Electric Properties of Tissues

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ELECTRIC PROPERTIES OF TISSUES

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1. INTRODUCTION

The electrical properties of biological tissues and cell suspensions have been of interest for over a century for many reasons. They determine the pathways of current flow through the body and, thus, are very important in the analysis of a wide range of biomedical applications such as functional electrical stimulation and the diagnosis and treatment of various physiological conditions with weak electric currents, radio-frequency hyperthermia, electrocardiography, and body composition. On a more fundamental level, knowledge of these electrical properties can lead to an understanding of the underlying basic biological processes. Indeed, biological impedance studies have long been important in electrophysiology and biophysics; one of the first demonstrations of the existence of the cell membrane was based on dielectric studies on cell suspensions (1).

To analyze the response of a tissue to electric stimulation, we need data on the specific conductivities and relative permittivities of the tissues or organs. A microscopic description of the response is complicated by the variety of cell shapes and their distribution inside the tissue as well as the different properties of the extracellular media. Therefore, a macroscopic approach is most often used to characterize field distributions in biological systems. Moreover, even on a macroscopic level, the electrical properties are complicated. They can depend on the tissue orientation relative to the applied field (directional anisotropy), the frequency of the applied field (the tissue is neither a perfect dielectric nor a perfect conductor), or they can be time- and space-dependent (e.g., changes in tissue conductivity during electropermeabilization).

2. BIOLOGICAL MATERIALS IN AN ELECTRIC FIELD

The electrical properties of any material, including biological tissue, can be broadly separated into two categories: conducting and insulating. In a conductor, the electric charges move freely in response to the application of an electric field, whereas in an insulator (dielectric), the charges are fixed and not free to move. A more detailed discussion of the fundamental processes underlying the electrical properties of tissue can be found in Foster and Schwan (2).

If a conductor is placed in an electric field, charges will move within the conductor until the interior field is zero. In the case of an insulator, no free charges exist, so net migration of charge does not occur. In polar materials, however, the positive and negative charge centers in the molecules do not coincide. An electric dipole moment, p, is said to exist. An applied field, E_0, tends to orient the dipoles and produces a field inside the dielectric, E_p, which opposes the applied field. This process is called polarization. Most materials contain a combination of orientable dipoles and relatively free charges so that the electric field is reduced in any material relative to its free-space value. The net field inside the material, E, is then

$$E = E_0 - E_p. \tag{1}$$

The net field is lowered by a significant amount relative to the applied field if the material is an insulator and is essentially zero for a good conductor. This reduction is characterized by a factor ε_r, which is called the relative permittivity or dielectric constant, according to

$$E = \frac{E_0}{\varepsilon_r}. \tag{2}$$

In practice, most materials, including biological tissue, actually display some characteristics of both insulators and conductors because they contain dipoles as well as charges that can move, but in a restricted manner. For materials that are heterogeneous in structure, charges may become trapped at interfaces. As positive and negative ions move in opposite directions under the applied field, internal charge separations can then result within the material, producing an effective internal polarization that acts like a very large dipole.

On a macroscopic level, we describe the material as having a permittivity, ε, and a conductivity, σ. The permittivity characterizes the material's ability to trap or store charge or to rotate molecular dipoles, whereas the conductivity describes its ability to transport charge (3). The permittivity also helps to determine the speed of light in a material so that free space has a permittivity $\varepsilon_0 = 8.85 \times 10^{-12}$ F/m. For other media,

$$\varepsilon = \varepsilon_r \varepsilon_0. \tag{3}$$

The energy stored per unit volume in a material, u, is

$$u = \frac{\varepsilon E^2}{2}, \tag{4}$$

and the power dissipated per unit volume, p, is

$$p = \frac{\sigma E^2}{2}. \tag{5}$$

We can represent these tendencies by using a circuit model to describe the tissue (1,4). Consider a sample of material that has a thickness, d, and cross-sectional area, A. If the material is an insulator, then we treat the sample as a capacitor with capacitance

$$C = \varepsilon \cdot A/d. \tag{6}$$

If it is a conductor, then we treat it as a conductor with conductance

$$G = \sigma \cdot A/d. \tag{7}$$

A simple model for a real material, such as tissue, would be a parallel combination of the capacitor and conductor. Such a model is referred to as "Debye-type." Other, more complicated models are sometimes used, as will be described later. If a constant (DC) voltage V is applied across this parallel combination, then a conduction current $I_C = GV$ will flow and an amount of charge $Q = CV$ will be stored.

Suppose, instead, that an alternating (AC) voltage was applied to the combination:

$$V(t) = V_0 \cos(\omega t). \tag{8}$$

Here, V_0 is the amplitude of the voltage and $\omega = 2\pi f$, where f is the frequency of the applied signal. The charge on the capacitor plates now is changing with frequency f. This change is associated with a flow of charge or current in the circuit. We characterize this flow as a displacement current:

$$I_d = \mathrm{d}Q/\mathrm{d}t = -\omega C V_0 \sin(\omega t). \tag{9}$$

The total current flowing through the material is the sum of the conduction and displacement currents, which are 90 degrees apart in phase because of the difference in the trigonometric functions. This phase difference can be expressed conveniently by writing

$$V(t) = V_0 \mathrm{e}^{\mathrm{i}\omega t}, \quad \text{where } \mathrm{i} = \sqrt{(-1)} \tag{10}$$

and taking its real part for physical significance. The total current is $I = I_c + I_d$, hence

$$I = GV + C \cdot \mathrm{d}V/\mathrm{d}t = (\sigma + \mathrm{i}\omega\varepsilon)A \cdot V/d. \tag{11}$$

The actual material, then, can be characterized as having an admittance, Y^*, given by

$$Y^* = G + \mathrm{i}\omega C = (A/d)(\sigma + \mathrm{i}\omega\varepsilon), \tag{12}$$

where * indicates a complex-valued quantity. In terms of material properties, we define a corresponding, complex-valued conductivity

$$\sigma^* = (\sigma + \mathrm{i}\omega\varepsilon). \tag{13}$$

Describing a material in terms of its admittance emphasizes its ability to transport current. Alternatively, we could emphasize its ability to restrict the flow of current by considering its impedance, $Z^* = 1/Y^*$, or, for a pure conductance, its resistance, $R = 1/G$.

