#### Master Degree in Information Technology Engineering for Health and Communication: Health Curriculum

# **Electromagnetic interactions and diagnostics**

# DIELECTRIC PROPERTIES OF BIOLOGICAL TISSUES



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- Tissue structure and composition
- Static and time-varying fields
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#### *Tissue structure and composition:*

- Challenging problem complexity and scale
- Microscopic and macroscopic structures
- Analytical and semi-empirical methods

Focus is made on the microwave range of the EM spectrum, for which closed-form solutions are available for simple tissues only.





#### *Tissue structure and composition:*

A biological tissue is a complex structure composed by:

- Water
- lons
- Membranes
- Macromolecules



#### *Tissue structure and composition:*

There are four main types of tissues:

- Epithelial, sheets of cells covering surfaces and lining cavities
- Connective, highly fibrous supporting, connecting and padding bones, cartilage, fat, etc.
- Muscular, elongated fibres able to contract
- Nervous, specialized to receive, process and conduct impulses



**Connective tissue** 



Muscle tissue





Epithelial tissue



Nervous tissue







#### *Tissue structure and composition:*

- Blood could be considered as a fifth class of tissues, but strictly speaking it is a particular kind of connective tissue.
- No pure tissue does exist, e.g., epithelial and connective tissues have nerves.
- All tissues are made of basic elements, the cells, which are made of molecules.
- Each cell consists of a protoplasm mass, including proteins, polysaccharides, nucleic acids and lipids, bounded by a membrane.



#### *Tissue structure and composition:*







#### *Tissue structure and composition:*



Protoplasm molecules:

- Intracellular water (65% of the human body water content)
- Interstitial/intercellular water (28%)
- Extracellular water/plasma (7%)

Those water fluids remarkably vary in ionic composition.



#### *Tissue structure and composition:*

Anion or Cation	Ion	Plasma	Interstitial	Intracellular
	Na+	142	145	10
Cations	K+	4	4	160
	Ca <sup>2+</sup>	5	5	2
	Mg <sup>2+</sup>	2	2	26
TOTAL		153	156	198
	Cl-	101	114	3
	HCO3-	27	31	10
Anions	HPO4-	2	2	100
	Protein	16	1	65
	SO4 <sup>2-</sup>	1	1	20

153

Unit

Atomic weight

*Ionic charge*  $\times$  1000  $\times$  *l* 



TOTAL

198

156

#### *Tissue structure and composition:*

It is interesting to note that, although the human body is mostly composed by water, most of the biological tissues calls for solid or semi-solid structure.

This is due to the presence of bound or hydration water.









A biological tissue can respond to a steady-state field in two basic ways:

- 1) Dielectric polarization
- 2) Static conductivity

The dielectric response is the result of:

- 1) Dipolar polarization, produced by the separation of a pair of opposite charges in either permanent dipoles (in polar molecules as methanol or water) or induced dipoles in non-polar molecules.
- 2) Space charge polarization, generated by free charges in the tissue coming from the outside or at the interfaces.



### Static and time-varying fields:

Dipolar polarization mechanism:

- 1) Atomic
- 2) Electronic
- 3) Orientational

Even though tissues usually contain permanent dipoles, at microwaves the key polarization mechanism is the orientational one. In addition, space-charge polarisation, which is not a dipolar effect, is also important at microwaves, in particular at the interfaces within heterogeneous materials as tissues.







The relative electric permittivity and conductivity of a tissue are the relationship between charge and current densities induced in the tissue when an electric field is applied:

- Electric polarization P
- $\mathbf{D} = \boldsymbol{\varepsilon}_0 \mathbf{E} + \mathbf{P} = \boldsymbol{\varepsilon}_0 \boldsymbol{\varepsilon}_s \mathbf{E} \qquad \mathbf{j} = \boldsymbol{\sigma}_s \mathbf{E} \qquad \bullet \quad \text{Static conductivity} \boldsymbol{\sigma}_s$ 
  - Static relative permittivity  $-\varepsilon_s$

Those apply for isotropic homogeneous media with a linear response to the field, at a macroscopic level, for which higher order terms can be neglected when considering small fields.







