The Electrical Conductivity of Living Tissues as it Pertains to Electrocardiography

I. Review of the Problem of Homogeneity vs. Nonhomogeneity, an Outline of the Technical Aspects of Tissue Resistivity Measurements, and a Critical and Experimental Analysis of Certain Pertinent Experiments

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Field analysis methods provide a convenient mathematical process for organization of electrocardiographic observations. The degree of divergence of calculated spatial orientations of heart forces from true orientations is dependent upon the magnitude of inaccuracy of the assumption that body tissues are electrically homogeneous. Preliminary to undertaking quantitative measurements of tissue resistivities in situ, technical difficulties of the problem have been surveyed, and previous studies have been analyzed. It is concluded that an accurate, quantitative measurement of such resistivity has not been made. If major inhomogeneity were found, current methods of application of field theory to electrocardiography might require extensive modification.

ELECTROCARDIOGRAPHIC theory and practice are tending to become increasingly dependent upon the assumption that the heart functions as an electrical dipole, immersed in a fluid of approximately uniform conductivity. This "homogeneous field" concept, originally formulated by Einthoven, has as its basic aim the delineation of the spatial orientation of the electromotive forces generated by the heart. The magnitude of error in such analysis is a direct function of the degree of inhomogeneity of the tissues. This is a problem which has attracted the attention of many investigators. We propose here (1) to survey some of the indirect and direct approaches which have been applied to the problem, (2) to outline the technical difficulties inherent in the direct approach, and (3) to investigate critically the validity and applicability of certain widely accepted experiments in this field.

I. SURVEY OF EXPERIMENTS FOR ESTABLISHING THE RESISTIVITY OF TISSUES

In the indirect approach to the problem of tissue resistivity, countless descriptions have been made of the effect of body build, heart position, respiration, pericardial calcification or effusion, pneumo-, hydro-, pyo-, or hemothorax, and myxedema upon electrocardiographic patterns. In these and a variety of other conditions, the effect is presumed to be the result of disturbed extracardiac electrical conduction rather
than of disturbed generation of electrical impulses by the myocardium. Some of these data (for example, the reduction of body surface potential differences accompanying pericardial effusion) have suggested that the conducting properties of body fluids and tissues vary appreciably. However, these descriptions have not produced convincing evidence of significant nonhomogeneity of normal body tissues, normally distributed.

Katz and his associates\(^1\) attempted a more definitive differentiation of body tissue conductivity by indirect methods. They found that

**Table 1.** Specific Resistivity ($\rho$) in Ohm Cm. of Various Excised Tissues

<table>
<thead>
<tr>
<th>Tissue</th>
<th>2500 K$\Omega$</th>
<th>300 K$\Omega$</th>
<th>0.5 K$\Omega$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>244–256</td>
<td>200–500</td>
<td>450</td>
</tr>
<tr>
<td>Spleen</td>
<td>167–189</td>
<td>240–500</td>
<td>450</td>
</tr>
<tr>
<td>Kidney</td>
<td>185–222</td>
<td>150–260</td>
<td>130</td>
</tr>
<tr>
<td>Lung</td>
<td>415–556</td>
<td>160–200$^\dagger$</td>
<td>170$^\dagger$</td>
</tr>
<tr>
<td>Brain</td>
<td>313–357</td>
<td>420–800</td>
<td>810</td>
</tr>
<tr>
<td>Muscle</td>
<td>143–200</td>
<td>160–250</td>
<td></td>
</tr>
<tr>
<td>Myocardium</td>
<td>180–250</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>118–149</td>
<td>120–180$^\S$</td>
<td>90$^\S$</td>
</tr>
<tr>
<td>Serum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat</td>
<td>2220–4350</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^*$ Osswald.\(^6\)
$^\dagger$ Rajewsky, Osken, Schaefer, Schwan, and Stachowiak.\(^5\)
$^\S$ Minced lung tissue, alveolar structure destroyed.

While the resistance of all tissues is relatively independent of frequency below approximately 10 K$\Omega$ and of many tissues below approximately 100 K$\Omega$. Above this critical frequency range, resistance progressively decreases as frequency increases. This high frequency effect, known as "disappearance," has been attributed mainly to the nonhomogeneous, membranous structure of tissues.

2. Specific resistivity varies considerably from tissue to tissue.\(^5\) \(^6\) (Table 1.)

3. While the resistance of many tissues varies from one specimen to another, the resistance of serum is constant within about 2 per cent from specimen to specimen and remains within the same limit among different species of mammal.\(^7\)

4. Despite the fact that the capacitance of tissues reaches enormous values at lower frequencies, it is not high enough to influence the current flow appreciably at frequencies below
10 Kc. Therefore only the resistivity of tissues may be important for the frequencies generated by the heart.

5. The extent to which the resistance of tissue is subject to change at very low frequencies can be judged by considering the data compiled in Table 2. This table lists the specific resistance of several tissues, each measured at two frequencies, while the last column lists the percent difference between these two resistance values for each tissue. The results are taken from Rajewsky’s monograph. Some measurements have been made even at much lower frequencies. One of the authors (Schwan) has found a resistance change of 0.24 per cent for frog muscle between 32 cps. and 100 cps., 6 per cent between 100 and 1000 cps., and 21 per cent between 1 and 10 Kc. This measurement would seem to indicate that the dispersion frequency for muscle is considerably lower than for the tissues listed in table 2.