Factoring $\mathrm{i}\omega\varepsilon_0$ in Equation 11 yields

$$I = (\varepsilon_r - \mathrm{i}\sigma/\omega\varepsilon_0)\mathrm{i}\omega\varepsilon_0 A/d = C\frac{\mathrm{d}V}{\mathrm{d}t}. \tag{14}$$

We can define a complex-valued, relative permittivity

$$\varepsilon^* = \varepsilon_r - \frac{\mathrm{i}\sigma}{\omega\varepsilon_0} = \varepsilon_r' - \mathrm{i}\varepsilon_r'', \tag{15}$$

with $\varepsilon_r' = \varepsilon_r$ and $\varepsilon_r'' = \sigma/(\omega\varepsilon_0)$. The complex conductivity and complex permittivity are related by

$$\sigma^* = \mathrm{i}\omega\varepsilon^* = \mathrm{i}\omega\varepsilon_0\varepsilon_r^*. \tag{16}$$

In physical terms, we can regard the conductivity of a material as a measure of the ability of its charge to be transported throughout its volume by an applied electric field. Similarly, its permittivity is a measure of the ability of its dipoles to rotate or its charge to be stored by an applied external field. Note that if the permittivity and conductivity of the material are constant, the displacement current will increase with frequency whereas the conduction current does not change. At low frequencies, the material will behave like a conductor, but capacitive effects will become more important at higher frequencies. For most materials, however, these material properties are not constant, but vary with the frequency of the applied signal. σ^* and ε^* are frequency-dependent. Such a variation is called dispersion. Biological tissues exhibit several different dispersions over a wide range of frequencies.

Dispersions can be understood in terms of the orientation of the dipoles and the motion of the charge carriers. At relatively low frequencies, it is relatively easy for the dipoles to orient in response to the change in the applied field, whereas the charge carriers travel larger distances over which a greater opportunity exists for trapping at a defect or interface. The permittivity is relatively high and the conductivity is relatively low. As the frequency increases, the dipoles are less able to follow the changes in the applied field, and the corresponding polarization disappears. In contrast, the charge carriers sample shorter distances during each half-cycle and are less likely to be trapped. As frequency increases, the permittivity decreases and, because trapping becomes less important, the conductivity increases (4,5). The dispersion can be characterized by an angular relaxation frequency $\omega_r = 2\pi f_r$ or, equivalently, by a relaxation time $T_r = 1/f_r$.

In a heterogeneous material, such as biological tissue, several dispersions are observed as illustrated in Fig. 1 (4), which shows the variation with frequency of the complex permittivity of Equation 15. For frequencies below about 10 kHz, the α dispersion is caused by counterion polarization along cell membranes. The extremely high values of permittivity reflect the trapping of charges at internal interfaces and are not related to dipole orientation. Note that even at the lowest frequencies a residual or DC conductivity σ_0 exists. The dispersion in the MHz frequency range originates in interfacial polarization of cell membranes, which act as a barrier for passive ion transport between the inner and the outer cell media. Basically, the membrane can be modeled as a parallel combination of a capacitor and a resistor. This so-called beta dispersion occurs in the frequency range where the reactance of the membrane capacitance short-circuits the membrane re-

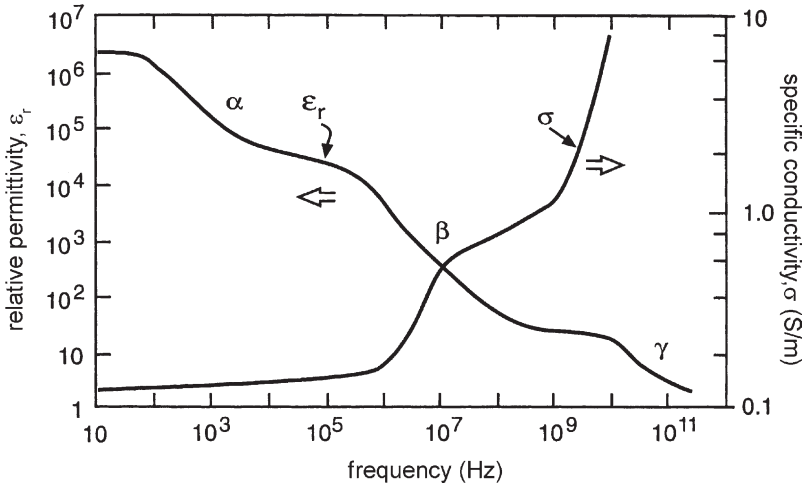

Figure 1. Typical frequency dependence of the complex permittivity of a heterogeneous material such as biological tissues (4).

sistance, so that the external electric field begins to penetrate into the cell interior. Additional contributions to this β dispersion can develop because of the polarization of proteins and other organic macromolecules. In the GHz range (10^9 Hz), γ dispersion is caused by the polarization of water molecules.

The relative importance of the permittivity and conductivity in determining the electrical properties of the tissue can be compared by taking the ratio of the displacement and conduction currents; $I_d/I_c = \omega\varepsilon/\sigma$. For frequencies below the MHz range, this ratio is very low, even with the large increase in permittivity of α dispersion. Hence, at low frequencies, biological tissue is essentially conductive in nature.

For a Debye-type response, which corresponds to parallel *RC* elements, dispersion can be represented as

$$\varepsilon_r^* = \varepsilon_\infty + \frac{(\varepsilon_S - \varepsilon_\infty)}{(1 - \mathrm{i}\omega\tau)} - \mathrm{i}\sigma_0/\omega\varepsilon_0 \tag{17}$$

and

$$\sigma^* = \sigma_\infty + \frac{(\sigma_0 - \sigma_\infty)}{(1 - \mathrm{i}\omega\tau)}, \tag{18}$$

where the time constant, $\tau = 1/RC$. ε_∞ and ε_S refer, respectively, to the relative permittivities at frequencies well above and well below the dispersion. σ_∞ and σ_0 refer, respectively, to the conductivities at frequencies well above and well below the dispersion.

The complexity of the dispersions illustrated in Fig. 1, however, cannot be readily described by three successive, simple Debye relaxations. The widths of the dispersions, in particular, are greater than predicted for simple *RC* parallel elements. A similar situation occurs for most materials. Therefore, in place of a simple *RC* element, a more general, empirical relation, the Cole–Cole response, is used in which

$$\varepsilon_r^* = \varepsilon_\infty + \frac{(\varepsilon_S - \varepsilon_\infty)}{(1 - (\mathrm{i}\omega\tau)^\alpha)} - \mathrm{i}\sigma_0/\omega\varepsilon_0 \tag{19}$$

and

$$\sigma^* = \sigma_\infty + \frac{(\sigma_0 - \sigma_\infty)}{(1 - (\mathrm{i}\omega\tau)^\alpha)}, \tag{20}$$

where α is a parameter that depends on the nature of the material. α is equal to 1 for a Debye-type dispersion and becomes smaller as the width of the dispersion increases.

Two physical interpretations exist for α factor. Some researchers regard a wide dispersion as an indication of numerous Debye-type dispersions with a distribution of simple relaxation times. Other researchers regard the spread as an indication that the fundamental charge-transport and dipole-reorientation processes are essentially cooperative in nature and that, as the degree of cooperation increases, α becomes smaller than 1.

