The Canine Heart As an Electrocardiographic Generator

Dependence on Cardiac Cell Orientation

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SUMMARY Traditionally it is assumed that during cardiac depolarization the macroscopic current generators that produce electrocardiographic voltages can be represented as a uniform double-layer source, coincident with the macroscopic boundary between resting and depolarized cardiac fibers as measured with extracellular electrodes ("uniform" hypothesis). A segment of this boundary is thus considered as a current dipole oriented perpendicular to the boundary. We present evidence that, contrary to the above, the effective dipoles largely parallel the long axes of cardiac fibers ("axial" hypothesis). Calculated potentials in volume conductors differ markedly in the two cases. The magnitudes of rapid local "intrinsic" deflections also differ markedly. In our experiments, potential fields produced by stimulation at several cardiac sites and measured magnitudes of intrinsic deflections during normal depolarization and that caused by stimulation support the axial hypothesis and are incompatible with the uniform hypothesis. Our results suggest that axial orientation of sources is sufficiently strong so that predictions assuming the uniform hypothesis would be seriously in error, although the axial theory alone does not exactly describe all the measured potentials. Axial orientation of current generators must be considered in quantitative prediction of electrocardiographic potentials. Further study of the geometry of the intracellular depolarization boundary and its relation to fiber direction and to the frequency of lateral intercellular junctions is required to describe the generators exactly.

THE ELECTROCARDIOGRAM (ECG) is of great utility in physiology and in cardiac diagnosis, but its shape has not been quantitatively predictable from a knowledge of intracardiac events. Such prediction, known as the electrocardiographic "forward" problem (usually dealing with ventricular depolarization and the QRS complex), has appeared feasible on the basis of available knowledge of (1) cellular electrical changes associated with depolarization of cardiac cells;1-3 (2) the sequence of these changes in the heart (pathway of depolarization);4,5 (3) geometry and conductivity of the torso and its contents; and (4) the physical theory describing current flow in three-dimen-

sionai, bounded, inhomogeneous conductors like the torso.6-17 If the forward problem were solved, it would greatly strengthen the scientific basis of electrocardiography. Although all necessary information seems available, past attempts to solve the forward problem during ventricular depolarization18-23 appear to us either qualitative and very difficult to evaluate or, when body surface maps that can be compared with real body surface maps have been produced, the studies do not show good agreement between the two. An explanation for failure to solve the forward problem may, we believe, be found in myocardial cellular anatomy, the electrophysiology of cardiac cell-to-cell conduction, and the manner in which cardiac cells generate external currents. These are the subject of this paper.

Cardiac cells are long and narrow (about 15 \(\mu\)m in diameter by 70 \(\mu\)m in length, with considerable variabili-
We do not feel that this approximation influences our conclusions as thereby and that the depolarizing process spans several cells simultaneously.

As depolarization propagates from cell to cell, currents are generated within the myocardium which give rise to electrocardiographic potentials at the torso surface. The ECG forward problem attempts to calculate these potentials in order to test our understanding of the total electrocardiographic system. Traditionally, calculations of extracellular potentials from depolarizing excitable tissue have been approached in two very different manners. Those dealing with nerves or single strands of muscle develop an analytic solution for potential within and around a long single cell and assume boundary conditions at the cell membrane approximating those for an experimentally measured action potential.\(^{16-17,20-22}\) It is usually assumed that membrane current is symmetric with respect to rotation around the cell axis and thus the resulting potential field is also axially symmetric. (Rall\(^{30}\) has calculated time constants of approach to equilibrium in the radial, angular, and longitudinal dimensions for passive currents. He shows that for long cells, symmetry about the cell axis is reached very rapidly.) The axially symmetric "core conductor model"\(^{34,35}\) is used to derive membrane current from experimentally measured intracellular action potentials. Potentials external to a cell are then calculated by integrating, over the entire cell, the membrane current divided by the distance to the observation point. Spach and co-workers\(^{20}\) have abandoned the use of the isochrones (boundaries between resting and active tissues) as potential sources and this implies abandonment of the uniform double-layer concept. They have questioned,\(^{44,45}\) as did Frank,\(^{18,19}\) the assumption that all parts of the myocardium which generate and unless conductivity and extracellular fluid spaces are identical along the wavefront.\(^{22,23}\) If the strength per unit area of this uniform double-layer source surface is constant, the potentials produced are directly proportional to the solid angle which that surface subtends.\(^{7,15,40}\) All that is important for determining the solid angle are the edges and holes of the wavefront (that is, where it terminates on endocardium, epicardium, or inactive tissue), and the exact description of activity at other positions is irrelevant.