To link microscopic to macroscopic polarization is a challenging task since the local field ( $E_1$ ) at the molecular level is very different from the macroscopic one (E). For N non-polar molecules per unit volume characterized by molecular polarizability  $\alpha$ , we have:

$$P_{induced \ dipole} = N \alpha E_{l}$$

Hence, we can get the static relative permittivity:  $\varepsilon_s = 1 + \frac{N \alpha E_1}{\varepsilon_0 E}$ 





By combining the static relative permittivity with a relationship between local microscopic field and the external macroscopic field:

$$\mathbf{E}_1 = \left(\frac{\mathbf{\epsilon}_s + 2}{3}\right) \mathbf{E}$$

Leads to the well-known Clausius-Mossotti formula for the static permittivity:

$$\frac{\varepsilon_{s} - 1}{\varepsilon_{s} + 2} = \frac{N_{0} \alpha}{3 v \varepsilon_{0}}$$
 • Avogadro's number –  $N_{0}$   
• Molar volume – v





A static permittivity model for rigid polar molecules which can orient according to an applied field was proposed by Debye (1929):

$$\frac{\varepsilon_{s}-1}{\varepsilon_{s}+2} = \frac{N_{0}}{3\varepsilon_{0}v} \left(\alpha + \frac{\mu_{g}^{2}}{3kT}\right)$$

- Permanent dipole moment  $\mu_g$
- Temperature T
- Boltzmann's constant k

However, the Debye model failed to reproduce the static dielectric constant of dense fluids.





This issue was overcome by Onsager (1936), who considered the molecule as a point dipole within a spherical cavity of molecular size dispersed in a host medium:

$$\frac{(\varepsilon_{s} - \varepsilon_{med}) (2 \varepsilon_{s} + \varepsilon_{med})}{\varepsilon_{s} (\varepsilon_{med} + 2)^{2}} = \frac{N_{0} \mu_{g}^{2}}{\varepsilon_{o} 9 \kappa T}$$









Further improvements were obtained by accounting for local forces between neighbouring dipoles. In fact, it was shown that fluctuations in the induced molecular moment gave rise to deviations in the local field:

$$\frac{(\varepsilon_{s} - \varepsilon_{med.}) (2 \varepsilon_{s} + \varepsilon_{med})}{\varepsilon_{s} (\varepsilon_{med} + 2)^{2}} = \frac{N_{o} g \mu_{g}^{2}}{\varepsilon_{0} 9 \kappa T v}$$

 Kirkwood intermolecular angular correlation parameter – g

This is called the Kirkwood-Frohlich model for static electric permittivity (1939). For g = 1, the Onsager formula is achieved.





## Static and time-varying fields:

The Kirkwood-Frohlich model was generalized by Cole (1957) for a mixture of polar molecules:

$$\frac{(\varepsilon_{\rm s} - \varepsilon_{\rm med}) (2 \varepsilon_{\rm s} + \varepsilon_{\rm med})}{\varepsilon_{\rm s} (\varepsilon_{\rm med} + 2)^2} = \frac{1}{9 \kappa T v \varepsilon_{\rm 0}} \left\{ g_{\rm A} N_{\rm A} \mu_{\rm g}^2 + g_{\rm B} N_{\rm B} \mu_{\rm g}^2 \right\}$$

where A and B refer to two different polar molecules.







Generally speaking, these models relating microscopic and macroscopic polarizations are not easily applied to biological tissues, which are highly complex dielectric materials, i. e., it is not a straightforward task to measure the molecular dipole moments of their constituent parts.

However, simpler biological materials as animal proteins in solution have been studied, which allow the estimation of molecular parameters necessary to understand the more complex dielectric behavior of the tissue of which they constitute.







Dielectric polarization in a tissue is due to the physical displacement of charge and takes time to develop: relaxation process.

The relaxation process generally becomes apparent when the applied field gives rise to a polarisation mechanism that relaxes at about the same rate as the field alternates.

Dielectric relaxation is the exponential decay with time of the polarization in a dielectric medium when an externally imposed field is removed. The relaxation time can be defined as the time during which the polarisation is reduced to 1/e times its natural value.

Dielectric relaxation results in a medium being dispersive since the dielectric constant decreases as the frequency increases.



#### Static and time-varying fields:



Tissue	T1 (msec)	T2 (msec)
Water/CSF	4000	2000
Gray matter	900	90
Muscle	900	50
Liver	500	40
Fat	250	70
Tendon	400	5
Proteins	250	0.1-1.0
Ice	5000	0.001

#### Hydrogen nuclei, B = 1.5 T







At microwaves, the most important relaxation process involves orientational polarization, where single or cluster of molecules rotate depending on their inner structures and outer arrangement.