The representation of the dispersion in a circuit model can then be achieved in two ways. First, several Debye-type RC elements connected in series could be used to represent the single, broad dispersion. This process is unwieldy. Second, and more commonly, the circuit model is generalized by the introduction of a "Constant Phase Element" (CPE) with a complex-valued impedance given by

$$Z_{CPE}^* = A(\mathrm{i}\omega)^{-n}, \tag{21}$$

where A is a parameter and $n = \alpha$. This CPE impedance reduces to a simple resistance for $n = 0$ and to a capacitive reactance for $n = 1$. For a diffusive process, $n = 0.5$. The Cole–Cole dispersion can be represented in circuit terms as the parallel combination of a resistor and a CPE. Other dispersions, such as Cole–Davidson and Havrilak–Negami, differ somewhat from Equations 19 and 20 and are used for many materials. However, the Cole–Cole model is generally used for biological materials.

3. COMPLICATIONS IN DIELECTRIC MEASUREMENTS OF TISSUES

The measurement of tissue dielectric properties can be complicated because of several factors, such as tissue inhomogeneity, anisotropy, the physiological state of the tis-

sue, and electrode polarization. Therefore, caution must be used in the design of the measurement procedure.

3.1. Inhomogeneity of Tissues

Tissue is a very inhomogeneous material. The cell itself is comprised of an insulating membrane enclosing a conductive cytosol. A suspension of cells can be regarded at low frequencies simply as insulating inclusions in a conducting fluid. The insulation is provided by the cell membrane. At frequencies in the MHz range, capacitive coupling across this membrane becomes more important. Beginning in this range, the dispersive properties of the membrane and ultimately the cytosol must also be considered. For a thorough discussion of how the dielectric properties of cell suspensions vary with frequency, see Kotnik and Miklavcic (6,7) and Pavlin et al. (8).

In tissue, the cells are surrounded by an extracellular matrix, which can be extensive, as in the case of bone, or minimal, as in the case of epithelial tissue. Tissue does not contain cells of a single size and function. For example, bone contains osteoblasts, osteocytes, and osteoclasts embedded in a collagen/hydroxyapatite matrix as well as bone marrow with stroma cells (9). The tissue is perfused with blood and linked to the central nervous system by neurons. It is thus difficult to extrapolate from the dielectric properties of a cell suspension to those of an intact tissue.

A large discrepancy exists between various data on electrical properties of biological materials found in the literature. Why is there such a wide range of values obtained by different researchers? Excised samples carry along with them various amounts of body fluids, and the lack of standardization of measurement techniques presents its own difficulties and probably widens the range of resistivity values. Moreover, there are seasonal, age, and disease-linked changes as well as those that accompany the physiological function of various biologic materials (10).

3.2. Anisotropy of Tissues

Some biological materials, such as bone and skeletal muscle, are distinctly anisotropic. Therefore, when referring to published conductivity and permittivity values, we need to check the orientation of the electrodes relative to the major axis of the tissue (e.g., longitudinal, transversal, or a combination of both).

Electrical anisotropy is often related to the physiological demands made on the tissue. Major bones and muscles of limbs are designed to produce and support significant longitudinal forces. For example, muscles are composed of fibers that are very large individual cells and are aligned in the direction of muscle contraction. Electrical conduction along the length of the fiber is thus significantly easier than conduction between the fibers in the extracellular matrix because the extracellular matrix is less conductive than the cell. Therefore, muscle tissue manifests typical anisotropic electric properties (4). The longitudinal conductivity is significantly higher than the transverse conductivity even when path differences in the charge transport are taken into account, especially in the low-frequency range (11). A similar anisotropy exists in the long bones of the body where charge transport is easier along the longitudinal axis than transverse to it.

Moreover, tissue anisotropy is frequency-dependent. Namely, if the frequency of the current is high enough, the anisotropic properties disappear (specifically for muscle tissue, that happens in the MHz frequency range). At higher frequencies, charge movement takes place over shorter distances so large-scale structures become less important and capacitive coupling across membranes becomes more important.

A practical problem occurs when measuring the electrical properties of anisotropic materials: how to accurately align the applied electric field and tissue fibers (12). Namely, it has been shown that perfect alignment is crucial for obtaining accurate longitudinal and transverse values. A study on skeletal muscle tissue shows (13) that a 5 degree misalignment from true perpendicular or parallel orientations would result in an 18% overestimate in the perpendicular direction and a 0.4% underestimate in the parallel direction when measuring specific conductivity.

3.3. Physiological Factors and Changes of Tissue

Any changes in tissue physiology should produce changes in the tissue electrical properties (14). This principle has been used to identify or monitor the presence of various illnesses or conditions such as body fluid shift, blood flow, cardiac output, and muscular dystrophy (15) by various impedance diagnostic techniques, such as impedance plethysmography, rheoencephalography, and thoracic impedance cardiograph. For a detailed discussion of the applications of bioimpedance methods in medicine and biotechnology, see (16,17).

Tumors generally have higher water content than normal cells because of cellular necrosis but also irregular and fenestrated vascularization. In addition, differences may exist in the membrane structure. Although an increased conductivity may be used to identify the presence of tumors (18), parameters associated with the fitting of the overall dielectric spectrum to a circuit model may be more reliable (19). In clinical practice, the presence of skin may complicate the interpretation of impedance changes in tissue, such as the breast (20). The higher conductivity of tumors in the MHz frequency range could lead to their selective targeting by radio-frequency hyperthermia treatment (21).

Fat is a poorer conductor of electricity than water. Changes in the percentage of body fat or water are reflected in tissue impedance changes. For example, Biggs et al. (22) estimated the whole-body fat percentage by measurement of the resistivity of the upper arm and leg at 50 kHz. Van Kreel et al. (23) determined the total body water content by measurement of body impedance at several frequencies. This method can even be applied to individual organs. For example, Schaefer et al. (24) correlated the complex permittivity of heart tissue with the level of ischemia.

In an extreme case, one can imagine that tissue death or excision would result in significant changes in electrical properties. Tissue metabolism decreases after the tissue

has been excised and, often, the temperature falls. If the tissue is supported by temperature maintenance and perfusion systems, the tissue may be stabilized for a limited period of time in a living state *in vitro* (*ex vivo*). If the tissue is not supported, however, irreversible changes will occur, followed by cell and tissue death (3). If the blood flow is interrupted, metabolism continues, but in an anaerobic way. Osmosis will cause cell swelling and tissue damage. As a consequence, the extracellular pathways narrow, which typically leads to an increase in the low-frequency impedance (<10 kHz). The time of occurrence of these phenomena is different for different tissues. Decreased blood flow also accounts for changes in tissue resistivity, because blood is a good conductor (12).

Conductivity changes caused by cell and tissue death have been studied by different researchers (10,12,25). The results show that in the first hour after the tissue sample has been excised, the specific conductivity is almost constant, although the change depends on the tissue type. Liver tissue shows changes after only 30 minutes from excision, brain tissue after one hour, and the muscle tissue two hours after excision. In all cases, the conductivity increases with time (10). Changes in the frequency range above 100 Hz are lower and take a longer time to occur. However, because tissue impedance at low frequencies is almost entirely ohmic, permittivity errors do not play any major role. For these reasons, considerable caution must be taken in the interpretation of electrical measurements that were performed on excised tissues.