Although the uniform hypothesis has been useful to provide a rough qualitative visualization of the origin of the ECG, we and others, as indicated earlier, have been generally unsuccessful in quantitative predictions of ECG potential maps using the solid angle approach, even when corrections for inhomogeneities and boundaries are made.\(^{20,21}\) Spach and co-workers have abandoned the use of the isochrones (boundaries between resting and active tissues) as potential sources and this implies abandonment of the uniform double-layer concept. They have questioned,\(^{44,45}\) as did Frank,\(^{18,19}\) the assumption that all parts of an isochrone (wavefront) generate equal current per unit area, and have advocated the use of potential fields as volume-conductor sources.

The validity of the uniform hypothesis is questionable unless all cells are identical in terms of the action potential they generate and unless conductivity and extracellular space are identical along the wavefront. Its validity will also depend on the geometry of cardiac cells and the relative frequency of branching and side-to-side intercellular junctions. If lateral junctions were infinitely frequent and if gaps between cells did not exist, then depolarizing regions within adjacent cells would join coherently to form a hole-free macroscopic wavefront of uniform strength, as illustrated in Figure 1A. Conversely, if lateral junctions were relatively infrequent, then the wavefront within each cell would tend to lie in a plane perpendicular to the cell axis, as hypothetically illustrated in Figure 1B. Each cell would then act as a dipole current source pointed along the cell axis. The effective strength per unit area of the result-
The configuration of Figure 1A is not likely to be the general case within the ventricular wall because anisotropy of conduction velocity and electrotonic spread, as well as results of anatomical studies, indicate relatively infrequent branching and side-to-side cellular junctions. Yet, it is also unlikely that pure axial symmetry will be the general case, and typically the truth will lie somewhere between Figures 1A and 1B. But we thus have raised the possibility that effective wavefront strength may be highly variable, although all cells are electrophysiologically identical—merely because of differences in orientation of intracellular depolarization gradients.

Thus, we determined to examine the validity of the uniform hypothesis using stimulation experiments in which simple, well localized excitation wavefronts are produced and resulting potentials are recorded from many points close to the wave. We wished to predict potentials close to a wavefront as a prerequisite for later predicting potentials at a greater distance. In these experiments, we accurately mapped the position of the wavefront in three dimensions, and compared actual measured potentials with potentials derived from the measured wavefront by the solid angle formulation. We also calculated potentials from the wavefront position via a new approach, a macroscopic extension of the axially symmetric single cell theory. We call this the "axial" hypothesis. It treats the partially depolarized portion of a myocardial fiber as an ideal dipole source pointing along the axis of that fiber. The boundary between resting and active tissue, as in the solid angle approach, is considered to be macroscopically smooth, and cells are assumed to be electrophysiologically identical and locally parallel, with uniform extracellular space (Appendix B).

The axial and uniform hypotheses not only predict very different shapes and magnitudes of fields, but also predict different electrical changes as a depolarization wave passes a recording electrode. When a wavefront surface passes a recording point within the myocardium, the solid angle subtended by that surface changes by $4\pi$ steradians; when the recording point is on an epicardial or endocardial surface, the change is $2\pi$ steradians. The "discontinuity" in potential should then be either $K,\Delta V$ or $K,\Delta V/2$, where $\Delta V$ is the cellular plateau voltage minus resting voltage, and $K, = 0.56-0.74$ (for $\Delta V = 120$ mV, then $K,\Delta V = 60$ mV). Thus, although the wave is not actually infinitesimally thin, we would expect from solid angle predictions to observe rapid changes in potential, referred to as "intrinsic deflections," with magnitudes clustering near $K,\Delta V$ and $K,\Delta V/2$ (that is, 60 mV and 30 mV). In contrast, as developed in the Appendix, the axial theory predicts a continuous variability of intrinsic deflections, equal to $K,\Delta V\cos^2\gamma$, where $\gamma$ is the angle between cell axes and wave propagation direction.

