LOW-FREQUENCY DIELECTRIC PROPERTIES OF BIOLOGICAL TISSUES: A REVIEW WITH SOME NEW INSIGHTS

W. Kuang, S. O. Nelson

ABSTRACT. *Low-frequency dielectric properties of biological tissues, characterized by α- and β-dispersions, are reviewed with emphasis on physical mechanisms. Ion activities, tissue microstructure and composition are discussed. A new mechanism associated with membrane permeability is included. The counterion layer (electrical double layer) phenomenon is discussed. Electrode polarization, which always causes problems with low-frequency dielectric measurements, is also discussed.* ***Keywords.*** *Dielectric properties, Electrical properties, Dielectric dispersion, Dielectric relaxation, Biological tissue, Electrode polarization.*

Radio-frequency and microwave dielectric properties of biological materials have been of interest in connection with high-frequency and microwave dielectric heating, absorption of electromagnetic energy by living systems, and for nondestructive measurements of nonelectrical properties such as moisture content of agricultural products. These applications, including health hazards of energy absorption, medical diagnostics, and electromagnetic heating of tissues for medical purposes have spurred research on determining dielectric properties of such materials. There has been much less concentration on studies of low-frequency properties of biological materials. However, the behavior of materials exposed to low-frequency electromagnetic fields, and a better understanding of these phenomena, may open up new applications and potentially useful measurements of important characteristics in the future. Recent studies, related to material impedance and ion conduction through artificial membranes (Kuang, 1996), have opened an opportunity to present this review of low-frequency properties. With increasing interest in biological engineering opportunities, this review is written to provide some basic background for those interested in pursuing such studies. Readers are referred to the review by Foster and Schwan (1989) and other references cited for greater depth in the subject.

Dielectric properties (electrical properties) of biological tissues have been of interest for many years. Information about tissue structure and composition, for example, water content or presence of a tumor, might be obtained by measuring the dielectric properties of the tissues. The understanding of interactions between electromagnetic energy and biological tissues must be based upon the knowledge of electrical properties of the tissues. This has many practical applications in agriculture, food engineering, and biomedical engineering.

Dielectric properties of biological tissues are frequency-dependent or dispersive. A significant change in dielectric properties over a frequency range, by convention, is called a dielectric dispersion. Although the dielectric properties of the tissues vary greatly from tissue to tissue, their typical behavior is characterized by three distinctly large dielectric dispersions, often referred to as α-, β-, and γ-dispersions (Schwan, 1957), as shown in figure 1. The α-dispersion usually occurs below a few kHz, the β-dispersion in the frequency region from tens of kHz to tens of MHz, and the γ-dispersion in the microwave frequency region. The γ-dispersion, arising mainly from polarization due to reorientation of water molecules, has been well studied and has found many applications in different areas (Thuery, 1991; Nelson, 1991; Metaxas and Meredith, 1983).

Heterogeneous structure and composition and ionic activities inside the tissues dominate the low-frequency dielectric behavior of the tissues. The β-dispersion is well known to arise principally from interfacial polarization (Maxwell-Wagner effect) of biological membrane systems. This was observed mainly by studying blood tissues

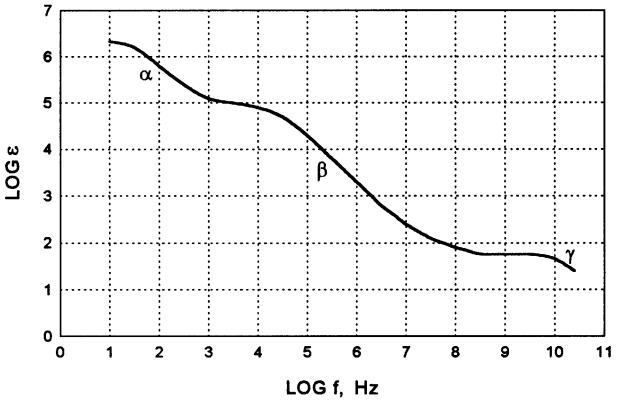

Figure 1–Typical frequency dependence of the dielectric constant of biological tissues. A measurement of muscular tissue (Schwan, 1957).

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(erythrocyte suspensions) early in this century (Hober, 1910; Fricke and Curtis, 1935; Schwan, 1957).

Dielectric studies of biological or any other electrolyte systems below a few kHz were very difficult, mainly because electrode polarization at these frequencies is significant. Partly for this reason, the mechanism of the α-dispersion of biological tissues has not been well understood. It is believed to be associated with a counterion layer (electrical double layer) polarization in the tissues (Foster and Schwan, 1989). Colloidal particle mechanisms have been well studied (Schwarz, 1962; Dukhin and Shilov, 1974; Chew and Sen, 1982; Fixman, 1983; Grosse and Foster, 1987) and should be applicable to tissues due to the presence of many macromolecules, subcellular particles, and cells in the tissues. Another mechanism associated with membrane permeability (ion passage in tissue) was recently investigated (Kuang, 1996).

This review focuses on mechanisms responsible for the low-frequency dielectric dispersions of tissues. General dielectric theory and biological systems are briefly introduced. Mechanisms responsible for the α- and β-dispersions, including a newly proposed mechanism associated with membrane permeability, are discussed next. Finally, the electrode polarization problem is discussed.

General Relaxation Theory

Definitions and Basic Concepts

Dielectric properties of a material basically reflect the electric charge movement inside the material in response to an external electric field. For example, dc conductivity of the material represents its free charge movement forced by the external field. Dielectric response of biological materials is always frequency dependent. A linear response means that the dielectric properties are independent of the external field strength, which is true when the external electric field is not very strong. Assuming a harmonic field **E** is applied to the material, a current density **J** inside the material will be induced:

$$\mathbf{J} = \sigma_s\mathbf{E} + j\omega\varepsilon_0\varepsilon\mathbf{E} = \sigma_s\mathbf{E} + j\omega\varepsilon_0(\varepsilon' - j\varepsilon'')\mathbf{E} \qquad (1)$$

where σ_s is the dc conductivity of the material, ω is the angular frequency of the applied field, ε_0 is the permittivity of free space, ε is the relative complex permittivity of the material, ε′ is the dielectric constant, and ε″ is the loss factor of the material. For biological materials, ε is usually dependent upon frequency. Equation 1 can be written as:

$$\mathbf{J} = (\sigma_s + \omega\varepsilon_0\varepsilon'')\mathbf{E} + j\omega\varepsilon_0\varepsilon'\mathbf{E} = \sigma\mathbf{E} + j\omega\varepsilon_0\varepsilon'\mathbf{E} \qquad (2)$$

where σ is the conductivity of the material. From equations 1 and 2, the electrical properties of a material can be completely represented either by the dielectric constant ε′, loss factor ε″, and dc conductivity σ_s, or by the dielectric constant ε′ and conductivity σ. The two representations are related by:

$$\sigma = \sigma_s + \omega\varepsilon_0\varepsilon'' \qquad (3)$$

For biological materials, σ_s is mainly due to ionic conduction; whereas, $\omega\varepsilon_0\varepsilon''$ results from dielectric relaxation. A common circuit representation is shown in figure 2.

