sin 60^\circ) &&= \mathbf{H} \cdot \mathbf{c}_{\mathrm{III}} \end{aligned} \qquad 12.$$

where **i** and **j** are unit vectors in the x and y directions, the x axis is directed horizontally from right to left, and the y axis is vertical and pointing down. The voltage in a lead is thus the dot product of two vectors, one characterizing the heart and the other the lead (18). Einthoven called **H** the *manifest heart vector*. Note that the three "lead vectors" $\mathbf{c}_{\mathrm{I}}$, $\mathbf{c}_{\mathrm{II}}$, $\mathbf{c}_{\mathrm{III}}$ form an equilateral triangle.

Einthoven stated that the manifest vector was the sum of the vector contributions of the individual regions of the heart contributing to the potential at each instant. He was, therefore, picturing the heart as a distribution of vector sources, and argued that as an approximation, the potentials recorded at the limbs reflected only the vector sum of all individual vector sources.

Einthoven was motivated at least in part by an attempt to explain variations of the ECG with respiration. If the ECG was the result of a manifest heart vector, then this vector (more particularly the mean vector) should rotate in a predictable way during respiration when the heart's position and orientation in the chest changed. Einthoven was able to find confirmation for his vector concept in such studies.

Doublet Hypothesis

An early picture of the nature of the electromotive forces in the heart was provided by the *negativity hypothesis*. The negativity hypothesis appeared in several forms, but for our purposes we can state that it infers that excited regions of the heart are electrically negative with respect to all other unexcited regions.

Craib studied potentials recorded at the surface of small muscle strips immersed in a conducting medium, and found a conflict with the negativity hypothesis (19, 20). He could explain his results by assuming that the electromotive force in the muscle strip was a doublet, i.e. a source sink pair separated by a small distance, which moved along the muscle strip in the direction of excitation. For excitation (depolarization), the positive pole preceded the negative pole while for recovery (repolarization), the negative pole preceded the positive one. Furthermore, especially for cardiac muscle, the separation between poles of the doublet was much greater for recovery than for excitation. The doublets for excitation and recovery were possibly separated by a neutral region.

Craib plotted voltages in the medium surrounding a strip of injured muscle and showed that the field was very similar to that of a dipole located at the site of injury. He also pointed out the validity and significance of superposition as applied to bioelectric sources in a volume conductor. His theory indicates that each region

of the heart acts as a dipole source and that electrograms reflect the superimposed effect of all these dipole sources in a volume conductor.

Shortly after Craib's papers appeared, Wilson and his co-workers published a paper that developed many of the mathematical consequences of the picture to be drawn from Craib's data (21). We will discuss this phase of Wilson's work in two parts. One deals with fields in a volume conductor arising from dipoles and double layers. The other deals with the relationship of the double layer to the membrane theory of electrical activity of cells.

Wilson calculated the field of a doublet moving along a line and showed that the potential at a point near the line was biphasic, with the separation between maximum and minimum equal to the product of the velocity of the excitation wave and the distance between source and sink. The curve resembled experimental curves, and using measurements from the surface of the auricle, Wilson estimated the separation between poles to be 3.6 mm. Later investigations using electrodes inserted in the ventricle have indicated that the width of the electromotive surface is about 1 mm (22). This point will be discussed further below.

The intact heart acts electrically like a syncytium and excitation tends to spread rather uniformly through the muscle mass. Since the separation between poles of the doublet is small, it follows that at each instant of time during excitation the cardiac sources lie in a thin sheet. Therefore, the cardiac sources during QRS can be represented by distributions of dipole moment, or double layers, over appropriate surfaces. These surfaces at each instant are drawn through the regions of the myocardium that are undergoing depolarization.

For a simple model, we can assume that at an instant of time the electromotive surface is uniform and takes on a cup-shaped appearance with a circular opening. This opening can be considered to be the superposition of two equal and opposite double layers. Thus the cup-shaped electromotive surface is equivalent to a closed double layer, which contributes no potential, plus an oppositely directed electromotive surface on the disk-shaped opening. From the superposition principle, the potential contributed by the original double layer is identical to the potential of the oppositely directed double layer on the disk closing the surface. Exactly the same result is obtained from Equation 8, since the net solid angle subtended by the cup is identical to the solid angle subtended by the opening.

Wilson showed that at a distance the potential of the disk behaves very much like that of a single dipole located at its center. He suggested that a dead region of myocardium would not be excited and hence would appear to be a hole in the double layer. Once more the superposition principle states that the contribution of this hole to the electric field is that of a double layer of opposite polarity. These concepts provide a qualitative explanation of many features of the surface electrocardiogram.

According to the membrane hypothesis, the interior of a cell at rest is negative in potential with respect to the exterior, and the cell is polarized. This potential difference appears across the cell membrane. When the cell becomes active the transmembrane potential changes, i.e. depolarizes. A cell can be represented electrically by a double layer $\mu = \sigma e$ at the cell membrane, assuming that the internal and external media of the cell are fluids of conductivity σ. A cell that is either uniformly polarized

or uniformly depolarized will not give rise to external fields. For an active cell, μ will be nonuniform, and the cell will act as an electric source.

Wilson applied this idea to a cylindrical cell. Suppose that a portion of the cell is still polarized, but that part of the cell has become depolarized. For simplicity, let the transition between the two regions of the cell be abrupt. The cell can then be portrayed as a uniform double layer spread over the polarized membrane. Since this surface is an open one, there will be an external field.

From the argument used above, the potential contributed by the cell is proportional to the solid angle subtended by a circular disk at the discontinuity between the polarized and depolarized regions of the cylindrical cell. For remote points the cell will then act as a dipole source of moment $\sigma e \pi R^2$, where e is the difference between the transmembrane potential in the depolarized and resting states and R is the radius of the cell. The current dipole moment per unit area contributed by the cell is then $\mu = \sigma e$. The dipole moment vector points in the direction of the spread of excitation. In general, excitation will spread so that a large number of cells are depolarizing simultaneously. The dipole moment to be assigned to the excitation surface is therefore

$$\mu = \sigma e \alpha \tag{13.}$$

where α represents the fraction of the total surface occupied by the cross sectional area of cells, as suggested by Plonsey (7), who also derived a modification of the equation to account for the difference between the internal and external conductivity of the cell.