It may happen that polar molecules do not rotate rapidly enough to attain equilibrium with the field:

- When molecules are very large;
- When a very high-frequency field applies;
- When high-viscosity tissues are in place.







In these cases, an out-of-phase polarization component arise that results in thermal dissipation of energy through ohmic current. This means that the tissue has non-negligible absorption properties, i. e., a lossy medium is in place which calls for complex-valued dielectric constant and electric conductivity:

$$\varepsilon^* = \varepsilon' - j \varepsilon''$$
  $\sigma^* = \sigma + j \omega \varepsilon_0 \varepsilon'$ 

The dielectric loss  $\varepsilon''$  and the electric conductivity  $\sigma$  contain contributions from both dielectric relaxation and ionic conductance processes. They are impossible to separate at a single frequency but their relative contributions can be isolated using information obtained at different frequencies.





In the simplest cases, Debye (1929) found that the polarization of a sample relaxs towards steady-state according to a first-order process with relaxation time  $\tau$ :



- High-frequency dielectric constant  $\varepsilon_{\infty}$
- Static relative permittivity  $-\varepsilon_s$

Rather than the relaxation time, the process is often expressed in terms of characteristics or relaxation frequency:  $f_c = (2 \pi \tau)^{-1}$ 









In more complex media, as in the case of biological tissues, mixture of substances and/or nonlinear relaxation processs may occur and, therefore, more advanced models accounting for the distribution of relaxation times are needed.

• Cole-Cole (1941): Empirical parametric model with symmetrically-distributed relaxation times







In more complex media, as in the case of biological tissues, mixture of substances and/or nonlinear relaxation process may occur and, therefore, more advanced models accounting for the distribution of relaxation times are needed.

• Cole-Davidson (1951): Empirical parametric model with asymmetrically-distributed relaxation times

$$\varepsilon^{\star} = \varepsilon_{\infty} + \frac{(\varepsilon_{s} - \varepsilon_{s})}{(1 + j \omega \tau)^{1 - \alpha}}$$

This model is usually adopted to describe dielectric properties of viscous fluids as glycerine.







In more complex media, as in the case of biological tissues, mixture of substances and/or nonlinear relaxation process may occur and, therefore, more advanced models accounting for the distribution of relaxation times are needed.

• Havriliak-Watts (1986): Empirical parametric model to describe dielectric relaxation of polymers (e.g., proteins, polysaccharides, nucleic acids, etc.)

$$\varepsilon^{\bullet} = \varepsilon_{\infty} + \frac{\varepsilon_{s} - \varepsilon_{\infty}}{\{1 + (j \,\omega \,\tau)^{\alpha}\}^{\beta}}$$

- Cole-Davidson  $\alpha = 1$
- Cole-Cole  $\beta = 1$





A different represention of the dielectric relaxation models: the Cole-Cole plots





As already mentioned, dielectric relaxation experienced by biological tissues in response to an externally applied time-varying field describes the process of partial orientation of permanent dipoles. It occurs according to the following dispersion mechanisms:

- 1) DIPOLAR RELAXATION
- 2) SPACE-CHARGE POLARIZATION
  - Interfacial or migration polarization
  - Counterion diffusion



Random distribution of ions inside the cell and in the extracellular media





Interfacial polarization under the effect of applied electric field

#### Static and time-varying fields:

#### ➢ DIPOLAR RELAXATION

In tissues several dipolar relaxation effects are observed:

- Globular proteins show dispersion at frequencies < 10 MHz;
- Partial orientation of polar sidechains contribute to dispersion in the range 100 MHz 1 GHz;
- 37 °C water exhibits single time-constant dipolar relaxation at f<sub>c</sub> = 25 GHz;

#### SPACE-CHARGE POLARIZATION: INTERFACIAL POLARIZATION

In a heterogeneous tissue a dispersion occurs due to the charging of interfaces within the medium, which produces a relaxation frequency dependent on the differences in bulk properties of the constituent materials. Interfacial effects can rule the properties of colloids and emulsions, but in biological materials at microwave frequencies, the effects of dipolar relaxation of liquid water are believed to be more important.