**Methods**

**PREDICTION OF POTENTIAL SHAPES FROM DEPOLARIZATION**

Five dogs were studied by two different techniques. In the first study, three dogs were anesthetized with pentobarbital, 30 mg/kg, iv, and the heart was exposed through a left-lateral thoracotomy. Multiterminal needle electrodes (terminals at 1-mm distance) were inserted in a close array into the lateral left ventricular wall. Two or more rings of electrodes were inserted around a central electrode, all perpendicular to the epicardium, such that a total of 15–20 electrodes were placed within a 3-cm diameter. The heart was covered with 400 $\Omega$-cm sucrose-saline to a depth of several centimeters during the recording to approximate an infinite homogeneous medium. Depolarization was initiated by stimulation along the central electrode either at the epicardium or within the wall. The time of local depolarization at each of the multiple recording electrodes was determined as the instant of most rapid negative-going change of the unipolar potential. After each experiment, the position of each electrode was carefully measured and the anatomy of the block of tissue with electrodes was reconstructed. The tissue was then grossly dissected to determine the orientation of cardiac muscle fibers. The recorded potentials could be compared with those predicted from the solid angle or axial theory.

In a second study we used a brushlike electrode consisting of single tungsten wires (0.125 mm in diameter), insulated except for the sharpened tips. Eight parallel wires 6 mm long protruded at right angles from a plastic block around a 6-mm diameter circle. An additional elec-
trode in the center was used for stimulation. This brush electrode was inserted into the left ventricular wall so that all nine wire tips lay 5 mm deep in a plane parallel to the epicardium. Stimulation currents just above threshold were applied to the central electrode, and the potentials were measured on the surrounding wires. The object was to examine potentials very close to a closed excitation surface at points where the local wavefront moved in many directions relative to cell orientation.

In the third study, two dogs were anesthetized as above and the heart exposed as before. Two multiple electrodes were placed into the left anterior papillary muscle, one near the tip and one in the body of the muscle. We stimulated at various points and observed potentials on the other electrodes. By stimulating near the muscle tip, we were able to generate a simple wave which initially traveled nearly along cell axes.

MEASUREMENTS OF INTRINSIC DEFLECTION MAGNITUDES

During extensive mapping of myocardial depolarization sequence in studies on the isolated, perfused dog heart, we had recorded unipolar potentials from hundreds of intramyocardial locations. For this study, we retrieved these records and tabulated the magnitudes of the rapid intrinsic deflections (slopes greater than about 10 mV/msec) which, for small recording electrodes, approximate the voltage difference across the local wavefront as it passes the electrode. In these studies, 71-terminal plunge electrodes were used (0.9-mm shaft diameter, with 0.05-mm wire tips exposed at 1-mm intervals). Recordings were made with 1-kHz band-width amplifiers and recorder, with an AC coupling constant of 0.3 seconds.

Results

EPICARDIAL STIMULATION

Figure 2 shows the isopotential contours expected according to the solid angle (A) and axial (B) formulations for a hemispherical boundary between depolarized and resting myocardium. Assumed fiber directions are described in the caption. All calculations are within an infinite, homogeneous medium. (Details are in Appendices A and B.) Figure 2C shows contours drawn from potentials recorded from a cup-shaped interface after stimulation 2 mm below the epicardium. The measured field shows regions of strong positivity ahead of the wave only in the direction of the cell axes, as predicted by the axial theory but not by the uniform hypothesis. In addition, negativity precedes the central part of the wave, which is traveling transversely to the fibers, also as predicted by the axial theory. This is clear evidence that the depolarization wavefront behaves as if cellular dipole current sources are oriented preferentially along the cell axes rather than normal to the wavefront.

From the uniform theory, we had previously thought that for such a simple wave (without superposition from other distant waves) one must always see positivity ahead of a wave. Here, however, we see negativity ahead of a wave when it is traveling transversely to the fibers, as predicted from the axial hypothesis. (This negativity is not always so striking, but the potentials in transverse direc-
dipoles were oriented along the cell axes. (The electrodes, including the central stimulation electrode, are in the middle of the left wall in a plane parallel to the epicardium.) Both the central figure and the egg-shaped figure in the upper left are hypothetical, but fiber direction is as indicated. As the wave travels along the cell axes toward both longitudinal electrodes marked L, a sharply rising positive potential ("spike") is seen (arrows), followed by a strong, sharply negative deflection as the wave passes the electrode. The two upper curves in the left insert of Figure 3 are predictions by the uniform and axial approaches (Appendix D). The positive spike in both "measured" and "axial" potentials and the lack of positive spike in potentials predicted by the solid angle calculation again confirm a preferential axial orientation of cellular dipoles.