Wilson pointed out that if the transition from polarized membrane to depolarized membrane were not abrupt, the picture would have to be modified by introducing a distribution of dipole moment along the axis of the cylinder, proportional at each point to dV_m/dx, where V_m is the membrane potential. The excitation wavefront will then have a thickness corresponding to the range where dV_m/dx has a significant value. If we assume that the excitation is moving with a velocity v, then

$$V_m(x, t) = V_m(x - vt) \tag{14.}$$

and

$$\frac{dV_m}{dt} = -v\frac{dV_m}{dx} \tag{15.}$$

A typical transmembrane action potential of a cardiac cell exhibits a depolarization phase during which V_m changes from about -90 mV to $+30$ mV in about a millisecond. The velocity v is of the order of a meter per second. Therefore dV_m/dx will occupy a region of about 1 mm, in agreement with experimental results. The value of e is then approximately 120 mV.

Following depolarization, the action potential exhibits a plateau phase during which V_m changes very slowly. Since a typical cell is about 100 μ long, and the duration of the plateau is typically 200 msec, during the plateau the membrane potential is essentially constant over the entire cell and it contributes no dipole moment. This phase corresponds to the neutral region suggested by Craib. In the normal heart there

is a period of time when most cells in the ventricles are in this state. The external fields are then very small, accounting for the flat S–T segment in the electrocardiogram.

Finally, we note that Wilson pictured an injured region of a cell as being permanently depolarized. An injured cell then acts as a dipole that is permanently present during the cardiac cycle. Injury currents are postulated to give rise to changes in the S–T segment, but the genesis of such changes requires further study.

Sequence of Excitation

Many important contributions to electrocardiography in the years following Einthoven's early work came from the laboratory of Lewis (23). Lewis studied the excitation process using electrodes at epicardial sites, and presented the earliest scheme of ventricular excitation. He concluded that the electrocardiographic deflections in the various leads at each instant during QRS depend primarily on the direction of the excitation wave at that instant.

Later investigators have used needle electrodes, which may be plunged into the wall of the heart (24–26). Each needle incorporates a linear array of closely spaced electrodes, each insulated from the others and typically separated by $\frac{1}{2}$ to 1 mm. Several plunge electrodes may be inserted simultaneously. Usually "bipolar" recordings are made from adjacent electrode pairs. Appearance of a voltage deflection is interpreted as indicating the passage of the excitation front between the electrodes.

Most data have been obtained on animals with a normal sequence of excitation, although some studies in abnormal situations have been reported (27). More recently, data have been obtained on resuscitated perfused human hearts in Durrer's laboratory (28). A picture has emerged of initial activity in the septum followed by activity in the wall, predominantly in an inside-out direction. Excitation studies have been reviewed by Scher (29). These studies are providing important data, especially for normal spread of excitation, but more data are needed.

In addition to knowing the sequence of excitation, it is important to know the amplitude of the double layer. Such information can be obtained from the potentials recorded at the myocardial electrodes. Consider electromotive forces distributed in a lamina bounded by the planes $x = 0$ and $x = d$. Let the distribution of dipole moment be $J^i(x)$. Then the potential difference V, between electrodes at $x = -a$ and $x = b$, is

$$V = \frac{1}{\sigma} \int_0^b J^i(x)\, dx \qquad 16.$$

If the electrodes are fixed and the lamina moves, V will be zero as long as no portion of the lamina lies between the electrodes. If the separation between electrodes is greater than d, V should rise to a flat peak and then return to zero. If the separation is smaller than d, the peak of V will decrease in amplitude.

By varying the separation between electrodes, one can determine the thickness of the lamina. As noted above, Vander Ark and Reynolds found the thickness to be somewhat less than a millimeter (22). The peak voltage would be an indication of the strength of the double layer. Vander Ark and Reynolds found peak values of about 90 mV, which would appear to be consistent with Equation 13. Since the peak values

observed in myocardial electrode studies are much the same in different parts of the heart, the strength of the double layer is apparently uniform. Furthermore, if the heart muscle is stimulated so that the excitation wavefront forms a closed surface, no potentials are recorded outside this surface (22). This observation is consistent with a uniform double layer. Selvester's data, however, disagree (30).

T Wave

During QRS, the electromotive forces are confined at each instant to thin sheets, at least for normal hearts; during T they are distributed throughout the ventricle. As we have noted above, the dipole moment contributed by a circular patch of membrane of a cylindrical cell is proportional to dV_m/dx, which in turn is proportional to $(dV_m/dt)/v$, where v is the velocity of propagation. The contribution of each patch of membrane to the potential δV in a lead is proportional to the dipole moment. Hence

$$\int \delta V \, dt = k \int \frac{1}{v} \frac{dV_m}{dt} dt \qquad 17.$$

If v is constant, the integral on the right is zero since V_m is the same at the beginning and end of the cycle. Therefore, if repolarization proceeds uniformly throughout the entire ventricle, the total area under QRS and T should be zero, or the area under QRS should be the negative of the area under T.

Wilson designated this area, or time integral, the *ventricular gradient* (31, 32), and Burger has provided a mathematical analysis (33). Nonuniformity in the recovery process will result in a nonzero ventricular gradient. There are practical difficulties in measuring the ventricular gradient because of uncertainty in determining the baseline level.

Wilson distinguished between changes in the T wave dependent on QRS, and abnormalities of T that occur independently. The former were called *secondary* changes and the latter *primary* changes. More recently, Harumi proposed a technique for constructing primary and secondary T waves based on the form of the downstroke of the action potential and the sequence of activation (34). The secondary T wave is constructed to make the ventricular gradient zero, and the primary wave is obtained by subtracting the secondary wave from the recorded T wave. Action potentials of the longest duration are assigned to the endocardium, those of shortest duration to the middle layers, and those of intermediate duration to the epicardium. Burgess has shown that this model accounts for the surface electrocardiogram during T (35).

Since the T wave is very sensitive to small changes in repolarization in different regions of the myocardium, it is quite labile. It was observed a number of years ago that it often became inverted after the patient drank ice water.

A small deflection that sometimes follows the T wave is designated the U wave. Its origin is uncertain, but it sometimes is associated with ionic disturbances, e.g. hypokalemia. Lepeschkin has provided a recent review (36).