The electrical properties of tissue also depend on its temperature. The mobility of the ions that transport the current increases with the temperature as the viscosity of the extracellular fluid decreases. A general increase of about 2%/°C occurs in the conductivity of tissue (2) in the frequency range below 1 GHz, up to a temperature of about 40°C. Above that point, the cell membrane begins to deteriorate and allows the cytosol to leak into the extracellular space. The rapid increase of conductivity with temperature was suggested to be used to monitor the progress of hyperthermia treatment (26).

3.4. Electrode Polarization

The measurement of tissue electrical properties, *in vivo*, is complicated (12). Two main sources of systematic error exist, electrode polarization and lead inductance, which become apparent at the lower and higher ends of the frequency range, respectively (27). Electrode polarization is a manifestation of molecular charge organization that occurs at the sample-electrode interface in the presence of water molecules and hydrated ions. In its simplest form, the phenomenon can be modeled as a frequency-dependent capacitor in series with a resistor. The effect increases with increasing sample conductivity, and its consequences are more pronounced on the capacitance than the conductance of ionic solutions as well as biological samples.

In a cell suspension, a counterion layer can form at each electrode. The potential drop in this layer reduces the electric field available to drive charge transport in the bulk suspension, resulting in apparently low suspension conductivity. As the frequency increases, the counterion layer is less able to follow the changes in the applied signal, the potential drop at the suspension/electrode interface decreases, and the apparent conductivity of the suspension increases. The nature of the ions in the layer is determined by both the suspension and the material of the electrode. Hence, changing either the electrode material or the nature of the suspension will modify the magnitude and frequency response of this electrode polarization.

The process is more complicated in tissue. Insertion of electrodes can first cause the release of electrolytes from the surrounding tissue and, later, the development of a poorly conductive wound region may occur. This region can shield part of the electrode from the ionic current and thus reduce the polarization effects compared with an ionic solution equivalent in conductivity to the intracellular fluid. As with a cell suspension, the material of the electrode plays an important part in determining its polarization impedance, the relative importance of which decreases with increasing frequency. It is good practice to measure tissue impedance *in vivo* after waiting a sufficient time for the electrode polarization processes to stabilize. The waiting time will depend, in general, on the nature of the electrodes and the type of tissue. If possible, one should perform a preliminary experiment in which impedance spectra are taken every few minutes until no further changes occur in order to determine the waiting time. A typical time might be on the order of 30 minutes.

Two different electrode setups are used to measure the electric properties of biological materials; the two-electrode method and the four-electrode method (28).

3.4.1. Two-electrode Method. This method is suitable for alternating current measurements. We can not use it as such for direct current measurements because of the electrode polarization that consequently gives incorrect results for the conductivity of the sample between the electrodes. For alternating current measurements, the frequency range over which electrode polarization is important depends to some extent on the system being measured and the electrode material. For cell suspensions, it is important up to nearly 100 kHz, whereas for tissue measured *in vivo*, it is significant only up to about 1 kHz. By varying the separation of the electrodes (29), the contribution of the electrode polarization can be determined and eliminated.

3.4.2. Four-electrode Method. This method can be used for direct and alternating current measurements. Two pairs of electrodes are used: the outer (current) electrodes and the inner (voltage) electrodes. The current from the source passes through the sample. Voltage electrodes of known separation are placed in the sample between the current electrodes. By measuring the current as the voltage drop across a resistor in series with the sample and the voltage drop across the inner electrodes, one can determine the specific conductance of the sample between the inner electrodes. The advantage of this method is that the polarization on the current electrodes has no influence on the voltage difference between the voltage electrodes.

Polarization at the voltage electrodes is negligible for direct and alternating currents because of the high input impedance of the measurement system. Some authors recommend the two-electrode system with a polarization error correction (12). They believe the four-electrode method does not completely eliminate the polarization on voltage electrodes. Some authors report 20% higher results when measuring muscle resistance with the two-electrode technique without error correction (30).

With direct current measurements, care must be taken to use small currents to avoid electrochemical injection of ions at the electrodes and nerve stimulation if the measurements are conducted *in vivo*.

In the MHz frequency range and higher, lead inductance becomes an important factor as the inductive couplings between the leads to each other, to the measuring instruments, and to nearby metal surfaces produce extraneous voltage drops that increase with frequency. It is good practice to identify and then reduce the effects of electrode polarization at low frequencies and lead inductance at high frequencies by replacing the sample to be measured by a saline solution for which the electrical properties should not vary with frequency until the GHz frequency range.

4. DIELECTRIC PROPERTIES OF SOME TISSUES

Large differences exist in electric properties of biological materials. These differences are determined, to a large extent, by the fluid content of the material. For example, blood and brain conduct electric current relatively well. Lungs, skin, fat, and bone are relatively poor conductors. Liver, spleen, and muscle are intermediate in their conductivities. An excellent, detailed review of the electrical properties of various tissues over a wide range of frequencies can be found in the series of three articles by Gabriel et al. (27,31,32). Of particular interest is their use of Cole–Cole response function, given by Equations 19 and 20, to parameterize the dielectric properties of tissue. Such parameterization allows one to calculate a reasonable estimate for the conductivity and permittivity at any frequency for different tissue types.

In the literature, we usually find data on specific conductivity and relative permittivity only at frequencies above 100 Hz. For most tissues, data below that frequency are very scarce or do not exist at all. The reason is not lack of interest, but because electrode effects can produce significant experimental errors for that frequency range. The results that have been published indicate that the impedance at frequencies under 100 Hz is almost entirely resistive and that the capacitive component accounts for only around 10% in most tissues. Between 100 Hz and 100 kHz, most tissues, with the exception of the anisotropic tissues, show almost no frequency-dependence.

We will now briefly present the electric properties of skeletal muscle, tumor, and skin and give the permittivity and specific conductivity ranges of some other tissues. The basic principles described earlier can be used to understand the differences in the electrical properties of various tissues.

4.1. Skeletal Muscle

Data on skeletal muscle are the most abundant in the literature. As a result of the anisotropy of this tissue, the data are usually presented separately for the transverse and longitudinal directions, although some results with random orientation have been reported. In Figs. 2–5 we have compiled some data from the literature (13,27,28,30–34). The tissue samples were taken from different species and the measurements were made at different times after excision and with two different measurement methods (two and four-electrode technique). Therefore, the scatter of the data is rather high, especially in the low-frequency range. The anisotropy is also more pronounced in the low-frequency range. However, these differences are greater in the conductivity data than in the permittivity data, where fewer measurements are available.