In contrast, as the wave approaches electrodes T transversely, a negative dip is seen (arrows), as predicted from axial dipole orientation. Then, as the wave passes the electrode, a sharper negative deflection occurs. This major negative deflection is slower and shows a more variable rate of change than is seen on the longitudinal electrodes. It is less than that predicted by the uniform theory, but much greater than that predicted by the axial theory. The presence of this intrinsic deflection at the transverse electrodes is possibly due to (1) some laterally oriented cellular dipoles, or the fact that (2) the wavefront near the electrode is not coherent, or (3) the wavefront at the electrode is not traveling exactly transversely to cell axes. Electrodes B at intermediate angles record potentials intermediate between L and T.

Although the electrodes are only 3 mm from the stimulation point, the distributed nature of the wavefront would not, we believe, account for the contrasting positive and negative potentials preceding local depolarization at L and T.

The consistent differences between potentials at longitudinal and transverse electrodes are more evidence for rejecting the uniform double-layer assumption and for considering fiber direction in understanding potentials generated during myocardial depolarization.

**PAPILLARY MUSCLE STUDY**

Figure 4 illustrates results of the papillary muscle study. Those electrodes where the wave arrived first (wave traveling directly from stimulus along the cell axes) experienced the largest intrinsic deflections (up to 57 mV) and the largest pre-arrival positive spikes (up to 12 mV). Later arrival times (wave arriving by oblique propagation) were accompanied by reduced intrinsic deflections (about 25
The conductivity factor $K_\text{V}$, extracellular fluid space, or showing, however, is a variation of such other factors as generally proceeds from endocardium to epicardium.

Spherical depolarization wavefront $W$, assuming that all cellular sources are oriented exactly along the cell axes. For propagation along the cell axes ($\psi = 0^\circ$), an initial pre-arrival positive deflection occurs, followed by a strong negative-going discontinuity, $\Delta$ (the intrinsic deflection), equal to $K_\text{V}\Delta V$. As propagation becomes more transverse to the cell axes ($\psi$ increases toward $90^\circ$), the positive pre-arrival deflection decreases and then becomes negative. Also, the intrinsic deflection (equal to $K_\text{V}\Delta V\cos\psi$) is reduced, disappearing completely for $\psi = 90^\circ$. (See Appendix D.)

If the average angle between fibers and wavefront direction were about 60 degrees, we might expect nearly 80% of the values to cluster near $K_\text{V}\Delta V \approx 60$ mV. The axial theory, however, predicts a small intrinsic deflection (equal to $K_\text{V}\Delta V\cos\psi$) with little or no positive spike. This agrees with axial predictions in which intrinsic deflections should be equal to $K_\text{V}\Delta V = 60$ mV for propagation along cell axes with a positive spike, and smaller intrinsic deflections with no spikes would be seen for large oblique angles of approach. (Figure 5 illustrates these features for an expanding, closed spherical wave.)

**INTRINSIC DEFLECTION MAGNITUDES**

Figure 6 shows histograms of rapid intrinsic deflection magnitudes for three dog hearts. The distributions are smooth and singly peaked, with means of 15-23 mV, and tail off between 50 mV and 70 mV. No significant differences were found between right wall, left wall, and septum.

Also, because over 80% of these electrodes were deep in myocardium, according to the solid angle theory one reasonable. One might argue that what Figure 6 is really showing, however, is a variation of such other factors as the conductivity factor $K_\text{V}$, extracellular fluid space, or tissue viability surrounding the electrode. Since axial conduction would account for the potential magnitudes in Figure 6 as well as the other findings reported above, it appears unnecessary at present to invoke these other factors, but they should be investigated.

**Discussion**

Several findings invalidate the hypothesis that the boundary between resting and active myocardial tissue behaves as a uniform dipolar-sheet current source. First, there are strong positive potentials in the direction of the cell axes around cup-shaped waves that indicate strong preferential axial orientation of the cellular electrical sources rather than orientation normal to the wavefront.