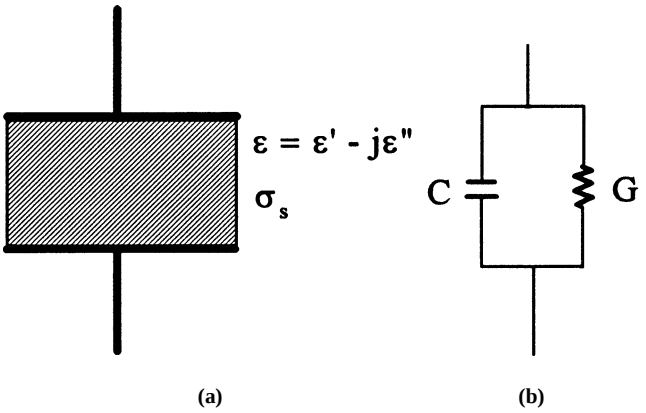


Figure 2–(a) Sample holder of ideal parallel plates; (b) frequency-dependent, measured circuit model, in which C is capacitance and G is conductance.

The dielectric constant and loss factor are not independent of each other. For linear and causal dielectric response, the Kramers-Kronig relations give a necessary connection between them (Kronig, 1926; Daniel, 1967; Böttcher and Bordewijk, 1978), which can be written as:

$$\varepsilon'(\omega) - \varepsilon_\infty = \frac{2}{\pi}\int_0^\infty \frac{u\varepsilon''(u)}{u^2 - \omega^2}\,du \qquad (4)$$

$$\varepsilon''(\omega) = -\frac{2\omega}{\pi}\int_0^\infty \frac{\varepsilon'(u) - \varepsilon_\infty}{u^2 - \omega^2}\,du \qquad (5)$$

where ε_∞ is the dielectric constant at very high frequency, and u is a real variable of integration. These relationships are useful in interpreting the frequency-dependent behavior of dielectrics, based on measurements of the dielectric properties (Jonscher, 1983).

Dielectric Relaxation

Polar molecules in materials will reorient under the influence of an external electric field, thus contributing to the polarization and exhibiting a phenomenon called dielectric relaxation. Free charges inside a heterogeneous material can be blocked by interfaces inside the material, also causing dielectric relaxation. Dielectric relaxation is always a frequency-dependent process. In accordance with the frequency dependence, dielectric properties of a material are characterized by relaxation time constants. A single-time-constant response is described by the Debye equation:

$$\varepsilon = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + j\omega\tau} \qquad (6)$$

where ε_∞ is the dielectric constant at frequencies much higher than $1/(2\pi\tau)$, ε_s is the static, or very low frequency, dielectric constant, and τ is the relaxation time. Note that

this time τ is different from that associated with ionic conduction, $\varepsilon_0\varepsilon_s/\sigma_s$. From equation 6, the dielectric constant and loss factor can be written as:

$$\varepsilon' = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + \omega^2\tau^2} \tag{7}$$

$$\varepsilon'' = (\varepsilon_s - \varepsilon_\infty)\frac{\omega\tau}{1 + \omega^2\tau^2} \tag{8}$$

The conductivity of a dielectric with a single-time relaxation can be expressed (Foster and Schwan, 1989) as follows in agreement with equations 3 and 8:

$$\sigma = \sigma_s + (\sigma_\infty - \sigma_s)\frac{\omega^2\tau^2}{1 + \omega^2\tau^2} \tag{9}$$

where

$$(\sigma_\infty - \sigma_s) = \frac{\varepsilon_0(\varepsilon_s - \varepsilon_\infty)}{\tau} \tag{10}$$

The single-time response is rare except for some pure polar compounds. For dielectric properties with multiple relaxation times, the relative complex permittivity is written as:

$$\varepsilon = \varepsilon_\infty + \frac{\Delta\varepsilon_1}{1 + j\omega\tau_1} + \frac{\Delta\varepsilon_2}{1 + j\omega\tau_2} + \ldots \tag{11}$$

where ε_∞ is the dielectric constant at very high frequency, τ_i is the relaxation time of the ith dielectric dispersion, and $\Delta\varepsilon_i = \varepsilon_{si} - \varepsilon_{\infty i}$ is the dielectric increment for the ith dielectric relaxation. Accordingly, the dielectric constant and loss factor can be written as:

$$\varepsilon' = \varepsilon_\infty + \frac{\Delta\varepsilon_1}{1 + \omega^2\tau_1^2} + \frac{\Delta\varepsilon_2}{1 + \omega^2\tau_2^2} + \ldots \tag{12}$$

$$\varepsilon'' = \Delta\varepsilon_1\frac{\omega\tau_1}{1 + \omega^2\tau_1^2} + \Delta\varepsilon_2\frac{\omega\tau_2}{1 + \omega^2\tau_2^2} + \ldots \tag{13}$$

and conductivity can be written as:

$$\sigma = \sigma_s + \Delta\sigma_1\frac{\omega^2\tau_1^2}{1 + \omega^2\tau_1^2} + \Delta\sigma_2\frac{\omega^2\tau_2^2}{1 + \omega^2\tau_2^2} + \ldots \tag{14}$$

where

$$\Delta\sigma_i = \frac{\varepsilon_0\Delta\varepsilon_i}{\tau_i} \tag{15}$$

For closely distributed relaxation times, which always seems to be the case in a certain frequency region, equation 11 can be replaced by an integral:

$$\varepsilon = \varepsilon_\infty + (\varepsilon_s - \varepsilon_\infty)\int_0^\infty \frac{f(\tau)}{1 + j\omega\tau}\,d\tau \tag{16}$$

where $f(\tau)$ is the distribution function of the relaxation times. The general approach in interpreting experimental data is to infer the $f(\tau)$ and identify the underlying physical mechanisms. Such an attempt involves modeling physical processes and is usually very complicated (Foster and Schwan, 1989).

Another purely empirical approach mainly serves to parameterize the data without clarifying the underlying mechanism. One such widely used equation is (Cole and Cole, 1941):

$$\varepsilon = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + (j\omega\tau)^{1-\alpha}} \tag{17}$$

where, here, $0 \le \alpha \le 1$ is an adjustable parameter, indicating the relaxation time distribution. For example, data from tissues and other biological materials can usually be fitted to the above equation, with α = 0.3 to 0.5 (Foster and Schwan, 1989), which indicates a very broad spectrum of relaxation times.

GRAPHICAL REPRESENTATION

Graphical representation is very useful in showing dielectric relaxation. According to equations 6 to 9, a single-time relaxation (Debye-type) can be graphically shown as in figure 3. Note that only figure 3b includes the influence of the dc conductivity. Other representations for easily showing relaxation behavior can also be obtained from equations 7 and 8. They are:

(a) Cole-Cole plot: $\left(\varepsilon' - \frac{\varepsilon_s + \varepsilon_\infty}{2}\right)^2 + \varepsilon''^2 = \left(\frac{\varepsilon_s - \varepsilon_\infty}{2}\right)^2$

(b) ε' vs $(\omega\varepsilon'')$ line: $\varepsilon' = \varepsilon_s - \tau(\omega\varepsilon'')$

(c) ε' vs (ε'' / ω) line: $\varepsilon' = \varepsilon_\infty + \frac{1}{\tau}\left(\frac{\varepsilon''}{\omega}\right)$

as shown in figure 4, which are useful tools in showing how well experimental data follow the Debye-type relaxation and for estimating dielectric parameters from the experimental data.

Multiple time relaxations, expressed by equations 11 and 14, are composed of many single-time relaxations (Debye-type). These single-time relaxations may overlap, appearing like one dispersion. However, their frequency dependence and Cole-Cole plot become more flattened, compared to a single-time relaxation, as illustrated for one example in figure 5.