The application of conclusions drawn from studies of excised tissues to resistivity of body tissues in situ is subject to two main criticisms. First, resistivity might change with time after death of the animal. It has been found to take as long as six hours, and in many cases as long as 40 hours before measurements of resistivity in excised tissues begin to change. When it occurs, the change is greater in the low frequency range than in the higher range in which the dispersion effect is normally present; it is considered to be due to the breakdown of all membranes. Experiments have shown that the change does not begin until metabolism has almost completely stopped. Thus, in the first few hours after death, resistivity should remain approximately the same as before death, provided that the distribution of cells and fluids is not significantly altered. This constitutes the second major criticism. It is obvious that this requirement is easily fulfilled with blood, but impossible to fulfill with, for example, lung. Thus, the material collected in Table 1 is difficult to evaluate. Tissues were cut into small sections to fill the conductivity cells, and no special care was taken to avoid loss of blood. The results are therefore of limited significance as measurements of absolute values of resistivity of the living tissues in situ. They are of value in demonstrating the effects of frequency upon resistivity measurements and the constancy of resistivity for several hours after the death of the animals.

Eyster, Maresh and Krasno studied the resistivity of living tissue in situ. They attached electrodes to one forelimb and one hindlimb of a living dog. At a fixed frequency and potential difference, the effect on impedance of severing successive body tissues was studied. They concluded that nearly 60 per cent of the total conductance of the trunk was in the dorsal muscles and vertebral column. They also found that the total impedance was decreased by 11 per cent when a rapid blood transfusion was administered. They concluded that differences in resistivity were of sufficient magnitude to be important in electrocardiographic studies. This method does not lend itself well to exact quantitation of resistivity of individual tissues and has been subject to the criticism that the frequencies employed in measurement were much higher than those with which we are concerned in electrocardiography. The latter criticism was avoided in the studies of Burger and Van Milaan. They measured the specific resistance of various parts of the body to direct current. The gradient of potential difference drop between electrodes was measured from intermediary electrodes. After computations of the cross sectional area of the tissue investigated, an approximation of the specific resistance of individual tissues was made. In their subsequent investigations with body models, they considered the specific resistivity of lungs to be four times that of other body tissues concerned.
in the conduction of electrical forces generated by the heart to the periphery. A major influence of nonhomogeneity of this magnitude upon the distribution of forces was demonstrated.

Kaufman and Johnston applied special electrodes directly to the tissues of living dogs. From their results, they concluded that "errors in theoretical studies of the form of the electrocardiogram, made by considering the tissues which surround the heart uniform with respect to their specific resistivity, are of no practical importance." Because of the importance and wide acceptance of this study, it has been subjected to critical analysis described below.

![Simple Wheatstone bridge for measurement of resistance](image1)

**FIG. 1.** Simple Wheatstone bridge for measurement of resistance.

The difficulties inherent in the performance of such an experiment as was done by Kaufman and Johnston are great. Thus it would seem advisable to sketch out briefly the principles and technics involved in the performance of this type of measurement.

II. TECHNICAL DIFFICULTIES IN MEASUREMENT OF TISSUE RESISTANCE

An ascending scale of complexity attends each step from the measurement of the resistance of a length of solid wire to that of a volume of electrolyte in simple solution, to that of excised tissue, and finally to living tissue in situ.

Wire. Let us first consider the measurement of the resistance \((R_x)\) of a short length of solid wire. This may be accomplished easily by the use of a Wheatstone bridge, as shown in figure 1. The variable resistor \((R)\) is adjusted to produce a minimum deflection of the meter \((G)\). The resistance of the wire \((R_x)\) is then equal to that of the variable resistor, provided that the values of the fixed resistors \((r)\) are equal. The frequency and voltage of the generator may be varied at will without changing the balance of the bridge.

*Electrolyte.* Suppose next it is desired to measure the resistance between two wires immersed into an electrolytic solution. If this system is attached to the bridge, it is found that the bridge cannot be balanced permanently when direct current is applied because the measured resistance drifts to higher and higher values with the passage of time.

![Modified bridge for measurement of resistance and capacitance](image2)

**FIG. 2.** Modified bridge for measurement of resistance and capacitance.

However, with alternating current instead of direct current, a balance independent of time may be attained by the addition of a variable condenser, \((C)\) (fig. 2). The fact that it has been necessary to add to the bridge in parallel with the variable resistance a capacitance, in order to achieve balance, suggests that the electrolytic system must be represented by some combination of resistances and condensers rather than merely by a resistance as was the case with the solid wire. A more careful investigation will show that the electrolytic solution between the two wires which serve as electrodes has itself a certain capacitance and that this capacitance is equal to the capacitance of the variable condenser, \((C)\), at very high frequencies. As the frequency is decreased, however, the capacitance \(C\) increases though the capacitance of the solution itself remains constant. This effect is due to phenomena which take place at the interfaces between the electrolyte and the electrodes and is called "polarization." Under the influence of the current passing through these inter-
faces, a voltage is developed which is proportional to the amount of current flowing and can be characterized by a resistance. Further investigation shows that this resistance, \( R_{\text{pol}} \), in series with a capacitance \( C_{\text{pol}} \). The resistance \( R_{\text{pol}} \) and the capacity \( C_{\text{pol}} \) of the electrolyte are therefore at each electrode in series with the impedance of the interface represented by polarization resistance \( R_{\text{pol}} \) and polarization capacity \( C_{\text{pol}} \) (fig. 3). The total combination is equal to the \( R-C \) combination in the adjustable arm of the bridge. The values \( R \) and \( C \) are therefore not identical with resistance and capacitance of the electrolyte, for the polarization resistance and polarization capacitance must also be taken into account. The extent to which polarization influences the values of \( R \) and \( C \) depends on temperature, design and material of the electrodes and their distance of separation, concentration of the electrolyte, and quite markedly on the frequency in use. But polarization is nearly independent of the applied voltage so long as this voltage is not too high. Figure 4 shows how polarization influences the measured resistance \( R \) as a function of applied voltage and frequency. So long as the voltage across the electrolytic cell does not exceed approximately 1 to 10 volts, depending on circumstances such as cell design and electrolyte, the resistance is not influenced by a change in the voltage. At higher voltages the polarization resistance is more noticeable with smaller electrode area than with larger area. Resistance as a function of frequency is constant at high values of \( f \) and starts to increase at first slowly and then more and more rapidly when the frequency changes. The effect is again more pronounced with smaller electrode area.