Tissue Conductivity

The solution to the volume conductor problem depends on the passive electrical properties of body tissues. Many experimental studies have been made, but more data

are needed. Geddes & Baker (37) have summarized these studies. We will only touch on some key points here.

Since tissue resistivity is a function of frequency, we will consider briefly the frequency content of the electrocardiogram. Scher & Young (38) have shown that frequency components in the range above 100 Hz are very small compared with the fundamental. Berson & Pipberger (39) have shown that the gross shape of the electrocardiographic waveform is not changed significantly when the upper frequency response is extended beyond 60 Hz, although to reduce amplitude errors below 100 μV, a cutoff frequency greater than 100 Hz is required. On the other hand, small notches and slurs of clinical significance are readily discernible in the waveform when recorded with wideband equipment. Langner & Geselowitz (40) have shown that a bandwidth of 1000 Hz is sufficient for reproducing these high-frequency components without loss of detail.

Wilson (21) cites a private communication from K. S. Cole in which Cole states that skin effect would not enter much below a frequency of 10^8 Hz, while changes in tissue conductivity with frequency would begin in the vicinity of 1000 Hz. Hence, neither of these effects is important for the electrocardiogram. The fact that skin effect or induction can be neglected means that there is no coupling between the electric and magnetic fields, and that the velocity of propagation is effectively infinite.

Schwan & Kay (41, 42) have shown that phase shifts of tissue are very small below 1000 Hz, which is consistent with Cole's observation. Hence, for electrocardiography, all tissues are resistive, and we are dealing with a quasi-static problem in which the potentials are instantaneously related to the sources and do not depend on their previous history. Schwan's measurements also confirmed that the tissues were linear, in that for current densities below the excitation level, current density was proportional to electric field intensity.

Resistivity measurements by Burger (43, 44) and by Rush (45) have shown that heart and skeletal muscle exhibit significant anisotropy. The volume conductor, therefore, is linear, resistive, inhomogeneous, and anisotropic. It may be considered to be composed of a number of regions in each of which the conductivity is uniform. The major inhomogeneities are evidently the high-conductivity intracavitary blood and low-conductivity lungs.

The basic equation relating the current density $\mathbf{J}$, the electric potential V, and the magnetic field intensity H, are therefore

$$\mathbf{J} = -\sigma \nabla V + \mathbf{J}^i = \nabla \times H \qquad 18.$$

where the distribution of electromotive forces $\mathbf{J}^i$ may be viewed equivalently as an impressed current density or as a current dipole moment per unit volume. If anisotropy is neglected, the conductivity σ is a scalar that is constant in each homogeneous region. Otherwise σ must be treated as a tensor.

Equivalent Generator

With the use of the appropriate boundary conditions, Equation 18 can be solved, in principle, to give V and H inside and outside the volume conductor, i.e. the torso. Of particular interest is the value of V on the surface of the volume conductor (surface

electrocardiogram) and the value of H in the region just outside the volume conductor (magnetocardiogram). This calculation is called the *forward problem.* Conversely, the calculation of sources from the surface potentials and/or the external magnetic field is called the *inverse problem.*

The inverse problem is really the problem of interest. Unfortunately, it has no unique solution. On the other hand, only a small set of the infinite number of solutions will be physiologically meaningful. The hope is that the set of "physiological" solutions for each subject is narrow enough to characterize unambiguously the actual sources in sufficient detail. Since it is most unlikely that it will be possible to calculate the actual electromotive forces from information available at the body surface, every solution to the inverse problem can be considered to be an "equivalent generator."

An *equivalent cardiac generator* may be defined as a set of time-varying sources in a torso-shaped volume conductor that gives rise to a surface potential identical to the surface electrocardiogram. The conductivity of the volume must be specified; it may be inhomogeneous. The sources will depend on the conductivity specified. One might choose a homogeneous conductor for mathematical convenience. If an inhomogeneous conductor is selected, the equivalent sources will be different from those in a homogeneous conductor. Under certain circumstances, for example, a complex source in an inhomogeneous conductor may "look" from the surface very much like a dipole in an isomorphic homogeneous conductor.

The manifest heart vector is an approximate equivalent generator. A Helmholtz double layer is an exact one. An example is a double layer on the body surface whose moment is proportional to the surface electrocardiogram. A much more interesting example is a double layer on the epicardial surface of the heart (46). There seem to be just three categories of equivalent sources: multipoles, multiple dipoles, and distributions on closed surfaces.

The equivalent generator can be considered to be a physically meaningful representation of the surface potential information. It must be defined so that the sources are uniquely determined from the surface data. In addition, the equivalent sources may be determined from a knowledge of the actual sources. The actual sources, however, cannot in all likelihood be determined from the equivalent sources. Much current research is devoted to attempts to generate sources that resemble very closely the actual sources by imposing constraints on possible solutions based on features of the anatomy and physiology. This topic will be discussed below in greater detail.

Vector Lead Systems

The decade of the 30s saw further advances in basic aspects of electrocardiography, notably from Wilson's laboratory. Also during this time, the precordial leads were introduced (47), together with so-called "unipolar" leads, which used as a reference the junction of three equal resistors connected to the limb lead electrodes (48, 49). The dipole concept continued to dominate thinking in the field. It was evident that Einthoven's theory had two serious shortcomings. For one, it gave only two components of the dipole, whereas the heart vector could clearly be oriented anywhere in three-dimensional space. For another, it provided only a crude theory for relating the surface potentials to the heart vector. A number of schemes were proposed to

correct these shortcomings. These schemes may be designated *orthogonal lead systems* and are designed to provide three leads, each proportional, ideally, to one of the orthogonal components of the vector.

There is still no universal agreement over the designation of the electrocardiographic axes. One commonly accepted right-handed system defines the x axis as right to left, the y axis as head to foot, and the z axis as front to back. With y directed downwards, the xy plane is the frontal plane, the xz is the transverse plane, and the zy is the sagittal plane.