### Static and time-varying fields:

#### SPACE-CHARGE POLARIZATION: COUNTERION DIFFUSION

This is a surface phenomenon arising from ionic diffusion in the electrical double layers close to charged surfaces. This effect is more important at sub-microwave frequencies and may explain why tissue data show relaxations much broader than predicted by the Debye theory.



Condensed counter-ions migrate along polymer backbone







#### Showcase: Pure water single-Debye dielectric model

The dielectric constant of pure water obeys the single-relaxation Debye model for polar molecules:

Static dielectric constant (dimensionless) – 
$$\epsilon_{w0}$$

HF dielectric constant (dimensionless) – 
$$\epsilon_{w\infty}$$

Relaxation time (s) – 
$$\tau_w$$

Note that all the parameters involved in the Debye model depend also on water temperature, with  $\varepsilon_{w\infty}$  being just slightly dependent (it belongs to the range 4.1 – 4.9).







#### Showcase: Pure water single-Debye dielectric model

The relaxation time of pure water as a function of temperarure (°C) is given by (Stogryn, 1971):

 $2\pi\tau_{\rm w}(T) = 1.1109 \times 10^{-10} - 3.824 \times 10^{-12}T + 6.938 \times 10^{-14}T^2 - 5.096 \times 10^{-16}T^3$ 

• The relaxation frequency of pure water lies in the microwave region:

F<sub>c</sub> (0 °C) ≈ 8.9 GHz
f<sub>c</sub> (20 °C) ≈ 16.7 GHz

- It can be shown that the dielectric loss factor has its maximum value at  $f = f_c$ .
- This relatively simple model applies for frequencies below 50 GHz (error less than 5%, less than 1% at frequencies below 10 GHz) and for 0 °C ≤ T ≤ 30 °C.

#### Showcase: Pure water single-Debye dielectric model




# Showcase: Saline water double-Debye dielectric model

The dielectric constant of saline water follows the double-relaxation Debye dielectric model (Ellison, 2006):

$$\varepsilon'_{\mathbf{w}} = \varepsilon_{\mathbf{w}\infty} + \frac{\varepsilon_{\mathbf{w}0} - \varepsilon_{\mathbf{w}1}}{1 + (2\pi f \tau_{\mathbf{w}1})^2} + \frac{\varepsilon_{\mathbf{w}1} - \varepsilon_{\mathbf{w}\infty}}{1 + (2\pi f \tau_{\mathbf{w}2})^2}$$

$$\varepsilon_{\mathbf{w}}^{\prime\prime} = \frac{2\pi f \tau_{\mathbf{w}1}(\varepsilon_{\mathbf{w}0} - \varepsilon_{\mathbf{w}1})}{1 + (2\pi f \tau_{\mathbf{w}1})^2} + \frac{2\pi f \tau_{\mathbf{w}2}(\varepsilon_{\mathbf{w}1} - \varepsilon_{\mathbf{w}\infty})}{1 + (2\pi f \tau_{\mathbf{w}2})^2} + \frac{\sigma_{\mathbf{i}}}{2\pi\varepsilon_0 f}$$

- Free space dielectric constant  $\varepsilon_0$
- Intermediate transitional state dielectric constant  $\epsilon_{w1}$
- Slow-process (bonds breaking) relaxation time  $\tau_{w1}$
- Fast-process (molecule rearrangement) relaxation time  $\tau_{w2}$

The two relaxation times result in a two local maxima in the dielectric loss factor spectrum ( $f_{c1} \approx 8.9$  GHz and  $f_{c2} \approx 201.8$  GHz at T = 0 °C, while  $f_{c1} \approx 16.7$  GHz and  $f_{c2} \approx 281.4$  GHz at T = 20 °C). Note also that the dielectric loss factor includes a term related to ionic conductivity due to the dissolved salt in the water solution.





# Showcase: Saline water double-Debye dielectric model

The applicable range of the double-Debye dielectric model is as follows:

> 0 ≤ T ≤ 30 °C
 > 0 ≤ S ≤ 40 psu
 > f ≤ 1 THz
 The water salinity S is defined at the total mass of solid salt (in grams) dissolved in one kg of solution. For pure water, of course, S = 0.