With small electrode area and low frequencies, polarization can be especially disturbing. Under these conditions, it is therefore necessary either to diminish polarization so much that it cannot influence the results or to correct for it by determining its exact influence. The most exact method to date for eliminating polarization resistance is to make two determinations of total resistance with two different spacings between electrodes. By subtracting the measured resistances corresponding to these two different electrode spacings, one obtains a resistance which corresponds to the difference between the two distances at which the measurements were taken, independent of polarization. The method has the disadvantage that two measurements have to be made in order to get one result. It is applicable when the resistance change which takes place upon varying the electrode distance is comparable to the measured resistance itself, that is, when the resistance which corresponds to the difference between two electrode spacings is not small compared to the resistance values measured in the bridge. If this is not the case, the precision of measurement is low and the overall gain in accuracy achieved by elimination of the polarization resistance from the measured resistance is offset by the increased inaccuracy thus introduced into the final resistance value. Another way to avoid polarization is by use of a four electrode system, in which two electrodes introduce current into the medium while two other electrodes measure the voltage drop across a portion of the medium caused by the current flow between the first electrode pair. This measurement can be made with a voltmeter which has a very high input resistance, for example, a vacuum tube voltmeter. Polarization will not be present then at the two voltage measuring electrodes since practically no current is passing through them because of the high input resistance of the voltmeter. However, with this method it is quite difficult to measure tissue capacitance.

![Fig. 3](http://circ.ahajournals.org/)

**Fig. 3.** Equivalent circuit of solution and electrodes with polarization present. \( R_{\text{pol}} = \) solution resistance; \( C_{\text{pol}} = \) solution capacitance; \( R_{\text{pol}} = \) polarization resistance; \( C_{\text{pol}} = \) polarization capacitance.

![Fig. 4](http://circ.ahajournals.org/)

**Fig. 4.** Influence of voltage and frequency on measured resistance in the presence of polarization.

Another method employed in the investigation of biologic material is based on the assumption that the polarization resistance of an electrolytic cell with biologic material is identical with the polarization which the same electrodes show when they are simply immersed in solution of the kind that surrounds the biologic material. For example, an exchange of tissue for physiologic saline solution should not change the electrode polarization. If this assumption is true, the polarization of a special set of electrodes can be measured while immersed in Ringer solution. Resistance and capacitance of this Ringer solution are well known, and since the total resistance, as illustrated in figure 3, has to be equal to the \( R-C \) combination in the variable bridge arm, \( R_{\text{pol}} \) and \( C_{\text{pol}} \) can be determined by calculation. The knowledge of these values then enables us to correct any measured resistances and capacitances of tissue for polarization. As far as we know, no detailed material has been published which bears on the above mentioned assumption that electrodes
show the same degree of polarization when placed in tissue as when placed in Ringer solution. In fact, one of us (H.S.) made a series of measurements with highly concentrated blood and found that the polarization capacitance is much smaller in blood than in serum and further, that it is a function of the volume concentration of the blood. It is, therefore, our belief that material which has been investigated on the aforementioned basis should be reviewed to determine the extent to which a smaller polarization capacitance than originally assumed might affect the results.

In most cases it is much simpler to reduce polarization effects than to correct for them. Platinum electrodes, especially when covered with a layer of platinum black, cause much less polarization than other metal electrodes. Furthermore, if it is possible to make the electrodes large and to maintain a sufficiently great distance of separation between them, it is nearly always possible to suppress the influence of polarization on the resistance at least. In cases where electrode area and distance cannot be sufficiently large, the use of higher frequencies is of value. However, it is necessary in each situation to investigate the extent to which polarization is apparent before final measurements are taken. The simplest way of checking polarization is to change the frequency and see if the resistance of the electrolytic system changes. Electrolytes are frequency independent up to extremely high frequencies (order of 10⁶ cps), so any change in measured \( R \) or \( C \) found with electrodes immersed in an electrolyte while varying the frequency must be caused by polarization at the electrode-electrolyte interface.

The effect of temperature on the electrolyte itself is not great (approximately 2 per cent decrease in resistance per degree centigrade increase). To control this we simply make all the measurements at a constant temperature. The size, shape, and spacing of the wires, and the shape and size of the container will also exert direct influence on the resistance and capacity. To eliminate these variables, after the geometry of the container and electrodes has been fixed, a solution of known specific resistance can be introduced into the container, and resistance and capacity determined at a specific voltage, frequency, and temperature. If we then let \( \rho_s \) represent the resistivity* of the standard solution and \( R_k \) its resistance, while similar quantities with subscript \( x \) stand for the corresponding resistive values of the solution to be tested, the relationship among these quantities may be expressed as follows:

\[
\frac{R_x}{R_k} = \frac{\rho_x}{\rho_k} \quad \text{or} \quad \rho_x = R_x \rho_k / R_k.
\]

The value \( \mu = R_k / \rho_k \) should be dependent only upon the geometry of the cell, and hence it is called the cell constant. Thus by this means one may calibrate any system consisting of electrodes placed in a container of any shape or size, with the aid of a standard solution.

Apparently, therefore, in measuring the resistance of electrolytes, unless we go to sufficiently low voltages, high frequencies, and large electrode areas, \( R \) and \( C \) as measured by the bridge will be functions of the electrode characteristics as well as of the solution. Thus, to measure successfully the \( R \) and \( C \) of the solution only, we must select and adjust the electrode material, size, surface condition, voltage, and frequency; otherwise, our measurements will be distorted by an \( R \) and \( C \) derived from the measuring system.