Second, potential changes occur before local depolarization external to closed-surface depolarization waves. These potentials are incompatible with a uniform dipolar-sheet representation, but are again consistent with a preferential orientation of generators along the cell axes.

Third, magnitudes of rapid intrinsic deflections are highly variable, in contrast to predictions of the uniform hypothesis, and are related to the angle between the wavefront and the fiber direction, again as predicted from assuming a preferential axial orientation. We believe that the magnitudes of the rapid components of the intrinsic deflection are approximately proportional to the effective strength of the wave in the immediate vicinity of the electrode. The wide variation in these measured magnitudes, as illustrated in Figure 6, thus indicates in itself a wide variation in effective wavefront strength. If this variation is systematic and due to fiber orientation, as we believe, it must be considered in quantitative predictions of electrocardiographic potentials.

These results are not (with hindsight) particularly unexpected considering the longstanding knowledge of cardiac excitation velocity anisotropy, anisotropy of electrotonic spread, a knowledge of cardiac cell geometry, and the frequency of intercellular contacts in the rabbit heart, as well as a knowledge of the behavior of electrical fields within and around long cylindrical cells. The widespread use of the uniform theory by ourselves and by others thus appears to be a failure to consider the effects of cell-to-cell conduction and cell geometry on extracellular potentials. Plonsey has made a beginning toward considering these and similar matters in depth.

**Figure 6** Histograms of rapid intrinsic deflection magnitudes observed during extensive mapping of excitation in three isolated, blood-perfused dog hearts. These serve as an indication of variation in local wavefront source strength. Discussion in text.
Vander Ark and Reynolds measured voltage variations on the epicardium. They found that the largest voltages occurred when propagation was parallel to the muscle fibers and that for cross-fiber propagation the waveforms were prolonged, with multiple notching and a lack of sharp intrinsic deflections. The mean voltages (total peak-to-peak changes) in this latter case were 29.5% less than with parallel movement, even without distinction between rapid and slow phases and without correction for distant superposition. Conduction velocity was also reduced by 51.8%. They did not, however, conclude that this difference implied a variability in effective wavefront strength with fiber direction, probably because of their study of the closed-surface wave. It is our opinion that their closed-surface wave study was insufficient to resolve the question of uniformity of wavefront strength for two reasons. First, they did not show how much voltage would be expected at various distances from the wave if the wave were not uniform (we present such an analysis in Appendix D). Thus, there is no reason to believe that their choice of electrode position and amplifier gain was adequate for testing uniformity. Second, they recorded with bipolar endocardial-epicardial electrode pairs which, according to the analysis in Appendix D, both would measure the same voltage, even for a nonuniform wave. Also, our own study of a closed-surface wave (Fig. 3) shows external potentials for electrodes within the muscle only briefly in advance of local depolarization. These potentials fall off so rapidly with distance that it probably would be impossible to measure them from electrodes on heart surfaces, but they nevertheless result from significant wavefront strength nonuniformities. (There may be some small voltage changes preceding local depolarization in Figure 7 in their paper.)

To supplement the voltage vs. fiber direction study of Vander Ark and Reynolds, we studied epicardial unipolar potentials, utilizing 50 measurements with poststimulus propagation parallel to muscle fiber direction and 100 measurements for propagation not parallel to fiber direction. We measured rapid intrinsic deflections and total (peak-to-peak) voltage changes. These are summarized in Table 1. They indicate that there are substantial differences in potentials between parallel and nonparallel propagation, especially in the rapid deflections.

The data presented above indicate that a macroscopic wavefront cannot be considered a uniform double-layer source and that systematic changes in effective wavefront strength and direction are determined by cellular geometry and by interconnections between cells. We believe that this accounts for the fact that the forward problem remains largely unsolved. We see no reason why the clear improvement in qualitative prediction of potentials external to a macroscopic depolarization interface W should be examined experimentally, especially in regions of Purkinje fiber penetration and in trabeculated regions. The question of uniform packing of myocardial cells and of intracellular-extracellular volume ratios may need exploration. Finally, fiber directions must be measured everywhere in the heart and described in some way appropriate for numerical processing. We hope that we and other investigators can then proceed toward a solution of the electrocardiographic forward problem by incorporating a knowledge of cell-to-cell conduction and myocardial fiber direction.