We will not dwell here on the various earlier lead systems but will jump to the work of Burger in the 1940s. Burger (18) investigated the relationship between a dipole source and body surface potentials by constructing a phantom, or tank model, of the torso, inserting a dipole into the phantom, and measuring potentials at the surface. In this way he was able to develop a relationship between the dipole and the voltage it would contribute to a particular lead. Burger noted that from considerations of superposition, the voltage in any lead arising from a dipole source is equivalent to the dot product of two vectors, the lead vector and the vector describing the dipole. This conclusion is valid even for unhomogeneous conductors. Burger determined the lead vectors for the three limb leads. These three lead vectors form a triangle called the *Burger triangle*. If a fourth point is chosen, such as a point on the back, then there are three equations available to determine the three orthogonal components of the vector. Furthermore, these equations can be solved in analog fashion by connecting appropriate resistor networks to the four electrodes to weight the voltages (50). Burger's lead system is the first modern *corrected* orthogonal lead system, where the word *corrected* has come into use to distinguish this type of vector system from the more primitive intuitive approaches. It is a term that has probably outlived its usefulness.

The lead vector may be plotted in an appropriate three-dimensional space designated *image* space by Burger. Frank, also using a tank model, measured the lead vectors for the entire surface of the torso (51). He then plotted the data by showing the locus of the lead vector in image space. In this way he presented in a three-dimensional picture information relating the voltage in any lead to the heart vector. Frank also proposed a scheme for obtaining the orthogonal components of the vector from voltages recorded at seven electrodes at the body surface (52).

While Frank's approach was much the same as Burger's, there were two important differences. One had to do with the consideration of inhomogeneities. This is an important consideration that enters into all the lead systems we are now discussing. Unfortunately, perhaps, various investigators have made different assumptions concerning inhomogeneities and therefore their lead systems, even ideally, are not necessarily designed to give the same heart vector. Frank chose to work with a homogeneous torso, while Burger included inhomogeneities, notably that of the lungs.

The other difference in Frank's approach is that he sought a lead system that was insensitive to dipole location over a reasonable volume of the heart region. Frank was guided by the hypothesis that the dipole approximation was a good one, that is, that potentials on the body surface could be reproduced quite accurately during the

cardiac cycle by a fixed-location dipole of variable moment. He had provided experimental support for this hypothesis by measuring a large number of electrocardiograms on a single subject. He then used a tank model of this subject's torso and placed an artificial dipole inside. He found he was able to adjust the orientation and magnitude of the dipole, keeping its position fixed, to give surface isopotential contours very similar to those actually recorded on his subject at instants during QRS (53).

Frank postulated that while all individuals exhibited similar dipolar behavior, the position of the dipole might vary. His lead system, then, was designed to give the dipole components independent of the dipole position. If Frank succeeded in his endeavour, his vector lead system has an interesting property in that, from the superposition principle, it cannot distinguish between a single dipole or distribution of dipoles in the region of interest. In all cases it will give the vector sum of these dipoles.

Burger's concept of the lead vector can be generalized for a distributed dipole source $\mathbf{J}^i$. From superposition, the potential in a lead is given by

$$V = \int \mathbf{J}^i \cdot \mathbf{Z}_T \, dv \qquad 19.$$

where $\mathbf{Z}_T$ may be looked upon as the lead vector associated with dipole $\mathbf{J}^i dv$. Schmitt called $\mathbf{Z}_T$ the transfer impedance (54, 55). From Equations 6 and 19 it is evident that the lead field $\mathbf{E}_L$ and transfer impedance $\mathbf{Z}_T$ are equivalent, as pointed out by Brody (56, 57).

The lead field approach of McFee is particularly useful in visualizing the contribution of a distributed source to the potential in a lead, including a coil designed to detect the magnetic field (15, 58). McFee applied this concept to develop a lead system that would give the vector sum of the dipole sources in the heart (59). If we designate this vector sum, or heart vector, by $\mathbf{H}$, then

$$\mathbf{H} = \int \mathbf{J}^i \, dv = \mathbf{i} \int J_x^i \, dv + \mathbf{j} \int J_y^i \, dv + \mathbf{k} \int J_z^i \, dv \qquad 20.$$

If a lead V_x has a lead field $\mathbf{i}E_{Lx}$, which is uniform and parallel to the x axis in the heart region, then

$$V_x = \int \mathbf{i}E_{Lx} \cdot \mathbf{J}^i \, dv = E_{Lx}\mathbf{H}_x \qquad 21.$$

The lead system proposed by Schmitt & Simonson (54) was also designed to give the heart vector. Since Schmitt was guided by the transfer impedance concept, he moved a dipole source in the heart region of a tank model and measured surface potentials, while with the lead field approach a current is injected into surface electrodes through a resistor network and the electric field is measured in the heart region. Schmitt used a homogeneous conductor while McFee's model incorporated inhomogeneities. Although Frank's lead system was based on a single dipole equivalent source, rather than on the integral of the distributed source, in practice it was equivalent, as we have noted. Other investigators have proposed orthogonal lead systems or modifications. Reviews are available (60, 61).

As we have seen, Burger's work prompted a number of investigators to work on the problem of developing schemes for accurately determining the heart vector. In turn, these and other investigators turned their attention to the following questions: How accurate are the proposed lead systems? How do the waveforms of the various lead systems compare on a series of subjects? How sensitive are the lead systems to electrode displacement?

Clinical aspects of the subject have been excluded from this review. We will, however, conclude this section with this observation: Many cardiologists feel that the conventional 12-lead electrocardiogram is superior to the vectorcardiogram as a diagnostic tool. From the standpoint of computer diagnosis, the vectorcardiogram has the advantage that only three signals are used. There is as yet no firm evidence from computer studies that, using statistically derived criteria, one can do better diagnostically with the 12 standard leads than with the vector leads.

Forward Problem

In principle, the potentials on the surface of a volume conductor can be calculated, given the internal sources. Prior to the advent of the digital computer, such calculations were not feasible. Instead, investigators used two-dimensional models (57, 62), tank models, or sought solutions in simpler geometric configurations. Tank models have been mentioned in connection with the development of vector lead systems. A more recent example is the elaborate model constructed by Rush (63).

The first analytic solution is evidently that of Canfield (64) who, in an appendix to Craib's paper, showed that for a centric dipole p, the potential on the surface of a sphere of radius R is given by

$$V = k\frac{3p\cos\theta}{R^2} \qquad 22.$$

The potentials at the vertices of an equilateral triangle in the vertical plane through the center of the sphere bear the same proportional relation to the dipole moment as in Einthoven's original two-dimensional model. For a current dipole, $k = 1/4\pi\sigma$, where σ is the conductivity of the sphere.