**Excised tissue.** Now let us pass on to the consideration of the measurement of body tissue. Based on experience gained from the experiments described above, if we wish to carry out a crucial experiment we would probably excise a specimen of the tissue to be investigated, large enough to fill the conductivity cell, place it in the cell, plunge the electrodes into it, adjust the frequency and voltage, make the measurement, and finally calibrate the cell with a known solution. This is a satisfactory procedure and, if correctly executed, will yield the correct results. How, though, should the electrode area, voltage, and frequency be decided upon? Let us first consider factors other than polarization which determine the size of these variables. The volume of tissue available will determine the maximum area for the electrodes. If we are measuring resistance for application to problems in electrocardiography, it would seem desirable to select a frequency in the range of those present in the pattern of voltage fluctuations produced by the heart. This can usually be done. The voltage, in turn, should be as small as it is practical to work with, consistent with the accuracy required in order not to damage or to heat up the tissues. After all of these variables have been decided upon, the apparatus should be checked for polarization by holding constant all but one variable and varying this one, preferably frequency, over a reasonable range (for example, a factor of three on each side of the working value).

* The resistivity \( \rho \) of a homogeneous conducting material is related to its resistance \( R \) by the following formula, where \( l \) = length of material sample and \( A \) = cross-section area.

\[
R = \int_{0}^{l} \frac{\rho \, dl}{A}.
\]

If the material has a constant cross-section area along its whole length, the above formula reduces to \( R = \frac{\rho \, L}{A} \). Thus \( \rho \) is a function of the nature of the material, not of its shape. The unit of resistivity is the ohm centimeter. This is the resistance measured between 2 opposite faces of a centimeter cube of the material.
If the measured $R$ remains constant, one has the assurance that there is only an insignificant polarization effect present. In this sort of experiment, it has been found possible to make the electrode area sufficiently large to meet the frequency and voltage requirements and thus to perform the experiment, though not down to frequencies near those present in the electrocardiogram. Such measurements have been made by Cole, Fricke, Curtis, Rajewsky and many others.

**Tissue in situ.** The measurements described above leave much to be desired in answering the question of whether or not the human body is a homogeneous conductor. Because of the radical change in blood distribution and disturbed physiology of the tissue, there is no way of knowing how much the tissue may be changed when it is removed from its natural environment. Thus it would be much better to measure the tissue in situ. A measurement can, of course, be made by introducing the electrodes into the tissue, but under these conditions there is no cell with measurable boundaries and a new method must thus be found to calibrate the electrodes.

To understand this new situation, let us perform the following experiment. Place a pair of electrodes, of fixed size and maintained a fixed distance apart, into successively larger containers each filled with solution of the same resistivity, and measure $R$ and $C$ between the electrodes. One finds on doing this that as the cell gets large compared to the distance between the electrodes and to their area, the $R$ and $C$ values become independent of size and shape of the container. Thus if the electrodes that are placed in the tissue are sufficiently small and close together the boundaries of the tissue may be neglected, and to calibrate the electrodes, we merely have to place them with the same relative spacing in a "very large" cell filled with solution of known resistivity. A more detailed discussion of this problem is found in reference 10.

In performing this experiment, however, the areas of the electrodes will have to be very much less than they were when the tissue was placed in a conductive cell since they must be small enough not to do serious damage to the organ in which they have been introduced. On the other hand, they must not be so small as to approach the size of the individual cells within the tissue under observation, for then one might get radically different measurements depending upon whether the electrode happens to be right against a cell, or in an interstice between cells. Because of this small electrode size, the minimum frequency at which the measurement can be performed without introducing polarization will be much higher than in the previous experiment.

If we are measuring resistance for application to problems in electrocardiography, it would at first seem necessary to perform the measurement with current of a frequency near to the frequency components present in an electrocardiogram. Thus the excised tissue work and the Kaufman and Johnston experiment have been dismissed by some (e.g., Katz) because they were performed at frequencies much higher than those present in the electrocardiogram. However, it appears possible that measurements made at any frequency up to about 10,000 cycles per second might be applicable to problems in electrocardiography. As discussed above, the effect of frequency begins to appear only at about 10 kilocycles and affects $R$ only to a small degree.

Table 2 shows this effect in more detail for various tissues. In addition frog muscle resistivity has been measured by one of the authors (H.S.) in the region from 100 Kc to 30 cps and has been found to be constant under 10 Kc as discussed above. Measurements have also been made by Schwan on blood from 50 cps to 2500 cps and by Dänzer from 1 Kc up to several megacycles. These measurements show no frequency effect below 100 Kc and at 100 Kc the effect is only about 1 per cent.

Convincing as these reasons may sound, the fact remains that no reliable measurements have actually been made upon living tissue in situ at low frequencies. Thus, we cannot say with certainty that an extrapolation from higher frequencies is really valid.

In performing any of these experiments, the electrodes would, of course, be made of some chemically inert electrical conductor. A convenient material for the purpose is platinum. Besides being chemically inert, platinum has the further advantage that it is possible to increase its effective surface area up to one hundredfold by plating onto it a spongy layer of platinum known as "platinum black." This platinum black layer will then markedly reduce the effect of polarization by increasing the surface area. However, care must still be taken not to let the electrode size decrease to that of a single cell of the tissue to be measured.

**III. Actual Measurements of Tissue in Situ**

The work which most closely approaches the application of the basic principles considered above is that of Kaufman and Johnston. In their experiment they made a pair of platinum-platinum black electrodes from wire 0.25 mm. in diameter insulated with glass down to the tips. They carefully determined the correct electrode spacing such that the tissue into which the electrodes were introduced could be considered infinite in extent compared to the distance between electrodes. They then measured the resistances in situ of tissues of living anesthetized dogs.

As a result of these studies, they drew the
following conclusions. "Measurements on the living tissues of the anesthetized dog show that muscle, normally inflated lung, and liver have resistances of the same order of magnitude. These measurements establish experimentally the validity of the assumption that the errors in theoretical studies of the form of the electrocardiogram made by considering the tissues which surround the heart uniform with respect to their specific resistivity are of no practical importance."