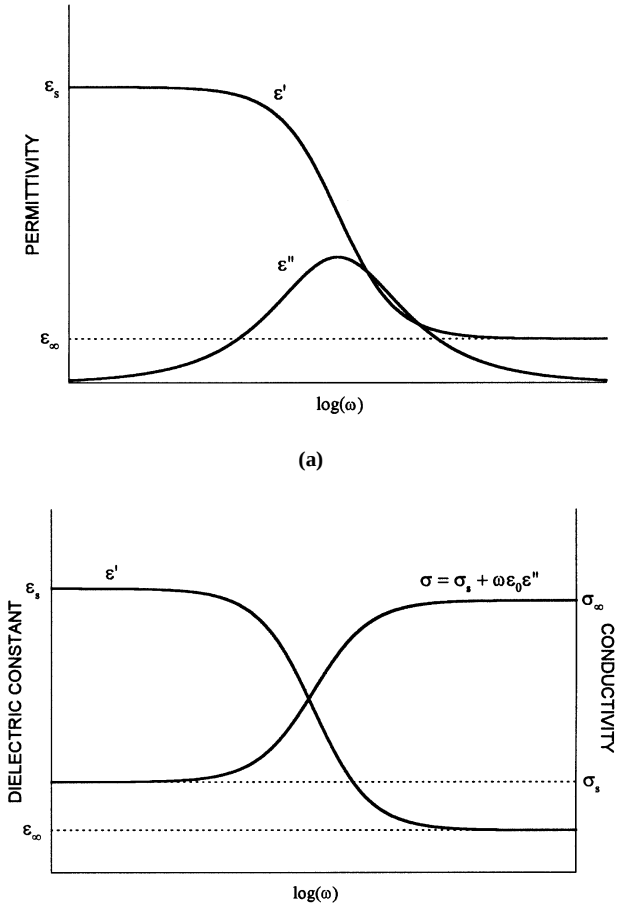


Figure 3–Frequency-dependence of single-time relaxation (Debye-type).

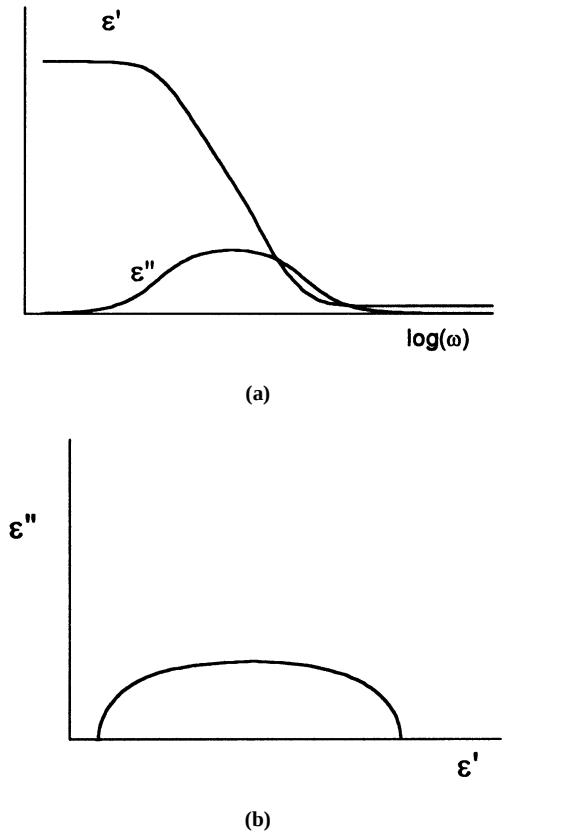


Figure 5–Dispersion arising from overlapping multitime relaxation. (a) frequency-dependence; (b) Cole-Cole plot.

When some of these single-time relaxations are well enough separated, i.e., their relaxation frequencies are far away from each other on the frequency axis, they may form separate dielectric dispersions, as shown in figure 6. Note that each of the separate dispersions may be a multitime relaxation including numbers of single-time relaxations.

INTERFACIAL POLARIZATION (MAXWELL-WAGNER EFFECT)

Interfacial polarization plays an important role at low-frequencies. It arises from induced charge accumulation or blocking at the interface of different materials under an external electric field. Both dilute particle suspensions and multilayer models have been studied. The dilute particle suspension model is appropriate for some tissues, such as blood. For tightly packed tissues, a multilayer model might be more appropriate. In the following, we will explain the interfacial polarization by two layers of different materials, as shown in figure 7. A single-time relaxation (Debye-type) for the two-layer system can be determined as follows. The circuits in figure 7(b), (c), and (d) are all equivalent (Foster and Schwan, 1989: Kuang, 1996), thus:

$$C = C_\infty + \frac{C_s - C_\infty}{1 + \omega^2\tau^2} \qquad (18)$$

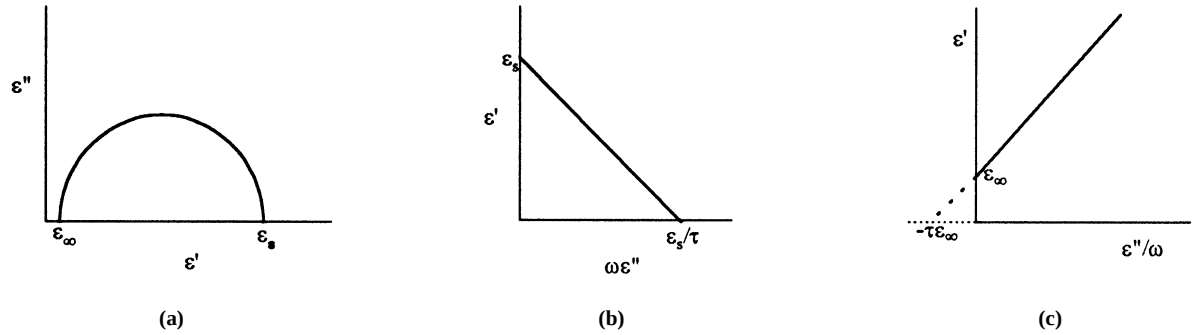
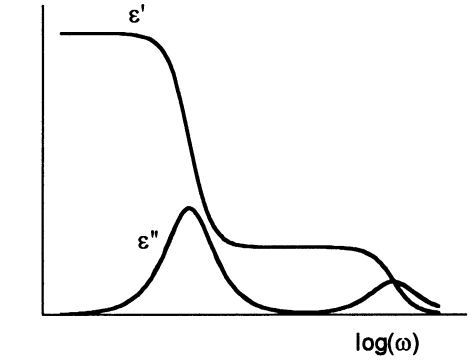
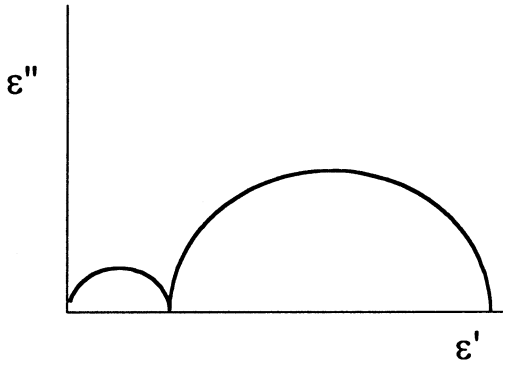


Figure 4–Other representations for a single-time relaxation; (a) Cole-Cole plot (semicircle); (b) ε′ vs ωε″ straight line; (c) ε′ vs ε″/ω straight line.