4.2. Tumor

A tumor is an abnormal mass of tissue surrounded by one or more normal body tissues. It has no useful function and grows at the expense of healthy tissues. As noted previously, many tumors have a significantly different electrical conductivity and permittivity from normal, surrounding tissues. This fact was attempted to be used in diagnosing tumors. For this reason, electrical impedance measuring and imaging systems are being designed and tested to screen for tumors. A study by Smith et al. (35) on tumors in liver tissue showed a significant difference in electrical properties between healthy liver tissue and tumors. Results show that tumor conductivity is 6–7.5 fold higher than liver conductivity; the difference in permittivity values is 2–5 fold. However, the dielectric properties of tumors cannot be generalized as large differences exist between different tumor types and even between tumors of the same type. Electrical properties also depend a great deal on the size or the development stage of the tumor. Namely, the tumor core can already exert tissue necrosis (35,36).

4.3. Skin

Skin is a very interesting tissue because of its highly inhomogeneous structure, which thus leads to inhomogeneous dielectric properties. Generally, skin has three different layers: the epidermis, dermis, and subcutaneous tissue. The epidermis is the outer layer of skin. The thickness of the epidermis varies in different types of skin. It is the thinnest on the eyelids at 0.05 mm and the thickest on the palms and soles at 1.5 mm (3). The epidermis contains different layers, but the one that defines its dielectric properties the most is the outermost layer, the stratum corneum. That layer is composed of dead, flat skin cells that shed about every two weeks. Although it is very thin (typically around 20 μm), it contributes a great deal to the dielectric properties of the skin. Its high resistivity makes skin one of the most resistive tissues in the human body. Its main function is protection of the body from the external environmental factors. The lower-lying layers, hence the rest of the epidermis (important in the immune response), the dermis (which gives firmness and elasticity),

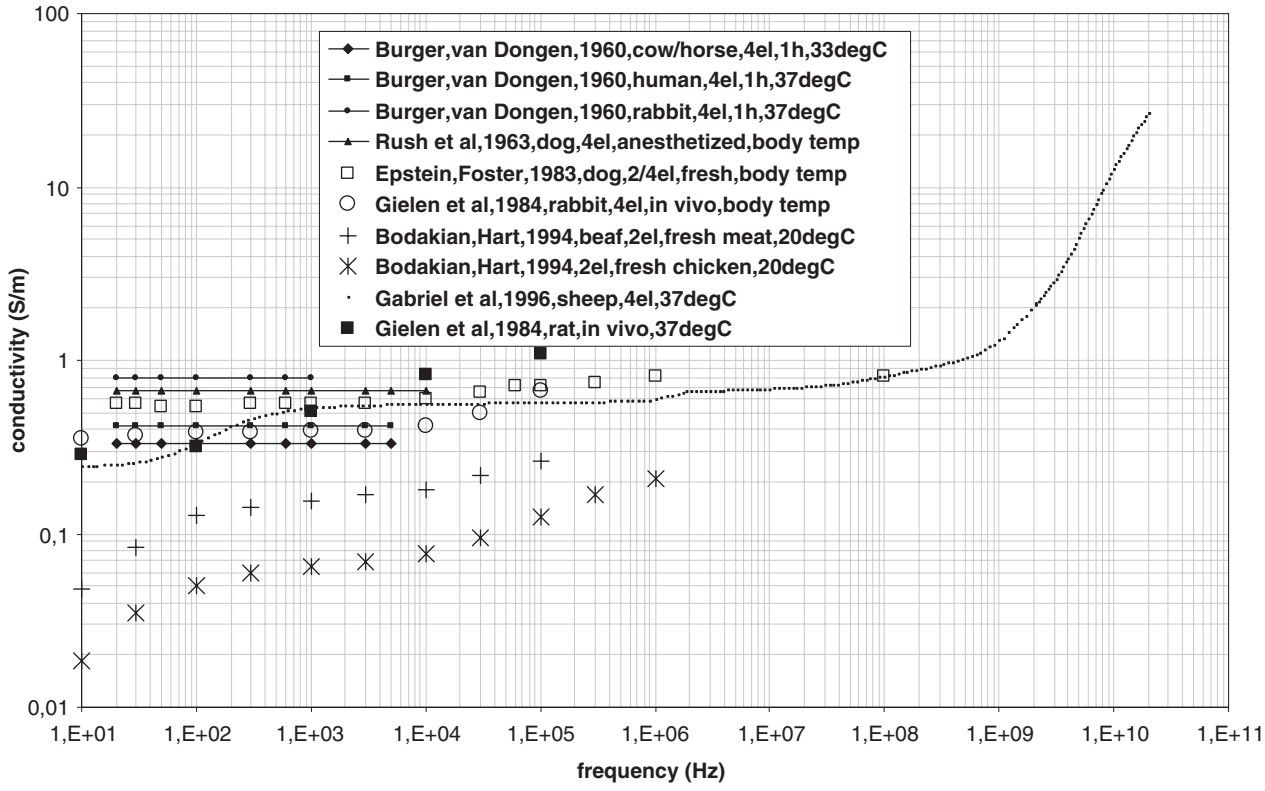

Figure 2. Specific conductivity for skeletal muscle, longitudinal direction.

and the subcutaneous tissue (fat, connective tissue, larger blood vessels, and nerves), all have much lower resistivities.

Especially in the low-frequency range (under 10 kHz), the impedance of skin is dominated by the stratum corneum even though this layer is very thin. Studies show that, for frequencies under 10 kHz, the share of stratum corneum in the total impedance of skin is around 50% (37), but at 100 kHz drops to around 10% (38).

In Figs. 6 and 7, we can see the specific conductivity and relative permittivity, respectively, of intact skin whose dielectric properties are dominated by stratum corneum (diamonds) and lower-lying layers of skin (boxes) (39,40). The measurements were made first on intact skin. The stratum corneum was then removed by cellulose adhesive tape stripping, and the measurements were repeated.

4.4. Dielectric Properties Data Ranges of Some Body Tissues

See Table 1 for data ranges of some body tissues (10,12,13,27,28,30,32–36,39–44).

5. USES OF BIOIMPEDANCE MEASUREMENTS

Today, bioimpedance measurements provide an important method for the noninvasive investigation of tissue structure and properties or for monitoring physiological change (i.e., "static" or "dynamic" human organism properties). One of the main problems one encounters using bioimpedance measurements is still the reliability of the results. The scatter of the data for the electrical parameters of tissues in Figs. 2–7 illustrates the problem of measurement reproducibility. Some of the scatter may result from problems in measuring technique, such as electrode polarization, but some may simply be caused by the individual variability among samples. At present, the relative importance of these two factors in determining the overall scatter is not clear. This scatter makes it difficult to establish criteria of normality or reference value for particular measurement results. However, in spite of the large differences between reported data on dielectric properties of different tissues, we can still find some very useful applications based on the measurements of the differences or changes in the specific conductivity or relative permittivity.