After an analysis of this work, we find it difficult to accept their conclusions for the following reasons:

(1) The divergence and variability of their results do not seem to prove that the resistivity of the tissues is uniform.

Table 3.—Resistivities of Tissues in Ohm Cm. as Reported by Kaufman and Johnston

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Range</th>
<th>Average</th>
<th>No. of Determinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>320–1532</td>
<td>649 ± 163</td>
<td>24</td>
</tr>
<tr>
<td>Liver</td>
<td>222–1083</td>
<td>596 ± 144</td>
<td>13</td>
</tr>
<tr>
<td>Blood</td>
<td>175–235</td>
<td>207 ± 19</td>
<td>4</td>
</tr>
<tr>
<td>Lung</td>
<td>615–897</td>
<td>756 ± 32</td>
<td>16</td>
</tr>
<tr>
<td>Heart</td>
<td>143–307</td>
<td>215 ± 35</td>
<td>12</td>
</tr>
<tr>
<td>Pericardium</td>
<td>405–434</td>
<td>419 ± 14</td>
<td>2</td>
</tr>
<tr>
<td>Fat</td>
<td>1757–2450</td>
<td>2006 ± 207</td>
<td>4</td>
</tr>
<tr>
<td>Serum</td>
<td>98–178</td>
<td>138 ± 40</td>
<td>2</td>
</tr>
</tbody>
</table>

(2) It can be demonstrated that polarization was present to a sufficient degree as to make difficult the interpretation of their results as measurements simply of tissue resistance.

Table 3 is a summary of their results. The two figures for each tissue in the column marked "range" represent the extreme values obtained from the series of measurements. These values are excerpted from their table 3. The next column gives the arithmetic mean and probable error of the single observation of each series of measurements. The last column tabulates the number of determinations that are averaged in each case.

Examination of table 3 shows probable errors of sufficient magnitude to mask approximately a 2 to 1 difference in resistivity between lung, liver and muscle tissues, while the extreme variations among measurements of these three tissues (222–1532) is a factor of 7. Furthermore, if the other types of tissue listed are considered, the difference in conductivity between tissues becomes much greater. At the worst, there is a 20 to 1 resistivity difference shown between serum and fat. The authors regard lung, liver, and muscle as the principle tissues concerned with the transmission of currents derived from the heart. The degree to which this assumption is justified is difficult to estimate. For example, by their results, the resistivity of fat is several times higher than that of other tissues. It seems possible that the irregularly placed fat pads immediately adjacent to the heart might exert an important influence upon the distribution of electromotive forces even if the other tissues were uniform.

However, the other tissues are not uniform, for while lung, liver and muscle conductivity difference is still less than one order of magnitude, an actual difference in tissue resistivities of 4 to 1, 2 to 1, or even less might make a significant difference in the distribution of heart potentials to the surface of the body. In order to evaluate the effect of combining several volume conductors of different resistivities, it would be necessary to know in detail the geometry of the distribution. Even a relatively simple configuration would be quite difficult to analyze mathematically. As previously stated, Burger and Van Milaan noted a very significant change in the distribution of potential differences on a model when a homogeneous medium was altered by the insertion in the space normally occupied by lung, of a mass with resistivity four times that of the original electrolyte.

Let us next consider the problem of polarization in the experiment under discussion. Certain of the results led to the suspicion that polarization had exerted an appreciable influence. If this were the case, the reported figures for tissue resistivity derived not from the tissue but from the measuring system. These suspicions were aroused especially by the following:

1. The capacities recorded when the electrodes were placed in the calibrating solutions were very much greater than one would expect in the absence of polarization, as can be concluded from figure 2 in Kaufman and Johnston's
A reactance of the order of 1.0 ohm would be anticipated in the absence of polarization rather than several hundred ohms as reported.*

2. A variation in cell constant was observed with changes of temperature and test solution concentration. It will be recalled that the cell constant should be independent of these factors.

For these reasons, it was decided to duplicate the electrodes used in this experiment, check them for polarization and at the same time see whether longer electrodes might eliminate polarization if it were found to be present with the short ones. Accordingly, electrodes were made by sealing lengths of 0.25 mm. diameter platinum wires (the diameter used by Kaufman and Johnston) in glass tubes. Two of these electrodes were mounted a fixed distance apart, coated with platinum black, and placed in a liter beaker of physiologic saline solution. They were then connected to a bridge whose operating frequency could be varied from 50 to 500,000 cycles per second. The relative accuracy of the bridge was at least one part in 100,000 for the resistance. (For this purpose, of course, such accuracy was not required, so the results have not been reported to this precision.) Details of the bridge will be described in another paper.16

The experiment was started with long electrodes. R and C were measured with the electrodes placed in the beaker of 0.9 per cent saline solution while the frequency was varied in several steps from 100 to 100,000 cps. The electrodes were then shortened, replatinized, and remeasured. The shortening was done in 5 successive steps, starting with a length of 7.6 mm. and ending with only the cross-section of the wire exposed, as was used by Kaufman and Johnston.

Additional runs were made at one length, varying the voltage and varying the electrode spacing. It was determined that for the particular values we chose, neither of these latter quantities was critical. That is, the measured value of R and C remained constant as both the voltage and the spacing were varied through the operating point to a reasonable distance on each side. The voltage finally chosen was 0.1 volts, while the spacing was 1.25 inches for the first three runs and 0.25 inches for the last two runs.

The results are presented graphically in figures 6 and 7. The series resistance (R_{ser}) and series reactance (X_{ser}) were calculated using the formula in figure 5 where R_{par} and C_{par} are the R and C observed on the bridge with a small correction made in C to allow for a small fixed bridge capacitance. Figure 6 is a plot of R_{ser} against frequency for five electrode lengths. The uppermost curve (marked 0.025 mm.) is the one approximately corresponding to the Kaufman and Johnston electrodes. Figure 7 is a similar presentation showing variation of
series capacitive reactance (\( X_{ser} \)) with frequency for the same series of electrodes.