Prompted by the electrocardiographic problem, investigators following Canfield have published solutions to a rather large number of configurations including spheres (65, 66), cylinders (67), spheroids (68, 69), and boxes (70). Probably the greatest contribution these studies have made is insight into the effect of inhomogeneities.

Brody (71, 72) pointed out that the intracavitary blood mass tended to enhance the contribution of the normal component of a dipole while diminishing that of the tangential component. This "Brody effect" follows from the method of images. Consider a dipole located near a spherical region of highly conducting material. The potential in the low-conducting region outside the sphere is equal to that of the dipole itself plus an image dipole. Since the image of a point source is of opposite polarity, the image for a dipole normal to the interface will be oriented in the same direction as the original dipole, thus tending to double the field. Conversely, the image for a tangential dipole will be oppositely oriented, thus tending to cancel the field.

In a cylindrical tank model experiment, Okada showed that a centric, highly conducting region tended to make a two-dipole source look more like a single dipole in an equivalent homogeneous cylinder (73). Geselowitz found the same result in a mathematical model with spherical symmetry and showed that the inhomogeneities representing blood and lungs altered the apparent location of an equivalent dipole in a homogeneous sphere (74, 75). The most elaborate mathematical model of this type has been analyzed by Bayley (76). Nelson has also provided a solution (77).

The "Brody effect" by and large has been confirmed in experimental studies where the conductivity of the fluid in the heart has been changed. The most recent report is from the laboratory of Nelson and co-workers (78).

McFee and Rush have studied the effect of anisotropy (79, 80). They showed that the anisotropy of the heart muscle tends to diminish the Brody effect for dipoles more distant from the endocardium, and that a low-resistance anisotropic layer at the surface of the body would tend to increase the apparent distance of an electrode from the sources. Evidently the uniform double-layer nature of the electromotive forces and the inhomogeneities tend to make the surface potentials look much more "dipolar" than one would expect from the fact that sources are distributed through a large region of the heart that is quite close to the chest wall. This topic has been discussed by Plonsey (81).

If anisotropy is neglected, an implicit solution for the potential in Equation 18 can be obtained directly from Green's theorem (82, 83). The result can be stated in two forms:

$$4\pi\sigma V = \int \mathbf{J}^i \cdot \nabla\left(\frac{1}{r}\right) dv - \sum_j \int (\sigma' - \sigma'')V\nabla\left(\frac{1}{r}\right) \cdot d\mathbf{S}_j \qquad 23.$$

$$4\pi V = \int \frac{1}{\sigma}\mathbf{J}^i \cdot \nabla\left(\frac{1}{r}\right) dv + \sum_j \int \frac{2E_j}{r}\frac{\sigma' - \sigma''}{\sigma' + \sigma''} dS_j \qquad 24.$$

where S_j is a surface separating regions of conductivity σ' and σ'', and $d\mathbf{S}_j$ is directed from the primed region to the double-primed one. In Equation 24,

$$E_j = \tfrac{1}{2}(E_n' + E_n'') \qquad 25.$$

where E_n is the normal component of the electric field at the surface of discontinuity.

Barr (82) pointed out that Equation 24 could be used to find a numerical solution for V. We will illustrate this procedure for the homogeneous case, although the result is easily extended to the general case. For a homogeneous conductor, the only surface is the boundary of the torso S_0, for which σ'' is zero. Hence, Equation 23 becomes

$$4\pi\sigma V = \int \mathbf{J}^i \cdot \nabla\left(\frac{1}{r}\right) dv - \int \sigma V \nabla\left(\frac{1}{r}\right) \cdot d\mathbf{S}_0 \qquad 26.$$

Let S_0 be divided into N elements, and assign a voltage V_k to the kth element. If we now evaluate V just inside element i, the contribution of that element on the right-hand side of the equation is just $2\pi\sigma V_i$. Hence

$$2\pi\sigma V_i = \int \mathbf{J}^i \cdot \nabla\left(\frac{1}{r}\right) dv - \sum_{k \neq i} \sigma V_k \Omega_{ik} \qquad 27.$$

where Ω_{ik} is the solid angle subtended at the centroid of element i by element k. There are N Equations 27 in the N unknown voltages, and a solution can be obtained by iteration. Refinements in the procedure were presented by Barnard, Lynn and co-workers (84, 85). Gelernter & Swihart (86) had earlier outlined a similar numerical technique based on Equation 24 (83).

The development of computer solutions to the forward problem has had a profound effect on electrocardiographic research. A number of laboratories are using programs based on either one of the approaches (87). Equation 18 can also be solved for the magnetic field. The solution given by Geselowitz (88) is

$$4\pi H = \int \mathbf{J}^i \times \nabla\left(\frac{1}{r}\right) dv + \sum_j \int (\sigma' - \sigma'')V\nabla\left(\frac{1}{r}\right) \times d\mathbf{S}_j \qquad 28.$$

If H is written in terms of a magnetic vector potential $\mathbf{A}$,

$$H = \nabla \times \mathbf{A} \qquad 29.$$

$$4\pi\mathbf{A} = \int \frac{\mathbf{J}^i}{r} dv - \sum_j \int (\sigma' - \sigma'')\frac{V}{r} d\mathbf{S}_j \qquad 30.$$

Availability of the computer solutions puts us in a position to solve the forward problem in detail for at least a single representative case. Such an experiment would involve taking an animal, measuring its surface electrocardiogram, its excitation patterns, its geometry, and comparing the calculated with the observed surface potentials. Rogers & Pilkington (89) obtained this type of data on a dog ("Coriolis"), but they have not reported a comparison of observed with calculated potentials in an inhomogeneous torso. Boineau & Moore (90), using the "Coriolis" data in part, have shown qualitative agreement between recorded and computed potentials at an instant during QRS for a dog with right ventricular hypertrophy.

There have been several other studies comparing observed and calculated potentials in dogs and humans, but none where all the details necessary for an exact comparison were present. Selvester (91) divided the heart into 20 regions and assigned a time-varying dipole moment to each region on the basis of human excitation data. He found that the vector sum of the dipole moments agreed with observed vectorcardiograms. Boineau (92) reported qualitative agreement between excitation in canine hearts and associated vectorcardiograms in several pathologies, although there were some discrepancies, possibly caused by inhomogeneities. Using his 20-dipole model of excitation, Selvester calculated potentials on the surface of a simulated human torso, which incorporated the inhomogeneity introduced by the lungs (93). He reported good agreement with body surface maps published by Taccardi (94), and concluded that inclusion of the lungs did not influence the isopotential contours in a major way.