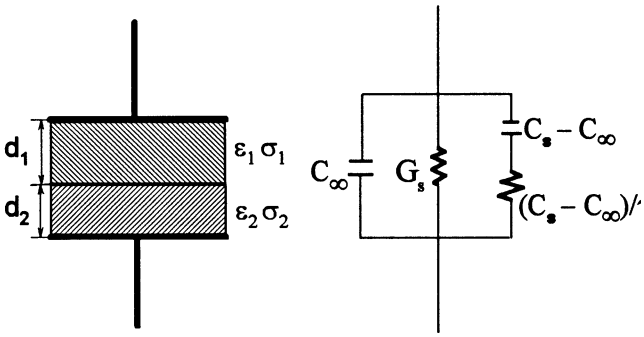


(a)

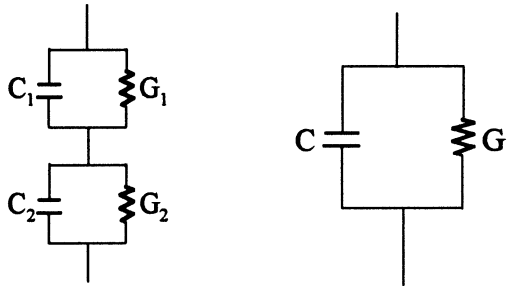


(b)

Figure 6–Dispersion of separate multitime relaxations: (a) frequency dependence; (b) Cole-Cole plot.



(a) (c)



(b) (d)

Figure 7–(a) Two-layer heterogeneous system. (b) An equivalent circuit; $C_1 = \varepsilon_0\varepsilon_1 A/d_1$; $G_1 = \sigma_1 A/d_1$; $C_2 = \varepsilon_0\varepsilon_2 A/d_2$; $G_2 = \sigma_2 A/d_2$. (c) Frequency-independent circuit model. (d) Frequency-dependent, measured circuit model.

$$G = G_s + (G_\infty - G_s)\frac{\omega^2\tau^2}{1 + \omega^2\tau^2} \tag{19}$$

where

$$C_s = \frac{G_1^2 C_2 + G_2^2 C_1}{(G_1 + G_2)^2} \tag{20}$$

$$C_\infty = \frac{C_1 C_2}{C_1 + C_2} \tag{21}$$

$$G_s = \frac{G_1 G_2}{G_1 + G_2} \tag{22}$$

$$G_\infty = \frac{C_1^2 G_2 + C_2^2 G_1}{(C_1 + C_2)^2} \tag{23}$$

$$\tau = \frac{C_s - C_\infty}{G_\infty - G_s} = \frac{C_1 + C_2}{G_1 + G_2} \tag{24}$$

For an ideal parallel-plate model, corresponding electrical properties can be expressed as a single-time relaxation (Debye-type) by equations 7 and 9, where:

$$\varepsilon_s = \frac{(\varepsilon_1\sigma_2 - \varepsilon_2\sigma_1)^2 d d_1 d_2}{(\varepsilon_1 d_2 + \varepsilon_2 d_1)(\sigma_1 d_2 + \sigma_2 d_1)^2} + \varepsilon_\infty$$

$$= \frac{d(\varepsilon_1 d_1 \sigma_2^2 + \varepsilon_2 d_2 \sigma_1^2)}{(\sigma_1 d_2 + \sigma_2 d_1)^2} \tag{25}$$

$$\varepsilon_\infty = \frac{d\varepsilon_1\varepsilon_2}{\varepsilon_1 d_2 + \varepsilon_2 d_1} \tag{26}$$

$$\sigma_s = \frac{d\sigma_1\sigma_2}{\sigma_1 d_2 + \sigma_2 d_1} \tag{27}$$

$$\sigma_\infty = \varepsilon_\infty^2\left(\frac{d_1}{d}\frac{\sigma_1}{\varepsilon_1^2} + \frac{d_2}{d}\frac{\sigma_2}{\varepsilon_2^2}\right) \tag{28}$$

$$\tau = \varepsilon_0\frac{\varepsilon_s - \varepsilon_\infty}{\sigma_\infty - \sigma_s} = \varepsilon_0\frac{\varepsilon_1 d_2 + \varepsilon_2 d_1}{\sigma_1 d_2 + \sigma_2 d_1} \tag{29}$$

where $d = d_1 + d_2$. The complex permittivity is provided by equation 6. The relaxation disappears when $(\varepsilon_0\varepsilon_1)/\sigma_1 = (\varepsilon_0\varepsilon_2)/\sigma_2$ for the two-layer system, i.e., there is no net charge accumulated at the interface under an external electric field.

A three-layer system has two single-time relaxations, but mathematical expressions for them are rather complicated (Hanai et al., 1993; Kuang, 1996). For systems with N-layers, there are (N – 1) time constants, and

graphical representation has to be used to clearly show the dielectric relaxations (Kuang, 1996).

COUNTERION LAYER OR ELECTRICAL DOUBLE LAYER

Ionic activities, represented by conductivity σ, contribute greatly to the low-frequency dielectric dispersion of biological tissues. This is evident upon examining equation 15:

$$\Delta\varepsilon_i = 1.13 \times 10^{11}\tau_i\Delta\sigma_i \qquad (30)$$

Because the relaxation time τ_i of the low-frequency dispersion is often greater than 10 ns, a little change in ion movement (small $\Delta\sigma_i$) will produce a very large dielectric dispersion (large $\Delta\varepsilon_i$).

There are free and bound ions in biological tissue. Ions in bulk electrolyte inside the tissue are free and randomly distributed in the absence of an external electric field. Ions at boundaries are subject to both a concentration gradient and the electric field attributable to a charged surface. These ions are bound and distributed in an orderly fashion, even in the absence of the external electric field, forming a counterion layer or electrical double layer, which plays a very important role at frequencies below a few kHz.

When an object is contacted by an electrolyte, the surface of the object can acquire a net electric charge or potential with respect to the bulk electrolyte. The surface charge can arise from dissociation of surface molecules and/or ion adsorption from the bulk electrolyte solution. A counterion layer or electrical double layer, a term more often found in electrochemistry, was used to describe this interfacial phenomenon (Lipkowski and Ross, 1993; Foster and Schwan, 1989; Martynov and Salem, 1983; Dukhin and Shilov, 1974; Schwan, 1957).

The electrical double layer has been studied for 100 years (Martynov and Salem, 1983; Gileadi et al., 1975). Helmholtz first introduced a capacitor model to describe an electrical double layer at a metallic electrode-electrolyte interface, in which all the excess charge on the metal is located at its surface, and the counterions in the electrolyte solution are held in a rigid layer parallel and very close to the electrode surface. This is probably the origin of the term “double layer”. However, the real physical situation is found to be much more complicated than the Helmholtz capacitor model. The ions in the electrolyte solution are not located in a rigid layer, but are continuously distributed throughout the volume. For metallic electrode-electrolyte interfaces, the electrical double layer never shows a pure parallel-plate capacitor behavior, and they are leaky, nonlinear (potential-dependent), and concentration-dependent. The “leaky” feature involves an electrochemical reaction and simply implies a conducting component in parallel with the pure capacitor.