In order to interpret \( R_{ser} \) and \( X_{ser} \), let us return once more to figure 3, the equivalent circuit of the solution and the electrodes. The actual capacity of the solution can be calculated approximately. It is about 4 micromicrofarads. This is so small compared to the measured capacity, that it may be safely disregarded. Thus, in figure 3, \( C_{sol} \) equals zero.

\[
\begin{align*}
\text{fig. 5. Relationship between simple series and parallel R - C circuits.}
\end{align*}
\]

\[
\begin{align*}
\text{fig. 6. Resistance of Kaufman and Johnston type electrodes of varying lengths vs. frequency when immersed in 0.1 N NaCl solution.}
\end{align*}
\]

Therefore, \( R_{ser} \) equals \( R_{tot} + R_{pot} \). Stated in words, this says that the series resistance is made up of two components, the resistance we are trying to measure, and the polarization resistance, while the capacitive reactance is due completely to polarization of the electrodes.

It is interesting to compare the reactance and resistance values as plotted in figures 6 and 7 with the values determined by Kaufman and Johnston. This comparison is done in table 4 for the frequencies which Kaufman and Johnston used in presenting the impedance loci of their pair of electrodes and for our electrode system having the lengths of 0.23 mm. and 0.025 mm. The columns I, II and III give the values as determined for the Kaufman-Johnston cell, our cell with the length \( l \) = 0.23 mm., and our cell with length \( l \) = 0.025 mm., respectively. A comparison of the

\[
\begin{align*}
\text{fig. 7. Capacitive reactance of Kaufman and Johnston type electrodes of varying lengths vs. frequency when immersed in 0.1 N NaCl solution.}
\end{align*}
\]

\[
\begin{align*}
\text{table 4.—Resistance and Reactance Values at Frequencies 500 to 10,000 cps.}
\end{align*}
\]

Column I: electrode system of Kaufman and Johnston. Columns II and III: our system with electrodes of lengths 0.23 mm. and 0.025 mm. The results shows that the Kaufman and Johnston system has values which are between those measured with our two sets of electrodes. This indicates that the effective length of the Kaufman-Johnston system is somewhere between 0.23 and 0.025 mm. Our presentation in figure

\[
\begin{align*}
\text{table 4—Resistance and Reactance Values at Frequencies 500 to 10,000 cps.}
\end{align*}
\]

\[
\begin{align*}
\text{values as determined for the Kaufman-Johnston cell, our cell with the length \( l \) = 0.23 mm., and our cell with length \( l \) = 0.025 mm., respectively. A comparison of the}
\end{align*}
\]

\[
\begin{align*}
\text{results shows that the Kaufman and Johnston system has values which are between those measured with our two sets of electrodes. This indicates that the effective length of the Kaufman-Johnston system is somewhere between 0.23 and 0.025 mm. Our presentation in figure}
\end{align*}
\]
7 shows that the reactance plotted in a log-log representation decreases linearly as frequency increases (i.e. the reactance decreases as a power function of the frequency). The slope of the log-log representation being approximately \(- \frac{1}{2}\) is in agreement with investigations of other authors pertaining to the influence of electrode polarization on the series reactance.\(^17\) This together with the fact that the absolute values of the reactance agree with those to be expected in the presence of polarization, shows that polarization is responsible for the reactance values in our electrode system. Since the Kaufman and Johnston system in saline shows the same behavior as our system, it is apparent that polarization was responsible for the reactance values in their system also. The relation of resistance to frequency was likewise essentially the same in the two experiments, and in each case behaved as would be predicted in the presence of polarization. Thus, the frequency dependence of both the resistance and the reactance is caused by polarization.

The difference between the R values determined by Kaufman and Johnston at 1 and 10 Kc is about 9 per cent. Our figure 7 shows that the difference between the 10 Kc value and the 100 Kc value contribute an additional 5 per cent to 10 per cent in the same direction. The resistance at extremely high frequencies is undisturbed by polarization. We may thus assume that the resistance values for the electrodes in saline, determined by Kaufman and Johnston at 1 Kc are about 15 per cent too high. This is in agreement with an estimate based upon Warburg's law. It predicts that the polarization resistance changes inversely with the square root of the frequency. The law has been shown to be valid as a first approximation by many authors.\(^18\) By its use we may extrapolate from the difference of 9 per cent as determined by Kaufman and Johnston between 1 and 10 Kc to infinite frequency to determine the true electrolytic resistance which was present in their case. Thus we find that the 1 Kc value differs about 13 per cent from the electrolytic resistor. This figure agrees well with our other estimate.*

Kaufman and Johnston recognized that polarization was present. The measurements which were corrected for polarization, and the amounts of such corrections are not specified. The foregoing discussion used their impedance loci as represented in their figure 2 in the “post biological” case. This case represents the calibration of their electrodes after a tissue measurement had been performed and differs in its resistance and reactance values (roughly 10 per cent and 30 per cent respectively) from the “pre-biological” calibration performed before the tissue measurement. In the postbiological calibration, both reactance and resistance are higher. It is well known that polarization resistance and reactance depend to a high degree on the amount of platinum black which covers the electrodes.\(^18\), \(^19\) This result is produced by an increase in effective electrode area. It seems possible that the introduction of the electrodes into the tissue changed the platinum black deposit, which is quite soft, either by rubbing off some of the platinum black or by adsorption of proteins. Such a change could result in a decrease of the effective area of the electrode. Figure 2 in Kaufman and Johnston’s paper represents one of their calibration tests which they took before and after each measurement. The degree of change between pre- and postbiologic calibrations in their other measurements may be determined by simple subtraction of the pairs of figures in their table 3. These differences, expressed in percentage of the postbiologic measurement, are shown in table 5.