Scher (95) compared potentials on the thorax of a dog arising from several artificial dipoles in the heart region with potentials in a tank model in which an actual heart-lung preparation was used to simulate these inhomogeneities, although the intracavitary blood was not included. He found considerable improvement when the heart and lungs were incorporated, as compared with the homogeneous tank model.

A comparison of observed potentials with those calculated in a precise realistic simulation should provide quantitative information about the effect of inhomogeneities. It is particularly important to know, for example, whether there are overlaps in potential patterns caused by variations in inhomogeneities and by variations in the sequence of activation. It will very likely be the case in these studies that data obtained for dogs cannot be extrapolated to humans.

A realistic simulation of the forward problem would incorporate, instant by instant, electromotive forces based on excitation data accumulated from studies with myocardial plunge electrodes. Several groups have turned their attention to models where the spread of activation is generated from initial conditions that specify where excitation starts (96). The initial conditions usually come from the myocardial electrode studies, although a simulation of the Purkinje system could be incorporated to determine the earliest points of activation. Spread through the myocardial mass is then assumed to proceed at a uniform velocity, although variation in velocity could be incorporated.

The earliest computer model of excitation of the heart was that of Moe (97). This model was a discrete one and used a two-dimensional array of cells. The basic idea is that a cell will become active if a sufficient number of its neighbors are active. Relative and absolute refractory periods are incorporated, and extension to a three-dimensional array is possible. A similar model had been used earlier in neural studies (98).

Inverse Problem

The inverse problem is the determination of cardiac sources from the surface electrocardiogram and magnetocardiogram. If no assumptions are made concerning the interior of the thorax, then the multipole expansion provides a canonical description of sources in terms of spherical harmonics. The first term of the multipole expansion is the dipole, and Wilson suggested that Einthoven probably had the multipole expansion in mind when he introduced the heart vector (49). Yeh (99) discussed multipoles in volume conductors and Geselowitz developed equations for relating the multipole coefficients to the potential on the surface of an arbitrary volume (100).

The multipole expansion takes the form

$$4\pi\sigma V = Re \sum_{n=0}^{\infty} \sum_{m=0}^{n} (a_{nm} + ib_{nm}) r^{-(n+1)} P_n^m(\cos\theta)\, e^{-im\phi} \qquad 31.$$

where (r, θ, ϕ) are the coordinates of a point in spherical coordinates. Following Brody (101, 102), we let

$$\Psi_{nm} = (2 - \delta_m^0) \frac{(n-m)!}{(n+m)!} r^n P_n^m(\cos\theta)\, e^{im\phi} \qquad 32.$$

where δ_n^0 is the Kronecker delta. It then follows from Equation 23 that (83)

$$a_{nm} + ib_{nm} = \int \sigma V \nabla \Psi_{nm} \cdot d\mathbf{S}_0$$

$$= \int \mathbf{J}^i \cdot \nabla \Psi_{nm}\, dv - \sum_j \int (\sigma' - \sigma'') V \nabla \Psi_{nm} \cdot d\mathbf{S}_j \qquad 33.$$

Equation 33 provides a relationship between the multipole coefficients and both the surface potentials and the internal sources. There are $2n + 1$ components a_{nm}, b_{nm} for a pole of order n. Equations analogous to Equation 33 were first derived by Gabor & Nelson (103), who interpreted the source not as multipoles but rather as discrete dipoles whose location and moment varied with time. In both interpretations $n = 1$ gives the moment of a single resultant dipole in a homogeneous torso. For $n = 2$, the multipole expansion gives the quadrupole, while with the Gabor–Nelson interpretation the five equations provide information about the three parameters that specify the dipole location. This redundancy can be removed using least squares (104), thus providing the instantaneous coordinates of the dipole location, or "electrical center" of the heart (105).

An experimental study of the moving electrical center for the human heart has been reported (106). As a clinical tool, the electrical center has two difficulties. For one, experimental errors in determining the locus will probably be quite large unless a large number of electrodes are used. For another, the dipole location can become meaningless when the source has large nondipolar components. For example, the "electrical center" for two collinear dipoles moves off to infinity as the dipole moments become equal and opposite (4).

Outside the body the magnetic field can be expressed as the gradient of a scalar function, that is,

$$\mathbf{H} = -\nabla U \qquad 34.$$

The magnetic scalar potential U can be expanded in multipoles analogous to V in Equation 31. If we designate the magnetic multipoles as α_{nm}, β_{nm}, then (107)

$$\alpha_{nm} + i\beta_{nm} = \frac{2 - \delta_m^0}{n + 1} \frac{(n - m)!}{(n + m)!} \int \mathbf{N}^1_{n-1,m} \cdot \mathbf{r} \times \left[\mathbf{J}^i\, dv - \sum_j (\sigma' - \sigma'') V\, d\mathbf{S}_j \right] \qquad 35.$$

where

$$\mathbf{N}^1_{n,m} = \nabla [r^{n+1} P^m_{n-1}(\cos\theta)\, e^{im\phi}] \qquad 36.$$

In terms of the external magnetic field,

$$\alpha_{nm} + i\beta_{nm} = (2 - \delta_m^0) \frac{(n - m)!}{(n + m)!} \int [r^n P^m_n(\cos\theta)\, e^{im\phi} H + \mathbf{N}^1_{n-1,m} U] \cdot d\mathbf{S}_0 \qquad 37.$$

Just as the contribution of the dipole term can be represented mathematically as the dot product of two vectors, the contribution of higher-order multipoles can be considered to be the product of two tensors (102). Furthermore, the lead field can

be expanded in spherical harmonics (15, 108)

$$\mathbf{E}_L = Re \sum_{n=1}^{\infty} \sum_{m=0}^{n} C_{nm} \nabla \Psi_{nm} \qquad 38.$$

so that

$$V = \int \mathbf{J}^i \cdot \mathbf{E}_L \, dv = Re \sum_{n=1}^{\infty} \sum_{m=0}^{n} C_{nm}(a_{nm} + ib_{nm}) \qquad 39.$$

R. M. Arthur (109) evaluated the dipole and quadrupole components of a human subject and found that on a root mean square basis the dipole accounted for 77% of the surface electrocardiogram, while the dipole plus quadrupole accounted for 86% during QRS. This experiment involved potential measurements at nearly 300 sites on the torso. Trost (110) subsequently developed a dipole-quadrupole lead system using 17 electrodes.