The electrical double layer is regulated by the ion concentration gradient and electric potential of the charged surfaces. An equilibrium is reached with the ions continuously distributed throughout the volume of the electrolyte solution. The most common treatment is the Boltzmann-type distribution, which was proposed by Gouy and Chapman (Gileadi et al., 1975). An approximate distribution is often exponential, as shown in figure 8. It produces a capacitance, for a unit area, expressed by (van Olphen, 1977):

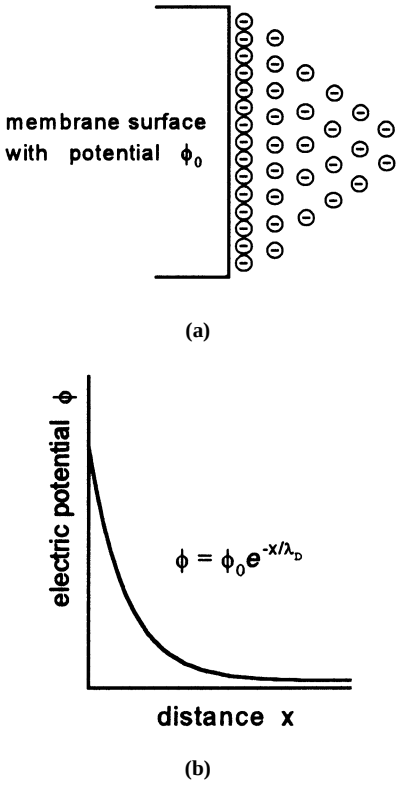


Figure 8–(a) Schematic view of ion concentration in electrical double layer; (b) electric potential distribution in double layer.

$$\varepsilon_0\varepsilon_s/\lambda_D \qquad (31)$$

where ε_s is the dielectric constant of the electrolyte solution; λ_D is the Debye screening length given by:

$$\lambda_D = \sqrt{\frac{\varepsilon_0\varepsilon_s kT}{2z^2q^2n_0}} \qquad (32)$$

where k is the Boltzmann constant, T is the absolute temperature, z is the valence of ions, q is the electron charge, and n_0 is the ion concentration of the electrolyte. The Debye screening length λ_D is usually very small, resulting in a very large capacitance. For 0.15M NaCl electrolyte, λ_D is about 0.8 nm.

If the electrical double layer is “leaky” (involving electrochemical reactions), as for a metallic electrode, the condition will be dynamic, often meaning a time-, potential-, and concentration-dependent process, and causing electrode polarization problems. For most biological materials, the electrical double layer is nonleaky and thus produces a pure capacitance.

BIOLOGICAL TISSUE MICROSTRUCTURE, COMPOSITION, AND PASSIVE ION ACTIVITIES

Biological tissues that form larger functional organs in living organisms consist of cells and an extracellular matrix. The extracellular matrix is a complex network of macromolecules, water molecules, ions, and other small molecules, and it helps to hold cells and different tissues

together. For some tissues, cells can migrate and interact with one another inside the matrix; whereas for other tissues, the cells are held in place by cell-cell adhesions or by a rigid extracellular matrix.

The extracellular matrix of plant tissues is rigid, in the form of cell walls (fig. 9), and cells do not migrate. The extracellular matrix in animal tissues has more forms and more functions. As shown in figure 10, connective tissues and epithelial tissues represent two extremes in the ratio of cells to the extracellular matrix. In connective tissues the matrices are plentiful and cells are sparsely distributed within them. It is the matrix, rather than the cells, that plays more roles in the tissue. In the epithelial tissues, by contrast, cells are tightly bound together into epithelial cell sheet. Extracellular matrices are scanty.

A major component of the tissues is water, accounting for up to 65 to 70% of the mass. Cell membranes are relatively permeable to water molecules, which can move either in or out of cells, regulated by osmotic pressure and the structure of the extracellular matrix. For tissues with rigid extracellular matrices, like plant cell walls and animal bone, which can act against osmotic pressure, it can be expected that most of the water will be kept inside cells or interstitial space of the tissues. It is well known that water

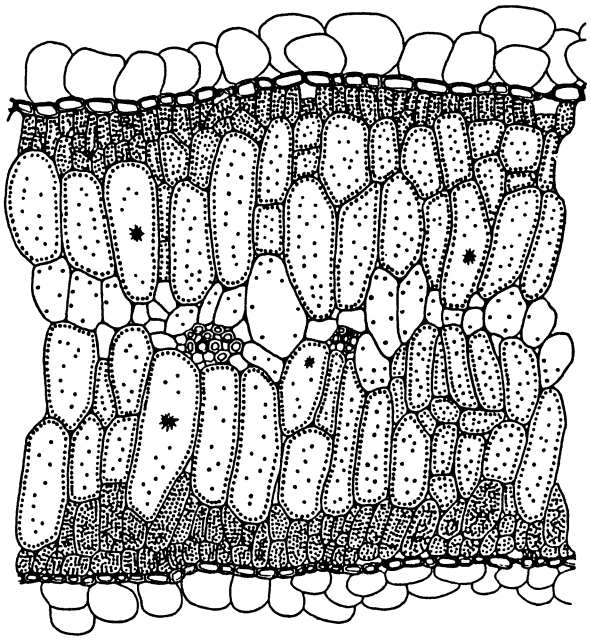


Figure 9–Cross-section of a leaf tissue (Fahn, 1990).

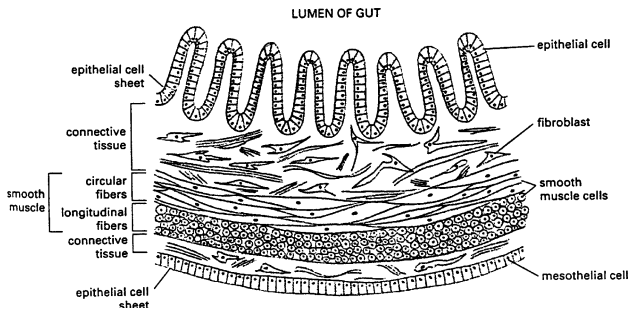


Figure 10–Cross-section of part of animal tissues (Alberts et al., 1994).

molecules contribute directly to higher-frequency dielectric response. However, they also play an important role at low frequencies by affecting ion activities, because ionic activity is an important factor in determining low-frequency dielectric response.

Other important components are cell membranes, “the barrier between life and death” (Fishman,1985). Cell membranes encompass cells and separate the intracellular region from extracellular space, acting as a barrier for ions and large molecules. Such a structure is repeated inside the cells. Many functional organelles such as the nucleus, mitochondrion, and chloroplast, are encompassed by membranes inside the cell and are separated from external fluids. Thus, a rather complicated membrane system is the major feature of a tissue. The membranes have many pores of around 0.5-nm dimensions (Kandel et al., 1991) and are thus semipermeable. The thickness of all the membranes is about 5 nm. The dielectric constant is about 2.3 (Pethig and Kell, 1987).

Free ions in the tissues can move through intermembrane space, and some of them may move through semipermeable membrane pores under external electric fields, contributing to the static conductivity of the tissues.

There are many interfaces between electrolytes and other components of the tissues, and therefore many counterion layers. Ions in the counterion layers, as mentioned previously, are somewhat bound, subject to rather strong built-in electric fields and concentration gradients that confine the ion movement. However, in places where the built-in field is perpendicular to the external field, the ions, under the influence of the external electric field, can move around in the counterion layers.