As noted previously, tumor diagnosis is one of the important applications of the measurements of bulk electrical properties of tumors and the surrounding tissues (35). Comparing dielectric properties of tumor and healthy surrounding tissues, one notices that a tumor has a much higher specific conductivity. The tumor tissue is more conductive at low frequencies because of its smaller volume fraction of intact cells, and at high frequencies because of its higher water content and its irregular and fenestrated vascularization. As stated above, the dielectric properties of the tumor and normal tissue appear to be distinctly different, by factors of 6–7.5 in the conductivity and 2–5 in the permittivity. Pronounced differences in the bulk electrical properties of a tumor and the surrounding normal tissue, if consistently present, could lead to a variety of

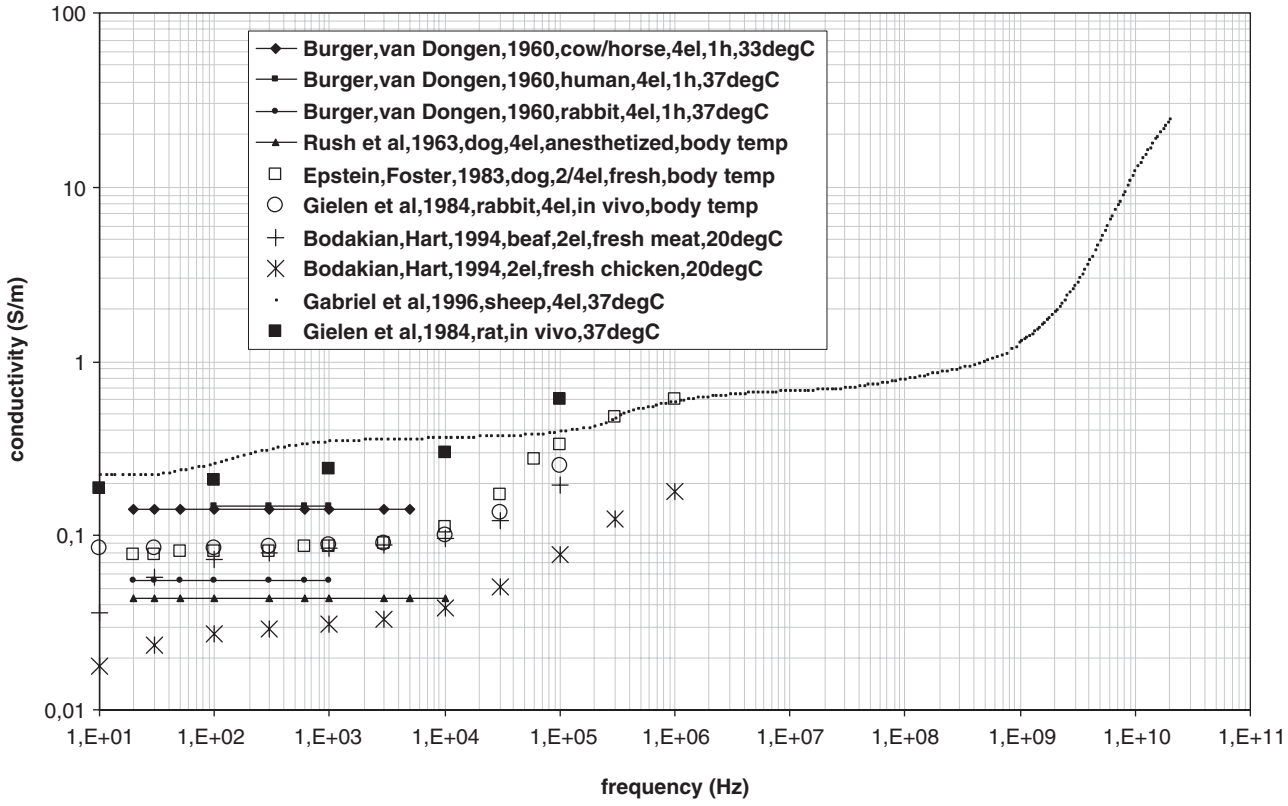

Figure 3. Specific conductivity for skeletal muscle, transverse direction.

clinical applications. Moreover, because we only need to measure the dielectric properties of tumors relative to normal surrounding tissue, the exact values for both are not critical.

Another application is monitoring of the changes in conductivity of the tissue during the process of the electropermeabilization (45–48). To effectively use electroporation in clinical applications, we need to detect whether the target tissue area has been permeabilized. This feedback could then be used to adjust the electroporation parameters during the treatment to make it more efficient. As the specific conductivity of tissue increases when permeabilized, its measurement can be used as an indicator of the level of the electropermeabilization in the tissue. Again, we are only dealing with relative changes in tissue dielectric properties before and after tissue electropermeabilization and not the exact absolute values. A feasibility study for electrical impedance tomography as a means to monitor tissue electroporation has been made (49). In this preliminary demonstration, the electroporated regions in liver were clearly distinguishable. However, more work needs to be done to bring this technique to clinical practice.

Electrical impedance tomography may also be used for other *in vivo* applications such as cryosurgery (50). Cryosurgery is a surgical procedure that destroys tissue by freezing it with a cryogen-cooled surgical probe that is in contact with the targeted tissue. However, although the extent of freezing can be monitored with an array of imaging techniques, the effective application of cryosurgery is still hampered by the fact that the extent of freezing does not necessarily correspond to the extent of tissue destruction. Substantial changes in tissue electrical properties caused by tissue destruction can be monitored by means of electrical impedance tomography in order to evaluate the effectiveness of the procedure.

A more commercially orientated application is measurement of the dielectric properties of meat products that could serve as a monitoring tool of their storage and preparation history (34). Dielectric properties of beef and chicken were measured on both commercially purchased and fresh meat, as well as thawed and cooked meat. The results show that the anisotropy of skeletal muscle is lower in the commercially purchased samples. In addition, the conductivity values are much higher for the commercial samples, particularly at low frequencies. Further changes are produced by freezing and cooking, which indicates that dielectric spectroscopy can be used to determine the storage/preparation history of meat products.

With bioimpedance measurements, it is also possible to estimate the ratio of muscle to fat mass because fat has lower conductivity than muscle tissue (3). The intention is often to determine total body water, extracellular/intracellular fluid balance, muscle mass, and fat mass. Application areas are as diverse as sports medicine, nutritional assessment, and fluid balance in renal dialysis and transplantation. Other applications of the theories of measuring electric properties of biomaterials, ranging from diagnostic to therapeutic applications or laboratory procedures, can be found in the literature (3,16,17).