In addition, the concept of a "coherent macroscopic wavefront" should be examined experimentally, especially in regions of Purkinje fiber penetration and in trabeculated regions. The question of uniform packing of myocardial cells and of intracellular-extracellular volume ratios may need exploration. Finally, fiber directions must be measured everywhere in the heart and described in some way appropriate for numerical processing. We hope that we and other investigators can then proceed toward a solution of the electrocardiographic forward problem by incorporating a knowledge of cell-to-cell conduction and myocardial fiber direction.

### Table 1. Magnitude in Millivolts of the Rapid Intrinsic Deflection and Total Voltage Drop Recorded on Unipolar Electrodes following Epicardial Stimulation

<table>
<thead>
<tr>
<th></th>
<th>Intrinsic (mV)</th>
<th>Total (mV)</th>
</tr>
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<tbody>
<tr>
<td>Parallel</td>
<td>46.2 (8.4)</td>
<td>52.2 (5.9)</td>
</tr>
<tr>
<td>Nonparallel</td>
<td>26.6 (8.4)</td>
<td>42.7 (3.6)</td>
</tr>
</tbody>
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Results are given as mean (sd). Differences in voltage between parallel and nonparallel propagation are significant at the 0.1% level. Discussion in text.

### Appendix

#### A. DESCRIPTION OF THE UNIFORM THEORY

The uniform theory considers the wavefront a uniform double-layer current source and gives the potential V at the point P within an infinite homogeneous conducting medium as the following integral over all points r on the macroscopic depolarization interface W:

$$ V(P) = \frac{1}{4\pi\sigma} \int \int \int n(r) \cdot \frac{\hat{n} \cdot (P-r)}{P-r} \, dA $$

where \( \hat{n} \) is the outward surface normal, \( \sigma \) is the conductiv-
ity, and \( m(r) \) is the dipole source strength per unit area at \( r \). (Units follow Plonsey.\textsuperscript{14}) If it is assumed that \( m \) is a constant and is equal to \( K_1 \sigma \Delta V \), where \( \Delta V \) is the cellular potential, then

\[
V(P) = -\frac{K_1 \Delta V}{4\pi} \Omega(P),
\]

(2)

where \( \Omega(P) \) is the solid angle subtended at \( P \) by the depolarization wave, and \( K_1 = 0.5 \) is a correction due to unequal intracellular and extracellular resistivities.\textsuperscript{5,7,11}

The field of Figure 2A was calculated in two different ways, each yielding the same result. The first was to find off-axis solid angles for Equation 2 using an expansion in spherical harmonics. The second was to do a numerical integration of Equation 1 over the hemispherical wave. The wave was broken into small area elements, and each was replaced by a dipole source at the element center, pointing normal to that element and having strength proportional to the area of the element. The potential at any point was then obtained by summing potentials produced by all the dipoles. Elements were progressively subdivided until no further change in the potentials occurred.

**B. DESCRIPTION OF THE AXIAL THEORY**

Both Equations 1 and 2 assume a cellular picture as in Figure 1A. If, instead, one assumes axial symmetry of cellular membrane currents as in Figure 1B, and assumes uniform locally parallel cell packing and, as before, that a smooth microscopically continuous surface can be drawn connecting the transitional regions of myocardium, then the potential is given as in Equation 1, except that the dipole sources now point along the local cell axis instead of normal to the surface, and the strength per unit area is reduced by \( \cos \gamma \) because of the "holes" now present in the wave (Fig. 1B). If we also assume that the maximum magnitude of \( \sigma \) is \( K_1 \sigma \Delta V \), then the potential becomes

\[
V(P) = \frac{K_1 \Delta V}{4\pi} \int _{|\mathbf{r}|} \frac{dA(r) \cdot (P - r) \cos \gamma}{|P - r|^3},
\]

(3)

where \( \hat{a}(r) \) is a unit vector pointing in the axial direction of the cells located at \( r \). (This integral does not simplify, as does Equation 1, and thus for most applications it must be evaluated numerically.)