α-Dispersion of Biological Tissues

Although α-dispersion of biological tissues was observed early (Schwan, 1957), direct studies on the tissues were difficult. It is believed that the α-dispersion is associated with counterion polarization (Foster and Schwan, 1989). However, mechanism details remain unclear. The difficulty lies in the complexity of the tissue structure and composition and the electrode polarization, which often renders true measurements impossible. Following are some studies on several models that can help us gain some insight into the α-dispersion.

Colloidal Particle Mechanism

Dilute suspensions of colloidal particles have been well studied (Grosse and Foster, 1987; Fixman, 1983; Chew and Sen, 1982; Dukhin and Shilov, 1974; Schwarz, 1962). A shell-shaped counterion layer is formed around the colloidal particles, as shown in figure 11. Under an external electric field, the ions move around, acting, as a whole, as a large dipole, compared to polar molecules, which produces a low-frequency relaxation. However, mathematical treatments are rather complicated even under simple physical assumptions. Schwarz (1962) proposed the first theory by studying spherical polystyrene particles in an electrolyte solution. He assumed that the ions under an external electric field are only diffused within the electric double layer, and obtained results that are approximated by the following equations representing the dielectric dispersion for colloidal particles:

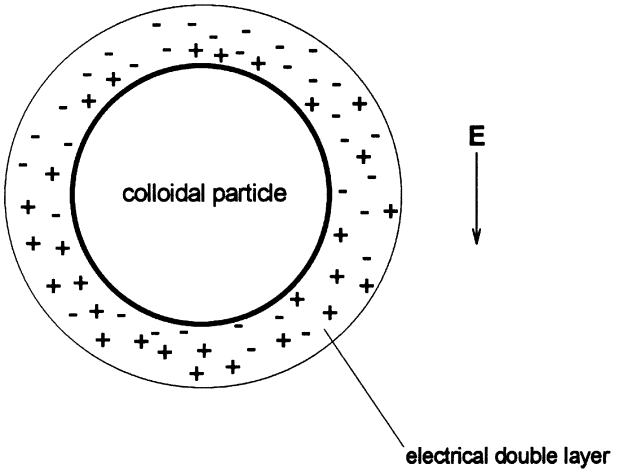


Figure 11–Colloidal particle with electrical double layer.

$$\varepsilon = \varepsilon_\infty + \frac{\Delta\varepsilon}{1 + j\omega\tau} \tag{33}$$

$$\Delta\varepsilon = \frac{9p}{(2 + p)^2} \frac{z^2 q^2 R \sigma_0}{\varepsilon_0 kT} \tag{34}$$

$$\tau = \frac{zqR^2}{2ukT} \tag{35}$$

where p is the volume concentration of the spherical particles, z is the valence of ions, q is the electron charge, R is the radius of the particles, σ_0 is the surface charge density, and u is the ion surface mobility which is adjustable. Schwarz's theory successfully accounted for the amplitude of the dispersion (Foster and Schwan, 1989).

Grosse and Foster (1987) modified Schwarz's theory by assuming a thin conducting layer around the colloidal particles, and that ionic movement under the external electric field is outside the electric double layer. They obtained a broad dispersion with the following parameters:

$$\varepsilon = \varepsilon_\infty + \frac{\Delta\varepsilon}{1 + (j\omega\tau)^{1-\alpha}} \tag{36}$$

$$\Delta\varepsilon = p\varepsilon_s \frac{9\left(\frac{R}{\lambda_D}\right)^2}{16} \frac{2 + \frac{R}{\lambda_D}}{1 + \frac{R}{\lambda_D}} \tag{37}$$

$$\tau = \frac{zqR^2}{ukT} \tag{38}$$

where ε_s is the dielectric permittivity of the electrolyte, λ_D is the Debye screening length of the electrical double layer, and u is the mobility of the ions in the electrolyte, which is different from that of Schwarz. The empirical value for α was found to be about 0.42 while R/λ_D is greater than 10. The measured dielectric increment of suspensions of polystyrene particles was found to be in reasonable agreement with equation 37.

Other categories of studies can also be found (Dukhin and Shilov, 1974; Fixman, 1983; Chew and Sen, 1982). Generally speaking, the colloidal particle mechanism is qualitatively explicit, whereas exact solutions are difficult to obtain even for the simple spherical polystyrene suspension. These theories have not yet been applied to real biological tissues (Foster and Schwan, 1989). Such a mechanism should be applicable to biological tissues, considering that there are many particles such as various macromolecules and even the cell itself in the tissues, which to some extent can be treated as a colloidal particle.

MEMBRANE PERMEABILITY

As mentioned, there are many ion passages in biological tissue, in the form of intermembrane spaces and membrane pores. A dispersion associated with ion permeability of artificial membranes was recently noted (Kuang, 1996; Kuang and Nelson, 1997). This mechanism can be explained by the passage of ions through the membrane pores, as illustrated in figure 12. The built-in electric field of the counterion layer around the passage is perpendicular to the external electric field. Therefore, ions in that part of the counterion layer can move under the influence of the external field. This is much the same as for colloidal particles, just different in geometry. More ion passages will produce a stronger dispersion. This was supported by experimental findings with artificial membranes (Kuang and Nelson, 1997). In fact, the dispersion of artificial membranes was much stronger than that of colloidal particles, because all the ion passages were confined to the plane of the membrane. Further quantitative investigation should be of interest for this mechanism. Because there are many such ion passages in biological tissues, this mechanism should be applicable to the tissues.

Examples for the α-dispersion of tissues are experimentally shown in figure 1 for muscular tissue and in figure 13 for plant leaf tissue, where evidence of the β-dispersion may also be noted.

β-DISPERSION OF BIOLOGICAL TISSUES

Almost all biological tissues, except some tissues such as blood, have membrane systems extending into all the tissues. Ion movement under an external electric field is largely blocked by the membrane systems. Small numbers of ions can go through the tissue by intermembrane or

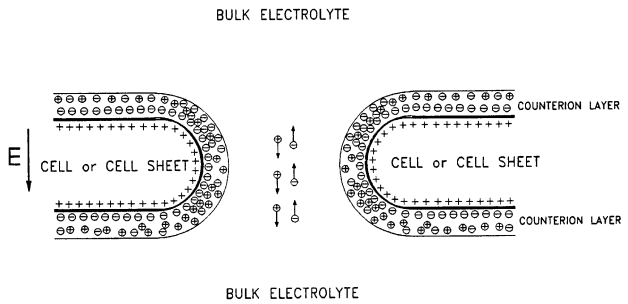


Figure 12–Counterion layer or electrical double layer around a large membrane pore.

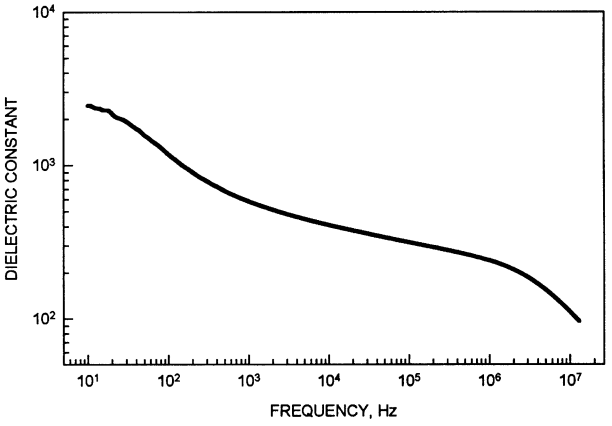


Figure 13–Dielectric constant of Cleyera leaf with conducting gel on electrodes to fill air gap between the leaf and the electrodes (Kuang, 1996).

intercellular spaces, contributing to the static conductivity of the tissue. There will be ions accumulated or blocked at membrane surfaces under the external electric field. A significant β-dispersion arises from such a membrane charging effect (Maxwell-Wagner effect) at frequencies from tens of kHz to tens of MHz, depending on the tissue structure and composition.