Fischmann & Barber (111) suggested that the electrical activity of the heart be represented by six dipoles that were variable in magnitude but fixed in position and orientation on the basis of anatomic considerations. They proposed that six "aimed leads" could be developed to record the individual dipole moments, each lead "responding to electromotive forces in a limited cardiac area." An aimed lead can be developed by letting E_L in Equation 38 be an impulse or delta function (108). If the heart is approximated by a spherical shell of mean radius R, then for a delta function at (θ_0, ϕ_0),

$$4\pi\sigma C_{nm} = \frac{2n+1}{nR^{n+1}} P_n^m(\cos\theta_0)\, e^{-im\phi_0} \qquad 40.$$

and

$$4\pi\sigma V_{\text{aimed}} = Re \sum_{n=1}^{\infty} \sum_{m=0}^{n} \frac{2n+1}{nR^{n+1}} (a_{nm} + ib_{nm}) P_n^m(\cos\theta_0)\, e^{-im\phi_0} \qquad 41.$$

V_{aimed} can be evaluated from knowledge of the cardiac multipoles.

Interest has increased in attempts to determine a physiologically meaningful generator directly from surface measurements. A number of investigators have turned to a multiple dipole equivalent generator in which each dipole represents activity in a local area of myocardium (91, 112–114). The multiple dipole approach is therefore equivalent to the aimed lead. It differs from the Gabor–Nelson formulation in that the dipole locations are fixed a priori.

The approach can be illustrated in the following way. Suppose at a given instant the electromotive forces in the heart form a uniform cup-shaped double layer, as was discussed above. Then the external electric field is identical to that of a disk-shaped double layer on the opening of the cup. Furthermore, if the distance to the disk is large, this field will be almost identical to that of a dipole at the center of the disk.

If no assumptions can be made concerning the source, the best one can do is to identify this equivalent dipole. If, however, it is known that the sources are located

only on the cup-shaped surface (and not on its opening), then it might be possible to learn something of the actual distribution. One could divide the surface into a number of segments and assign a dipole to each one. If there are M segments, then the voltages at N points on the surface of the volume conductor are related to the dipole moments p at each instant by

$$V = Ap \qquad 42.$$

where V is a column matrix of N elements, p is a column matrix of M elements, and A is a transfer coefficient matrix that is determined by solving the forward problem for each dipole source.

N is chosen greater than M to reduce errors. Equation 42 can then be solved by least squares, giving

$$p = (A^T A)^{-1} A^T V \qquad 43.$$

where A^T is the transpose of A. The question is how well the calculated dipole moments p agree with the original source distribution. Insight into the answer has been gained with the aid of simulations.

One conclusion is that a free moment inverse solution will very likely fail. In such a model the dipole locations are fixed, but their directions and orientations are unknown. If signal noise is introduced, or the assumed dipole locations are shifted, then the solution changes drastically (89). Hence, this model can lead to a mathematical solution that is unstable and physiologically not meaningful.

An alternative is not only to fix the dipole locations, but to orient them normal to the double layer surface with proper polarity, and to constrain their magnitudes to be nonnegative (112). Brody & Hight (115) tested this model by introducing signal noise and dipole dislocation noise. They concluded that while noise degraded the quality of the solution, the solution was not vitiated and that the method shows promise. One effect observed was that of crosstalk between dipoles, in that the contributions of certain pairs of dipoles cannot always be resolved. No similar studies of the effects of variation in inhomogeneities have been reported. An analysis of a simple two-dipole case was presented by McFee & Baule (9).

This approach to electrocardiography is extremely attractive and hopefully will bear considerable fruit. Some clinical success has been reported. Holt, Barnard and co-workers studied normal subjects and subjects with hypertrophy using a 14-dipole model of the heart in an inhomogeneous torso (114). Potentials were recorded at 126 skin electrodes. To a large extent the time course of the calculated dipole moments agreed with excitation data. Furthermore, a very good correlation with ventricular mass was obtained by calculating the total area under the dipole moment curves of the dipoles in the left ventricle and of those in the right ventricle. Attempts to utilize this approach for myocardial infarction have been somewhat less successful (116).

Of considerable interest are attempts to introduce a priori information about the time course of dipole moments into the inverse problem. It should be noted that in the study of Holt et al, this was not considered. A solution was obtained on an instant-by-instant basis, and each time instant was completely independent of any other. The fact that smooth continuous curves were obtained provides some

circumstantial evidence that the solutions are meaningful. Attempts to incorporate time constraints have by and large not proved fruitful thus far, but this is clearly also an area for future investigation (117, 118).

An equivalent generator that specifies information on the epicardial surface of the heart was mentioned earlier. Martin & Pilkington (119) have shown that the epicardial potentials are unique, but that it is probably not feasible to determine them from the torso potentials by using unconstrained solutions. It might be noted that it is also possible to use the normal current density at the epicardial surface or, as has been noted above, the Helmholtz double layer, which is proportional to the open circuit voltage on the epicardium. Finally, we might use a single layer that is proportional to the short circuit current, i.e. the current density at the epicardium when it is surrounded by a perfect conductor. These four representations have been studied by Grynszpan (107).

Note that Equation 41 is just the open-circuit potential on the surface of a sphere containing centric multipoles (74). From the Helmholtz theorem of the double layer, Equation 41 can then be interpreted as giving an equivalent double layer on a spherical surface representing the epicardium.

We conclude this section by noting the studies of isolated hearts in well-defined volume conductors, particularly spheres. Such experimental configurations eliminate the complexity introduced by an inhomogeneous torso of complex shape. Craib, for example, reported that the potentials of a terrapin heart in a spherical chamber resembled that of a dipole (19). Brody and co-workers have been studying isolated hearts in a precise spherical chamber (120).

Body-Surface Maps

Modern technology has made possible the acquisition of detailed information concerning the surface electrocardiogram. By recording time-coherent potentials at several hundred skin electrodes, it is possible to construct, instant by instant, isopotential contours describing the surface electrocardiogram. While the recording of such maps is not new, the procedure was used sporadically until quite recently. At the moment a number of laboratories are engaged in body-surface mapping (93, 94, 121–123).