Equation 3 describes the "axial" calculation for an infinite homogeneous medium. Equation 3 can be extended to a bounded homogeneous solution (as can Equations 1 and 2) by using it as the source term in the numerical computer algorithm of Barnard et al.\textsuperscript{10}

The field of Figure 2B for a hemispherical wavefront, with current generators assumed parallel to cell axes, was calculated by a numerical integration of Equation 3. As in Appendix A, the wavefront was subdivided into small area elements, and potentials were calculated by substituting for each element a dipolar source located at the center of the element. The strength and direction of each dipole, however, as indicated by Equation 3, are different than in Appendix A. The strength becomes the area of the element multiplied by \( \cos \gamma \), and the dipole points in the local fiber direction rather than normal to the wave surface. As before, elements were progressively further subdivided until no further change in calculated potential occurred. (\( \gamma \) is the angle between wave propagation direction and fiber direction at the wavefront element. The sign of fiber direction is always taken so that \( \cos \gamma \) is positive.)

By this same method, axial model calculations can be performed for any shape \( \sigma \), wavefront and for any fiber configuration, as long as the, area elements are small enough that fiber direction does not change significantly over any individual element.

**C. PREDICTIONS OF POTENTIALS BY THE AXIAL THEORY FOR INFINITE PLANE WAVE EXCITATION**

The following development leads to the axial model predictions for closed waves as illustrated in Figure 3.

Consider a closed spherical excitation wave of radius \( R \), centered on the origin, immersed in an infinite bed of homogeneous cell fibers oriented parallel to the \( z \) axis (Fig. 8). The depolarization wave in myocardium is extensive compared to its thickness, at locations where edge effects need not be considered.

Equation 3, for an infinite plane wave traveling in the \( z \) direction at an angle \( \gamma \) to the cell axes (all cells parallel and in direction \( \mathbf{a} \)) (Fig. 7), becomes

\[
V(P) = \frac{K_1 \Delta V}{4\pi} \cos \gamma \int _{\mathbf{a}} \frac{dA(r) \cdot (P - r)}{|P - r|^3},
\]

which integrates out as

\[
V(z) = -\frac{z}{|z|^2} \frac{K_1 \Delta V}{2} \cos^2 \gamma.
\]

This is constant on either side of the wave, \( +\Delta V \cos^2 \gamma \) ahead of the wave and \( -\Delta V \cos^2 \gamma \) behind it, and thus the "discontinuity" in crossing the wave is

\[
\Delta \phi = K_1 \Delta V \cos^2 \gamma.
\]

(4)

For small electrodes in intimate contact with active myocardium, this discontinuity is seen as a rapid negative deflection, the intrinsic deflection. Thus, when the depolarization wave in myocardium is extensive compared to its thickness, the axial model would predict a large variation in measured intrinsic deflections, depending on the angles between wavefront and fibers.

**D. PREDICTIONS OF POTENTIALS BY THE AXIAL THEORY FOR A CLOSED SPHERICAL WAVE OF EXCITATION**

The following development leads to the axial model predictions for closed waves as illustrated in Figure 3.

Consider a closed spherical excitation wave of radius \( R \), centered on the origin, immersed in an infinite bed of homogeneous cell fibers oriented parallel to the \( z \) axis (Fig. 8).

Equation 3 can be rewritten as

\[
V(P) = \frac{K_1 \Delta V}{4\pi} \int _{\mathbf{a}} dA(r) \cos \gamma \cdot \nabla_s \left( \frac{1}{|P - r|} \right),
\]

where \( \nabla_s \) is the vector gradient operating on the \( r \) variable. This is solved by expanding \( 1/|P - r| \) in an infinite series of spherical harmonics,\textsuperscript{44} then expressing \( \nabla_s \) in spherical coordinates, applying the derivatives in \( \nabla_s \) to the series expansion and then integrating term by term. (The resulting solution is symmetric with respect to rotations about the \( z \) axis, and thus is a function only of the distance \( P \) and
the azimuthal angle $\psi$.) The solution for $P$ inside the spherical wavefront becomes

\[ V(P,\phi) = -\frac{K_1}{3} \left[ 1 + \frac{2}{5} \left( \frac{P}{R} \right)^2 \left( 3\cos^2 \phi - 1 \right) \right]. \tag{5a} \]

and for $P$ outside the sphere,

\[ V(P,\phi) = \frac{K_1}{5} \left( \frac{R}{P} \right)^3 \left( 3\cos^2 \phi - 1 \right). \tag{5b} \]

At the wavefront surface, $\psi$ is equal to $\gamma$, the wave-fiber angle, so that the discontinuity in crossing the wave, as in the infinite plane wave case (Eq. 4), is again equal to $K_1 \Delta V \cos \gamma$.