Tissue structure is complicated and highly variable. The similarities between tissue building blocks, cells, are more in biological functions and composition and less in their exact structure. This makes physical modeling difficult. Simplifications are always made as in other research areas. There are two models: (1) the particle suspension model, in which cells are considered as particles with regular shapes in electrolyte; and (2) the multilayer model, in which membranes or other partly insulating components are stacked between electrolytes. Mathematical treatment with the particle suspension model is very complicated, requiring physical and hydrodynamic assumptions, which are usually appropriate for tissues like blood. On the contrary, the multilayer model is mathematically simple and precise, and it is still appropriate for most of the tissues; in fact, it is probably more appropriate for tightly-packed tissues such as epithelial tissues, muscular tissues, and most plant tissues. It should be noted that, in the multilayer model, there are ion passages in the membrane layer or insulating layer to facilitate static ion conduction.

Consider a two-layer model composed of a membrane layer of thickness t, and a bulk electrolyte of thickness d, as shown in figure 14. There are ion passages in the membrane, whose relative area is denoted by k. This gives a single-time dispersion according to equations 25 to 29 with the following dielectric parameters:

$$\tau = \varepsilon_0 \frac{\left[(1-k)\,\varepsilon_m + k\varepsilon_b\right] d + \varepsilon_b t}{\sigma_b\,(kd + t)} \qquad (39)$$

$$\Delta\varepsilon = \frac{\varepsilon_m^2\,(1-k)^2 (d+t) dt}{\left\{\left[(1-k)\,\varepsilon_m + k\varepsilon_b\right] d + \varepsilon_b t\right\}(kd+t)^2} \qquad (40)$$

where ε_m is the membrane dielectric constant, ε_b is the bulk electrolyte dielectric constant, and σ_b is the static

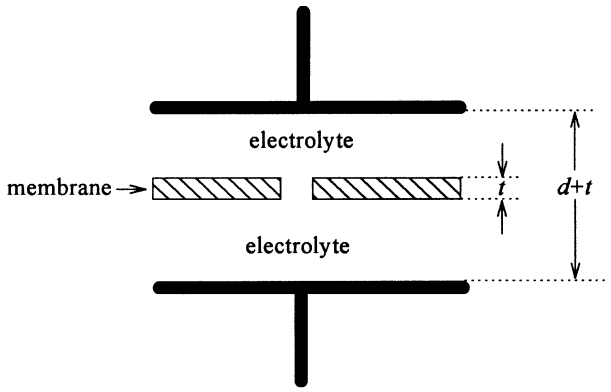


Figure 14–Two-layer tissue model. A′/A = k, where A is the electrode area and A′ is the ion passage area.

conductivity of the bulk electrolyte. When the ion passages make up only a very small portion of the total membrane area, i.e., k << 1, equations 39 and 40 can be simplified as:

$$\tau \approx \varepsilon_0 \frac{\varepsilon_m d + \varepsilon_b t}{\sigma_b t} \qquad (41)$$

$$\Delta\varepsilon \approx \frac{\varepsilon_m^2 (d+t)\, d}{(\varepsilon_m d + \varepsilon_b t)\, t} \qquad (42)$$

From equations 41 and 42, one can see that the ionic conductivity of the inside electrolyte will affect the relaxation frequency but not the dispersion magnitude, i.e., Δε will be mainly determined by the tissue microstructure. Table 1 shows calculations for typical tissue parameters for different values of electrolyte thickness d. Reasonable relaxation frequencies are obtained for β-dispersion. From table 1, one can see that the structural parameter t/d (membrane to electrolyte thickness ratio) has a large impact on β-dispersion. As t/d decreases, the dispersion becomes larger and shifts to lower frequencies. Note that t is the thickness of an insulating layer and does not have to be 5 nm (membrane thickness). For plant tissues, t is usually much larger than 5 nm because of the cell walls. For tissues with dry components or air gaps inside the tissue, t could be very large.

Water Content and Dry Constituents

Because d is the bulk electrolyte thickness and t is the thickness of the dry component, t/d could be related to water content. High t/d corresponds to low water content.

Table 1. β-dispersion for typical tissue parameters based on a two-layer model

Electrolyte Thickness d (μm)	Membrane/ Electrolyte Thickness Ratio (t/d)	Relaxation Frequency 1/(2 πτ) (MHz)	Dielectric Increment Δε
0.01	0.5	327	0.4
0.1	0.05	218	18
1	0.005	50	395
10	5×10^{-4}	6	4526
100	5×10^{-5}	0.6	45924

NOTE: σ_b = 1.5 S/m, ε_m = 2.3, ε_s = 78, t = 5 nm, k << 1.

Excised muscular tissue has a water content amounting to more than 60% and shows a large β-dispersion amounting to 10^5, as shown in figure 1. Broadhurst (1970) and Broadhurst et al. (1987) conducted measurements on several plant leaves with water content from 0% (dry sample) to 80% in the frequency range above 100 kHz. As water content decreased, the β-dispersion was found to decrease. Dry constituents dramatically increase the t/d value and thus decrease β-dispersion, as shown in figure 15 for bulk samples of rice weevils, which included air space between the insects (Nelson and Charity, 1972). As water content goes low, β-dispersion is largely reduced, as shown in figure 16 for wheat (Nelson and Stetson, 1976). This is also true for α-dispersion as shown in figure 17. Animal tissues usually have high water content, and a large β-dispersion can be observed (Foster and Schwan, 1989).

When there is less membrane structure in the tissue, such as dilute blood, water content does not have much influence and β-dispersion is small. This corresponds to increasing k in equation 40, thus reducing the β-dispersion (Δε). As blood cell concentration increases, corresponding to a decrease of k and a significant blocking of the ions, blood also produces significant β-dispersion (Foster and Schwan, 1989).

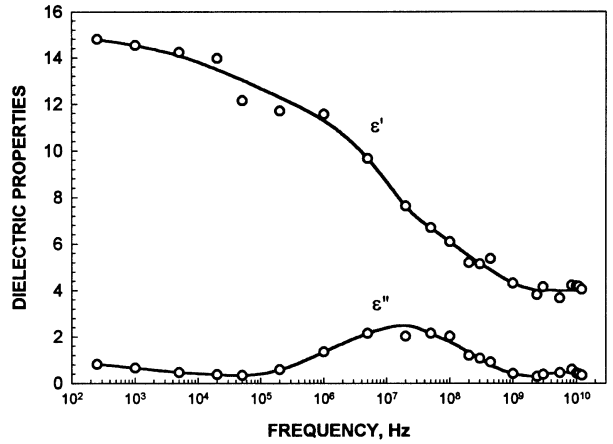


Figure 15–Dielectric properties of bulk sample of rice weevils (Nelson and Charity, 1972).