We conclude from these values that the figure 2 in Kaufman and Johnston’s paper represents

\[ R_{\text{post}} = \frac{k}{\sqrt{f}} \]

From this we get for two different frequencies \(f_1\) and \(f_2\)

\[ \frac{R_{\text{post}}(f_1)}{R_{\text{post}}(f_2)} = \sqrt{\frac{f_2}{f_1}} \]

The ratio of \(f_2\) and \(f_1\) is 10:1 in the discussed case. Hence \(R_{f_1} = 3.2R_{f_2}\) or \(R_{f_1} - R_{f_2} = 2.2R_{f_2}\). Kaufman and Johnston found \(R_{f_1} - R_{f_2} = 1890 - 1730 = 160\) ohm. Substituting this figure into the above equations, we find that \(R_{f_1} = 250 \Omega\) which is 13 per cent of \(R\) at 1000 cns.

* Warburg’s Law connects polarization resistance \(R\) with the frequency \(f\) as follows:

\[ R_{\text{post}} = \frac{k}{\sqrt{f}} \]
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a case with a relatively minor difference. In the majority of the other measurements, the difference between the resistance values with the cell immersed in the standard calibration solution before and after the tissue measurement was greater than that shown in their figure 2, and in many cases the difference was very much greater. From this it is reasonable to believe that in the majority of their measurements, the polarization was greater than in the case demonstrated by the authors in figure 2. The discussion of this figure led to our estimate of approximately 15% polarization disturbance when the above pair of electrodes was immersed in a 0.9% saline solution. It must be emphasized that this percentage figure represents only the additional polarization factor in the postbiologic and in the prebiologic measurements in saline, and is not an estimate of the total effect of polarization when the electrodes were used in tissue measurements.

Kaufman and Johnston took certain steps in order to correct for polarization. Their results were computed in the following way: "0.9% saline solution at body temperature was measured in a standard conductivity cell \( R_b \). The cell constant of the conductivity cell \( K \) was known to be 39.37. The same solution was measured with the point electrodes before and after each observation. The pre-biologic constant of the point electrodes was ascertained from the first reading, \( R_p \) (at 1000 cps) by the formula \( \mu = K \frac{R_p}{R_b} \). The post-biologic value

\[
\text{was ascertained from the second reading in the same way. The specific resistance of the tissue was computed by dividing the measured resistance of the tissue at 1000 cps by the cell constant.} \]

We feel that this method is subject to the following criticisms. Consider again our figure 5. By multiplying \( R_{ser} \) with \( C_{ser} \), the formula:

\[
(2\pi f)^2 R_{ser} R_{par} C_{ser} C_{par} = 1
\]

results. The presence of polarization increases both reactance and resistance. Therefore, the reactance values as published by Kaufman and Johnston cannot be too small. In the measurements at 1000 cps, from the tissue studies illustrated in their figures 3, 4 and 5, we find that the ratio \( X_{ser}/R_{ser} \) is in each case smaller than 0.1. In saline solution (their figure 2) it was less than 0.15. Thus the ratio: \( R_{par}/X_{par} = 2\pi f R_{par} \). \( C_{par} \) was, in all these examples, less than 0.15. Its square, which gives the difference between \( R_{ser} \) and \( R_{par} \) in relative units, is therefore less than 2.25 per cent. This demonstrates that it does not matter very much whether we express the resistance values in series resistances \( R_{ser} \) or parallel resistances \( R_{par} \). The difference is always smaller than 2.25 per cent as long as we consider only the frequency 1000 cps. The parallel combination \( R_{col} \) with \( C_{col} \) (fig. 4) may thus be transformed to a series combination without actually changing the resistive component and vice versa. Thus we recognize that, at least for the 1000 cycle values, the resistances of the tissue and of the saline solution, are falsified only by the polarization resistance \( R_{par} \).

Let us now consider what this means for the calibration procedure as applied by Kaufman and Johnston. We can assume that their standard conductivity cell was so constructed that polarization did not noticeably influence resistance measurements. Thus, the specific resistance of the saline solution, used for calibration of the point electrodes, has been deter-

\[
\begin{array}{cccccc}
\text{Muscle} & \text{Liver} & \text{Lung} & \text{Heart} & \text{Pericardium} & \text{Fat} & \text{Blood} & \text{Serum} \\
-2.8 & 13.9 & 3.0 & 7.0 & 7.2 & 11.6 & 20.5 & 82 \\
+2.2 & 37.3 & 7.0 & 7.7 & 32.0 & 28.6 & & \\
25.1 & 23.5 & 7.0 & 6.5 & & & & \\
37.5 & 2.6 & 18.2 & 5.6 & & & & \\
23.2 & 79.0 & 2.7 & 22.5 & & & & \\
2.4 & 168.0 & 25.7 & & & & & \\
11.4 & 12.3 & & & & & & \\
5.7 & 11.6 & & & & & & \\
17.6 & 11.5 & & & & & & \\
102.0 & 15.4 & & & & & & \\
91.0 & & & & & & & \\
\end{array}
\]

\[ \text{Table 5.—Percentage Differences Between Prebiologic and Postbiologic Calibrations (See text)} \]
mined correctly. Immersing the point electrodes in this saline solution we find a resistance

\[ R(\text{sal.}) = \mu \rho(\text{sal.}) + R_{\text{pol}}(\text{sal.).} \]

Introducing the point electrode system in tissue

\[ R(\text{tis.}) = \mu \rho(\text{tis.}) + R_{\text{pol}}(\text{tis.}). \]