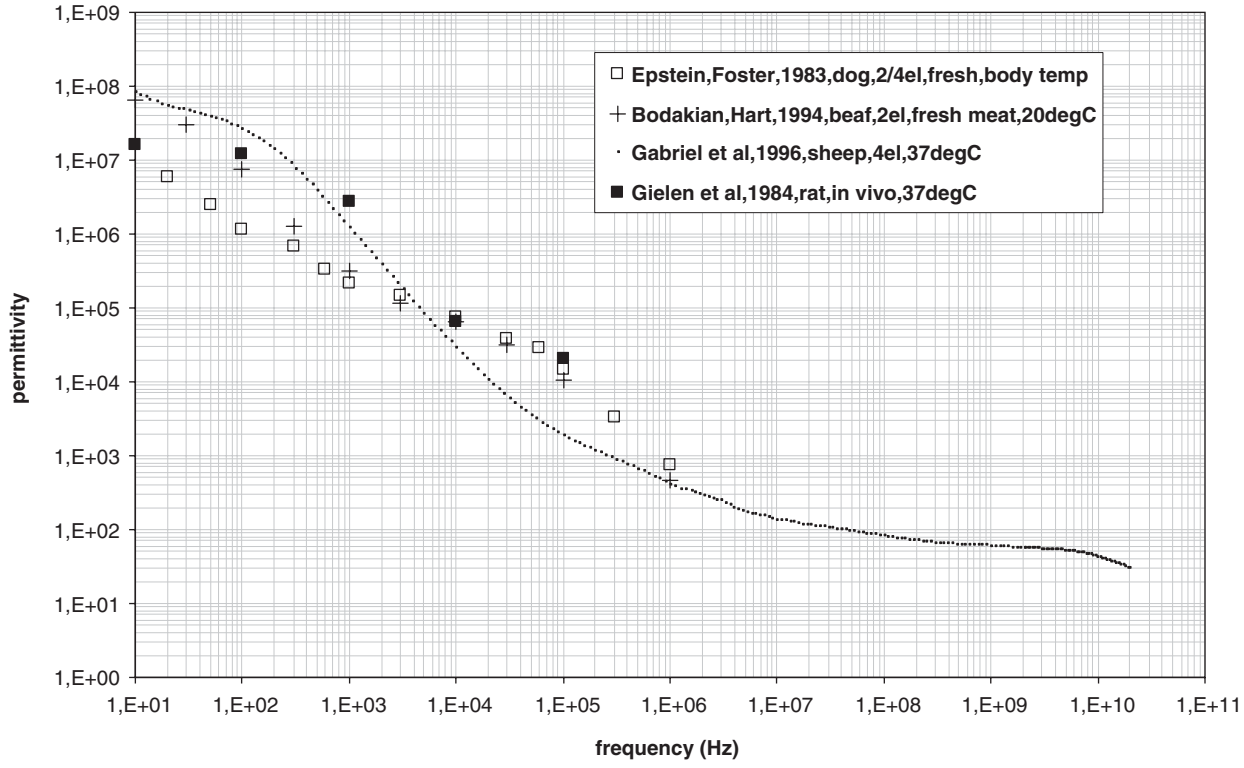

Figure 4. Relative permittivity for skeletal muscle, longitudinal direction.

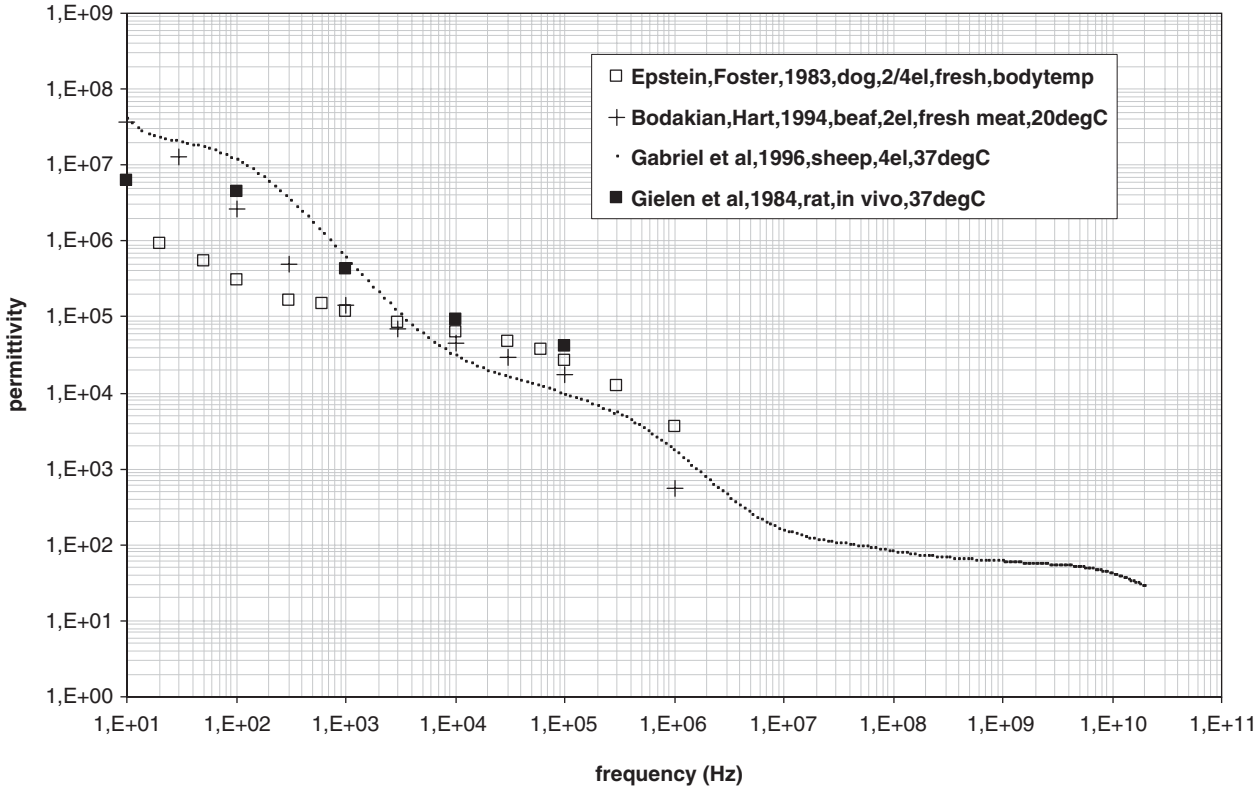

Figure 5. Relative permittivity for skeletal muscle, transverse direction.