Also, the potential $V$ outside the sphere goes to zero rapidly, as an inverse cubic, as shown in Equation 5b. In addition, the external potential is exactly zero for all angles $\psi$ such that $\cos^2 \psi = 1/3$ (e.g., $\psi = 54.7^\circ$), becoming negative for larger $\psi$ (cross-fiber propagation) and positive for smaller $\psi$ (longitudinal propagation). Because of the rapid falloff and this ($3\cos^2 \psi - 1$) dependence of Equation 6b, easily measurable potentials would be found only very near the wave, and only for $\psi$ nearly $0^\circ$ or $90^\circ$.

We have measured potentials near closed wavefronts, as described in Figure 3. The time curves illustrated there for the axial model were obtained from Equations 5a and 5b by allowing the sphere radius $R$ to expand from zero at a constant rate, while holding $P$ and $\psi$ constant. The curves of Figure 5 were obtained in the same way. Equation 5 is described in Figure 3. The time curves illustrated there for the axial model were obtained from Equations 5a and 5b.

Acknowledgments

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References

SUMMARY Much of our detailed understanding of renal function has come from studies, such as micropuncture, which require exposure of the kidney. In this study we have utilized a new method for assessing afferent arteriolar resistance in vivo to assess the influence of renal exposure on renal blood flow and preglomerular resistance in the rat. Exposure of the kidney did not reduce arterial pressure (111 ± 5.4 vs. 110 ± 5.5 mm Hg), but did reduce cardiac output (298 ± 32 vs. 235 ± 6 ml/kg per min; *P* < 0.02), and renal blood flow in the exposed kidney (5.90 ± 0.26 vs. 4.55 ± 0.19 ml/g per min; *P* < 0.001). Afferent arteriolar resistance, estimated from the size of microspheres reaching the glomeruli, was increased more strikingly (40%) than total renal resistance (29%), suggesting a quantitatively important influence of the surgery on glomerular capillary pressure. Equations, developed to allow the calculation of glomerular capillary pressure, suggested that glomerular capillary pressure was in the range of 50-60 mm Hg in the unexposed kidney, and fell to 45 mm Hg in response to trauma. We conclude that the surgery required to expose the kidney reduces renal blood flow and has a quantitatively important influence on glomerular capillary pressure—a response which must be considered when interpreting experiments which require surgery. The reduction in flow and capillary pressure may well be a useful part of the renal response to volume deficits and trauma.

SURGICAL trauma exerts a striking influence on renal perfusion and function, which has been well documented in several species. We recently devised a modification of the microsphere technique which makes it possible to assess afferent vascular dimensions and resistance without exposing the kidney. The known effects of surgical trauma on renal perfusion led us to examine the effect of the surgery required to expose the kidney on renal hemodynamics in the rat, and to explore the implications of the renal vascular response for glomerular dynamics. Our working hypothesis was that the surgery required to expose the kidney for micropuncture in the rat may have influenced the results of many experiments in which this maneuver is unavoidable. The results, moreover, provide further insight into the renal vascular and functional response to trauma.

**Methods**

**GENERAL TECHNIQUES AND PROTOCOLS**

Studies were performed in 46 male Sprague-Dawley rats weighing approximately 300 g. Standard laboratory chow and tap water were provided. Anesthesia was induced with pentobarbital sodium (40 mg/kg, ip) and maintained with occasional supplements of 5–6 mg/kg as required for surgical anesthesia with spontaneous respiration. Tracheostomy provided an airway. Rectal temperature (Yellow Springs Instrument) was kept between 36°C and 37°C with a lamp. Ventricular catheterization was achieved from the right carotid artery with a tapered, polyethylene (Clay-Adams PE 50) catheter. An identical catheter was placed into the aorta below the renal arteries from the femoral
The canine heart as an electrocardiographic generator. Dependence on cardiac cell orientation.

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