These equations provide a basis for the determination of the inherent error in the method for computation of specific resistance as employed by Kaufman and Johnston. We get from the first equation for \( \mu \):

\[ \mu = \frac{R(\text{sal.}) - R_{\text{pol}}(\text{sal.})}{\rho(\text{sal.})} = \mu_0 \left[ 1 - \frac{R_{\text{pol}}(\text{sal.})}{R(\text{sal.})} \right], \]

and from the second one

\[ \rho(\text{tis.}) = \frac{R(\text{tis.}) - R_{\text{pol}}(\text{tis.})}{\mu} = \frac{R(\text{tis.})}{\mu_0} \cdot \frac{1 - R_{\text{pol}}(\text{tis.})/R(\text{tis.})}{1 - R_{\text{pol}}(\text{sal.})/R(\text{sal.})} \]

The determination of the specific resistance, applying the formula \( \rho(\text{tis.}) = \frac{R(\text{tis.})}{\mu_0} \) as they did, leads to a result which has to be corrected for

\[ \frac{1 - \frac{R_{\text{pol}}(\text{tis.})}{R(\text{tis.})}}{1 - \frac{R_{\text{pol}}(\text{sal.})}{R(\text{sal.})}} \]

The resistance of the tissue is high compared with the resistance of the saline solution. The relative error of the discussed method is then given by the ratio \( R_{\text{pol}}(\text{sal.})/R(\text{sal.}) \). As previously discussed, this ratio is about 0.15 and may go up to much higher values. This is the inherent error when no attempt is made to correct for polarization at all. Therefore, the correction method used by Kaufman and Johnston did not eliminate the errors due to polarization.

In view of all the foregoing, we are led to feel that although the Kaufman and Johnston experiment was of considerable value as a first attempt to delineate this complex problem, a considerable amount of further work will be required to reach a definite conclusion concerning the variation of resistance from tissue to tissue.

Conclusions

The conclusions drawn from this survey are as follows: The question of electrical homogeneity of the body is not a yes or no type of question. It is not meaningful to ask simply, “Is the body a homogeneous conducting medium, or is it not?” It is well understood by all who have investigated the problem in recent years that the body is only “relatively” homogeneous. Thus the problem is one of determining whether the inhomogeneity is sufficient to require modification of the theoretic interpretation of electrocardiographic observations, and if so, in what way, and by how much.

Regarded from this viewpoint, the early, relatively qualitative attempts to answer the question are of little value except as indications that the body is not absolutely homogeneous. As between the recent direct and indirect approaches to the problem, it would seem that the direct approach of actually measuring the resistances of the various tissues within the body would be the most straightforward. Measurements of excised tissue indicate variations in resistance of different tissues over quite a wide range, but the figures may not be directly transposed to apply to tissues in situ or to electrocardiographic problems in general. The final step in the direct approach appears to be the measurement of resistance of living tissues in situ. The first attempt in this direction, while valuable as a pioneer effort, has not, in our opinion, yielded an unequivocal result. Thus, we feel the whole matter of relative resistivity of tissues is still an open question.

It has been found convenient to organize electrocardiographic observations by field analysis methods. A mathematical process has thus been introduced to correlate calculated spatial orientations of the electromotive forces generated by the heart with clinical and pathologic observations. Whether a true orientation might be of much greater value than a calculated semi-empirical orientation remains to be established, but a quantitative estimation of the deviation of calculated orientation from
true orientation will necessitate careful consideration of the relative resistivities and spatial arrangements of the various tissues surrounding the heart.

If major inhomogeneities of resistance of the tissues surrounding the heart were found to be present, electrocardiographic interpretation of local abnormalities of myocardial electrical generation might best be studied by the application of circuit analysis, rather than of field analysis methods.

**SUMMARY**

The validity of the field concept of electrocardiographic theory as currently employed is dependent upon the assumption that various body tissues are approximately uniform in electrical conductivity. The estimation of the relative resistivities of tissues has long been a subject of investigation. In this paper, the status of the problem is brought up to date.

1. Various indirect approaches to the problem are discussed. The reasons are indicated for the inconclusive and unconvincing nature of the results.

2. The complexity of the problem of direct measurement is suggested in an outline of the progressive intricacy of electrical measurements step-by-step from wire, to electrolyte in solution, to excised tissue, to tissue in situ.

3. Measurements of the resistivity of excised tissues are briefly reviewed. A wide range of variation has been found. These results cannot be directly applied to the problem of the resistivity of tissues in situ, and hence are of uncertain value in the study of electrocardiographic theory.

4. In the only quantitative study of electrical conductivity of individual tissues in situ, Kaufman and Johnston concluded that inconsequential error results from considering the tissues surrounding the heart uniform with respect to conductivity. We believe that acceptance of these conclusions must be reserved because: (a) From an analysis of the reported resistivity measurements, one finds a variation which would be expected to influence considerably the distribution of potential in an electrical field; and the degree of uniformity necessary "for practical purposes" has not yet been established. (b) From an analysis of their experiment, including actual repetition and extension of certain of the crucial procedures, the reported figures for resistivity have included a large, unknown quantity derived from the electrode system as a result of polarization.

5. It is concluded that: (a) An accurate, quantitative measurement of the resistivity of various individual body tissues in situ has not yet been made. (b) Dependent upon the magnitude of inhomogeneity found, extensive modification of field theory as currently applied to electrocardiography may be necessary. Calculated spatial orientations of the electromotive forces generated by the heart, deviating from true orientations to an unknown degree, may be usefully employed on a semi-empiric basis when correlated with clinical and pathologic observations. True orientations will require carefully consideration of the resistivities and spatial orientations of the various tissues surrounding the heart. (c) Inhomogeneity, if sufficient in magnitude, could prove to be advantageous to electrocardiographic interpretation by providing the conditions necessary for the study of localized abnormalities of electrical generation by the myocardium. If so, circuit analysis methods might be more practical than field analysis methods.

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The Electrical Conductivity of Living Tissues as it Pertains to Electrocardiography: I. Review of the Problem of Homogeneity vs. Nonhomogeneity, an Outline of the Technical Aspects of Tissue Resistivity Measurements, and a Critical and Experimental Analysis of Certain Pertinent Experiments

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