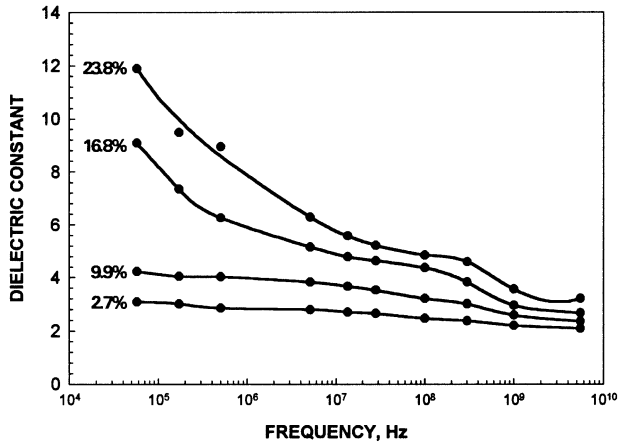


Figure 16–Dielectric constant of bulk wheat for indicated moisture contents (Nelson and Stetson, 1976).

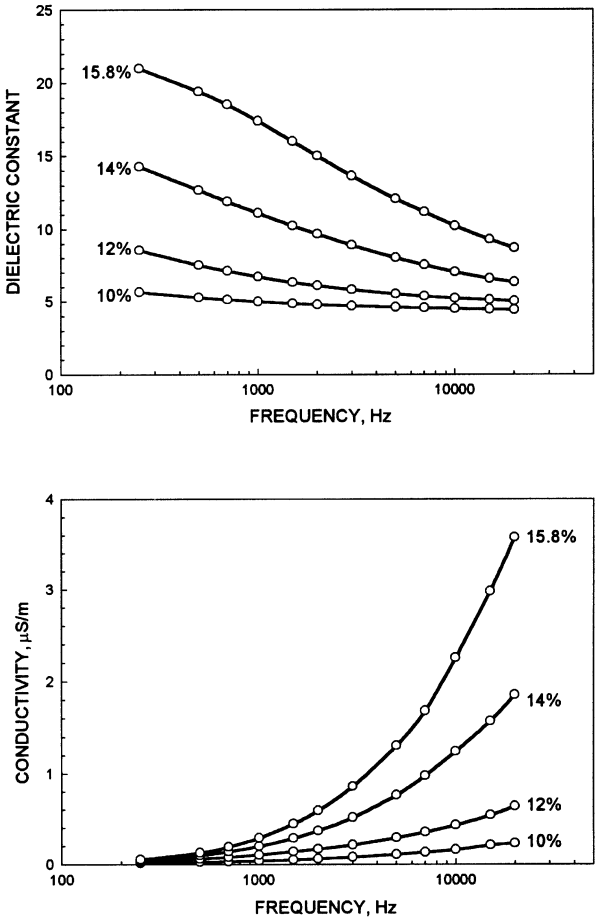


Figure 17–Dielectric properties of bulk wheat at indicated moisture contents (Stetson and Nelson, 1972).

The above discussion, based on the simple two layer model, just provides a general picture of the β-dispersion. In practice, β-dispersions of biological tissue vary greatly, depending upon particular tissue type, orientation, temperature, and experimental setup, etc.

ELECTRODE POLARIZATION

Electrode polarization affects low-frequency measurements on any moist and/or ionic materials by producing an extra impedance in series with the real sample, as shown in figure 18. Caused also by the counterion layer or electrical double layer on the electrodes, this electrode polarization impedance is always

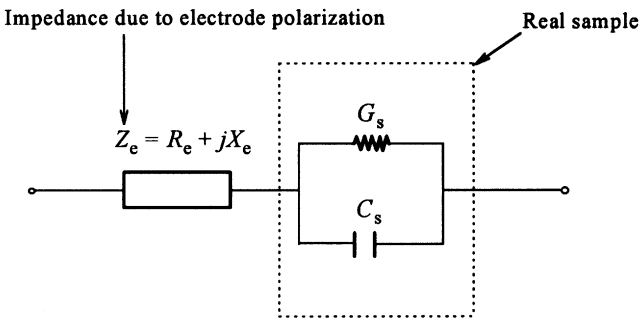


Figure 18–Equivalent circuit for modeling electrode polarization.

frequency-, concentration-, voltage-, and electrode-dependent, which makes low-frequency dielectric studies extremely difficult.

There are two types of techniques to deal with the electrode polarization effect. One is to reduce the relative magnitude of the electrode polarization artifact. That can be done in two ways: lowering the electrode polarization impedance, e.g., using platinum-black electrodes; or using higher impedance samples, e.g., increasing sample thickness. The real effect of this technique is to shift the electrode polarization influence to lower frequencies rather than eliminating it. Another technique is to correct for the electrode polarization impedance. The electrode polarization impedance is determined in some way by measurement, and then this impedance is subtracted from the measured impedance, thus, obtaining real sample data. It usually involves at least two experimental setups, and, by taking the difference, the electrode polarization impedance is supposed to be eliminated. An example is the sample thickness variation technique. This kind of technique is based upon an assumption that the electrode polarization impedance of the two setups are the same. However, the electrode polarization is still dependent on the current density or the applied voltage, and this technique should be used with caution. Many efforts to deal with electrode polarization are described in the literature, where the problems are treated in more detail (Schmukler and Buck, 1992; Schwan, 1966, 1968, 1992 ; Geddes, 1972; Bamford and Compton, 1986).

CONCLUSIONS

A review of the low-frequency dielectric properties (α- and β-dispersions) of biological tissues has been presented, with emphasis on the underlying mechanisms rather than on presentation of various biological tissue data. The α-dispersion is associated with a counterion layer that can take different shapes, depending on the object associated with it. Colloidal particles have a shell-shaped counterion layer producing one kind of α-dispersion. There are many ion passages in biological tissue formed by intermembrane space, intercellular spaces, and membrane pores, around which convex counterion layers are formed. This kind of counterion layer is believed to produce an α-dispersion in the same way as it does for the colloidal particles.

The β-dispersion is mainly caused by membrane structure, which blocks ion movement under an external electric field. When membranes stack more tightly, the β-dispersion becomes weaker. The β-dispersion is largely affected by water content. Less water content of the tissue means more air gaps or dry components, which will also block ion passage in the same way as membranes, thus, reducing the strength of the β-dispersion significantly.

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SYMBOLS

ε_0	permittivity of free space
ε'	dielectric constant
ε''	dielectric loss factor, excluding dc conductivity
ε	relative complex permittivity ($\varepsilon' - j\varepsilon''$), excluding dc conductivity
ε_b	static dielectric constant of bulk electrolyte
ε_m	static dielectric constant of membrane
ε_s	static dielectric constant or permittivity
ε_∞	dielectric constant at very high frequency
σ	conductivity (at certain frequency)
σ_s	dc conductivity or ionic conductivity
σ_b	dc conductivity of bulk electrolyte
τ	relaxation time
λ_D	Debye screening length of electrical double layer
ω	angular frequency
A	area of electrode occupied by sample
C	capacitance
C_s	dc capacitance; sample capacitance
C_∞	capacitance at very high frequency
d	distance between two electrodes; electrolyte thickness
E	electric field
G	conductance
G_s	dc conductance; sample conductance
G_∞	conductance at very high frequency
k	Boltzmann constant; relative ion pore area
n_0	ion concentration of electrolyte
q	electron charge
t	membrane thickness
T	temperature
u	real variable of integration, ion surface mobility
z	valence of ions