From a clinical standpoint, body-surface mapping is on one hand an advance and on the other a retrogression. It is a step forward in that it allows presentation of all the information available. It is a retrogression insofar as it takes us away from an ideal where a small number of tracings from a small number of electrodes may be made to yield a description of the source (e.g. heart vector) and the clinical information we seek.

Body-surface mapping is still in its infancy. A conference on the subject was held recently, and following is a summary of some of the conclusions we have drawn (123). At this point there are relatively few diagnoses that can be made from body-surface maps that cannot be made from conventional leads. There clearly is additional information present in the maps and perhaps this information is important diagnostically, but it has not yet been correlated with pathology. It may well be that body-surface mapping will indicate how to use more effectively the heart vector or its

extension to include the quadrupole. Alternatively, it may indicate more appropriate sites for unipolar leads. Investigators studying body-surface maps report that they have a better understanding of the conventional scalar and vector leads as a result.

There are indications that the contours that one sees are directly related to important electrophysiological and clinical events such as epicardial breakthroughs. Taccardi (124) has reported changes in maps during the S–T interval for abnormals. Apparently, with the use of multiple electrodes one can with confidence draw isopotential contours of very low amplitude. Equivalent information may be potentially available in the vectorcardiogram during S–T, but may be obscured by noise. This question requires further investigation.

A similar observation is that body-surface maps show that activity persists after the QRS, as conventionally recorded in scalar or vector leads, has returned to the base line. This observation is again apparently a consequence of the ability to draw contours corresponding to very small potentials recorded from a large number of electrodes. The question of whether these potentials can be accurately recorded in individual scalar or vector leads remains to be investigated.

Body-surface maps clearly show that on many individuals, at instants during QRS, multiple maxima and minima appear on the body surface. This feature of the maps has awakened interest in the question of whether these multiple extrema can be attributed in part to inhomogeneities or even to the shape of the torso in the absence of inhomogeneities, rather than completely to the generator (125).

Another question of interest is how few electrodes can be used to construct body-surface maps with reasonable accuracy. The multipole approach has led to some success in a 17-electrode system (109, 110). The Durham group (126) has shown that, using 24 electrodes, surface maps can be constructed accurately for a wide range of subjects. One difficulty inherent in studying isopotential contour maps is how to quantitate differences and similarities.

Magnetocardiography

The past decade has seen a dramatic improvement in the ability to measure biomagnetic fields. They are extremely small, about one million times weaker than the earth's magnetic field in the case of fields of cardiac origin and even smaller in the case of fields originating in the brain. Hence the detection of these fields has been a major experimental challenge. Nevertheless, it has been possible to develop instrumentation so that such fields can be measured almost routinely.

Stratbucker measured the magnetic field surrounding an isolated guinea pig heart (127). Shortly later, detection of the human magnetocardiogram was reported by Baule & McFee (58, 128), who used two coils in opposition. Each coil consisted of several million turns enclosing a ferrite core. This work was later verified by a Russian group using a similar technique (129), and by Cohen, who used a specially constructed shielded room and a magnetometer with a Josephson junction (130, 131).

The magnetic field contains information that cannot be gleaned, in theory, from measurements of potential, i.e. electrocardiogram or electroencephalogram, at the body surface. It remains to be seen whether this new information is actually available in practice. Another potentially useful aspect of magnetic measurements is that they

do not require electrodes and hence avoid the difficulties in measuring very low frequency phenomena associated with electrodes. Cohen has reported measurements at dc (132).

It follows from Equations 18 and 29 that

$$\nabla \cdot \mathbf{A} = -\sigma V \qquad 44.$$

$$\nabla^2 \mathbf{A} = -\mathbf{J}^i \qquad 45.$$

These equations indicate that the electric field is related to the divergence of $\mathbf{J}^i$ while the magnetic field is related to the curl of $\mathbf{J}^i$. A general analysis has been presented by Plonsey (133) and by Grynszpan (107), and Grynszpan has studied simplified models utilizing sources in a sphere and spheroid. An interesting result is that there is no magnetic field outside a volume conductor in configurations possessing axial symmetry (58). A radial source in a sphere gives no magnetic field, but if the sphere is perturbed slightly to a spheroidal shape, a significant magnetic field appears (107). From Equation 28 or 30, the effect of the external boundary can be removed mathematically, but this step requires a knowledge of the surface electrocardiogram.

Baule & McFee (58) pointed out that the lead field concept could be extended to the magnetocardiogram. Consider a small one-turn coil of area S. Then, from the reciprocity theorem, the voltage in the coil V_M is given by

$$V_M = \mu_0 S \frac{dH_n}{dt} = \int \mathbf{J}^i \cdot \mathbf{E}_L \, dv \qquad 46.$$

where H_n is the magnetic field intensity normal to the plane of the coil. $\mathbf{E}_L$, the lead field, is the amplitude of the alternating field in the volume conductor when the terminals of the lead, i.e. the coil, are energized with an alternating current of unit amplitude. Note that E_L is proportional to the rate of change of this current with time.

In Conclusion

From a biophysical standpoint, understanding in detail the relationship between external fields and internal bioelectric sources is an interesting and significant problem. From a biomedical engineering standpoint, where questions of utility and costs of patient care should enter, the usefulness of this research must be examined more carefully. It is probably not unreasonable to state that the fundamental work to date in biophysical aspects of electrocardiography has not yielded great gains in clinical electrocardiography. Furthermore, small gains achieved at the expense of much greater complexity, patient time, physician time, technician time, and total costs are of questionable value.

I do feel, nonetheless, that further work is clearly justified for the following reasons. For one, current electrocardiographic diagnosis leaves much room for improvement in accuracy (134). Since a considerable cost is involved in misdiagnosing cardiac disorders, either through false positives or false negatives, any increase in accuracy of diagnosis is important. Second, the ability of the physician to intervene to correct cardiac abnormalities has been increasing dramatically. A decision to intervene will

often require precise information about the electrophysiological state of the heart, which further research may show to be available in the surface electric and magnetic fields. Finally, more precise quantitative information about the heart, such as ventricular mass and the size of an infarct or ischemic region, would be of direct clinical value. The recording of electro- and magnetocardiograms is a noninvasive procedure.

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