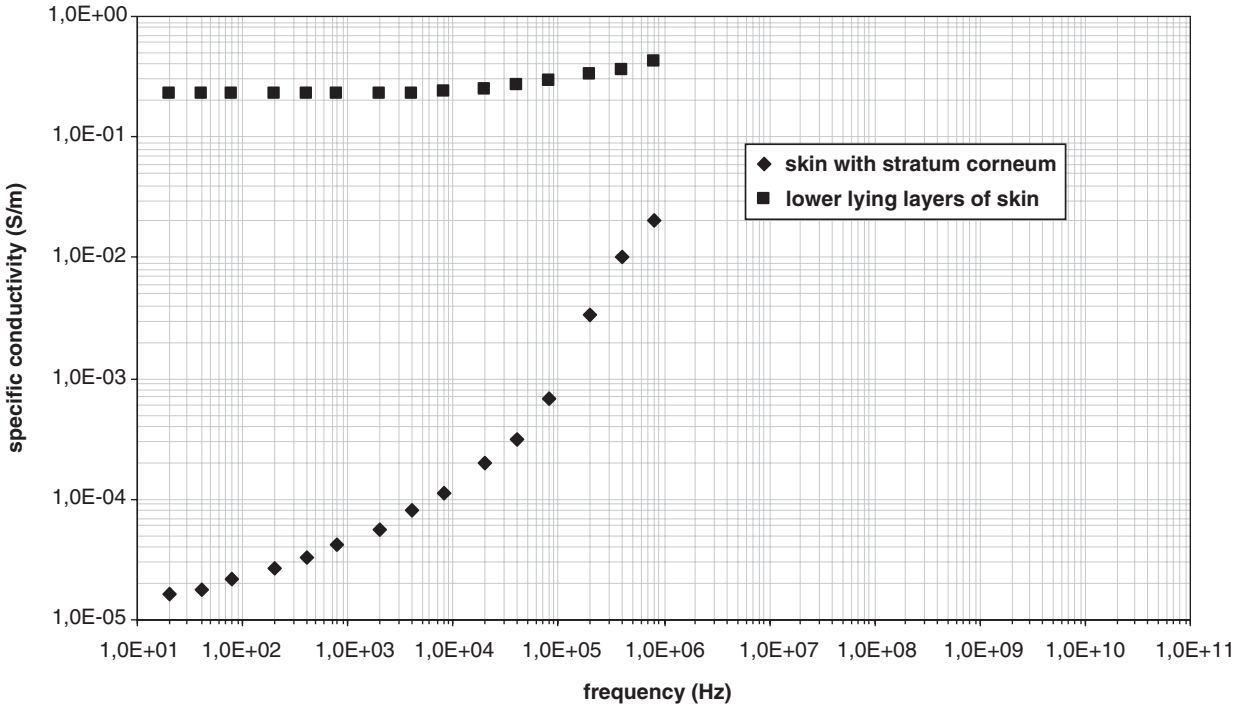

Figure 6. Specific conductivity of intact skin with dominating stratum corneum (diamonds) and lower-lying layers of skin alone (boxes).

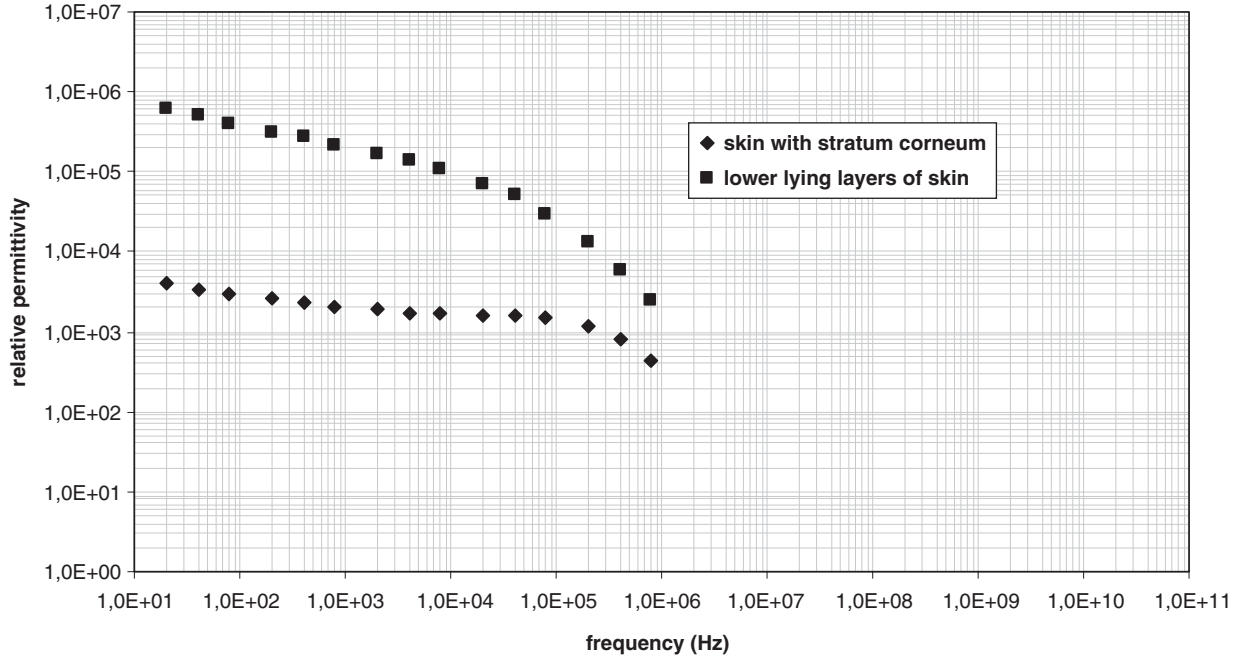

Figure 7. Relative permittivity of intact skin with dominating stratum corneum (diamonds) and lower-lying layers of skin alone (boxes).

Table 1. Data Ranges of Specific Conductivities and Relative Permittivities of Some Other Tissues in the Low-Frequency Range (10,12,13,27,28,30,32–36,39–44)

	Spec. Conductivity (S/m)	Rel. Permittivity
Tumor	0.22–0.4	60 000 (at 1 kHz)
Fat	0.02–0.04	10 000 000 (at 10 Hz)
Muscle		
Transversal	0.04–0.14	1 500 000–40 000 000 (at 10 Hz)
Longitudinal	0.3–0.8	10 000 000–66 000 000 (at 10 Hz)
Skin (dry)	0.00002–0.0002	1400–6600 (at 10 Hz)
Stratum corneum	0.0000125	10 000 (at 2 Hz)
Lower-lying layers	0.227	1 200 000 (at 2 Hz)
Bone	0.01–0.06	40000–1 000 000 (d.c.)
Blood	0.43–0.7	3000 (at 1 kHz)
Heart	0.06–0.4	7 000 000–20 000 000 (d.c.)
Kidney	0.6	30 000 000 (d.c.)
Liver	0.023–0.2	15 000 000–50 000 000 (d.c.)
Lung (inflated)	0.024–0.09	10 000 000 (d.c.)
Spleen	0.043	45 000 000 (d.c.)
Gray matter	0.033	50 000 000 (d.c.)
White matter	0.023	30 000 000 (d.c.)

Specific conductivities are given for direct current measurements (0 Hz); measuring frequencies for relative permittivities are stated in brackets.

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