It was found that this model calls for an error no larger than 1% (3%) [5%] in the frequency range 0 - 20 GHz (3 - 100 GHz) [100 GHz - 1 THz] with respect to actual pure water measurements.

It was also found that the model is accurate to within 3% with respect to actual sea water measurements in the frequency range 3 – 105 GHz).

#### Showcase: Saline water double-Debye dielectric model







To describe electrical and thermal properties of dispersive media as most of biological tissues is a challenging task. The problem usually translates in describing the effective dielectric properties of a two-phase dispersion in which one phase consists of particles dispersed in a second continuous phase. Both phases are usually regarded as homogeneous within themselves.

It was shown that, considering a time-varying field, the quasi-static approximation holds for dispersive media if the dimension of inclusions is small compared with the wavelength of the imposed field. Hence, the equation expressing the complex permittivity of the biological tissue is identical in formulation to that of the static permittivity. Accordingly, any formula valid for static permittivity may easily be transposed to the case of complex permittivity.



 $a = b, c \ll a$ Mixture models: a = b = cHost material Eh  $\frac{1}{2c}$ Inclusion material  $\varepsilon_i$ Eh 2**a** Eh  $a = b, c \gg a$ = ' 26/10/23 Prof. A. Buono



Maxwell (1881) was the first to derive a mixture equation, even if it was for the thermal conductivity of a dilute suspension of identical spheres.

Generalised Conductivity	Flux Vector J	Thermodynamic Force F	Kinetic Coefficient k		
electrostatic	electric displacement	electric field intensity	static permittivity		
	D	<u> </u>	ε,		
eletrodynamic	conduction current density	electric field intensity	static conductivity		
	j	E	σ		
magnetostatic	magnetic flux density	magnetic field intensity	magnetic permeability		
	В	н	μ		
heat conduction	heat flow	temperature gradient	heat conduction coefficient		
	q	grad T	λ		
diffusion	diffusion flow	concentration gradient	diffusion coefficient		
	М	grad C	D		

Generalized conductivity principle and transport coefficients





Consider a medium of static permittivity  $\varepsilon_{2s}$  in which spherical particles of static permittivity  $\varepsilon_{1s}$  and radius a<sub>i</sub> randomly fill a spherical volume of radius R. This volume is large enough to host a remarkable number of particles under the limit that the average distance apart of the particles largely exceeds  $a_i$ . An uniform electric field,  $E_0$ , is applied that induce on each particle a dipole moment p<sub>i</sub> (mutual polarization is neglected):  $p_i = (\frac{4}{3}\pi a_i^3) 3\varepsilon_0 \frac{\varepsilon_{1s} - \varepsilon_{2s}}{\varepsilon_{1s} + 2\varepsilon_{2s}} E_0 \xi_{2s}$ 



 $\mathbf{E}_0 \rightarrow$ 

### Mixture models:

The dipole moment P' of the spherical volume is calculated assuming it to be macroscopically homogeneous and characterized by permittivity  $\varepsilon_s$ :

$$P' = \left(\frac{4}{3}\pi R^3\right) 3\epsilon_0 \frac{\epsilon_s - \epsilon_{2s}}{\epsilon_s + 2\epsilon_{2s}} E_0 \epsilon_{2s}$$

Equating P' with the dipole moment of the N<sub>i</sub> particles within the volume ( $P_T = \sum N_i p_i$ ) we obtain the Maxwell mixture model.







$$\frac{\varepsilon_{s} - \varepsilon_{2s}}{\varepsilon_{s} + 2\varepsilon_{2s}} = \frac{\varepsilon_{1s} - \varepsilon_{2s}}{\varepsilon_{1s} + 2\varepsilon_{2s}}\phi$$

• Inclusion volume fraction –  $0 < \varphi < 1$ 

- It is thus clear that the static permittivity of a statistically isotropic and homogeneous mixture, where  $\varepsilon_{1s} > \varepsilon_{2s}$ , is bounded:
- > Above, by the static permittivity of sparse spherical particles  $\varepsilon_{2s}$  in a continuous medium of static permittivity  $\varepsilon_{1s}$ ;
- > Below, by the static permittivity of sparse spherical particles  $\varepsilon_{1s}$  in a continuous medium of static permittivity  $\varepsilon_{2s}$ .





Fricke (1924) introduced a shape factor accounting for the inclusions to be oblate/prolate spheroids:

$$\frac{\varepsilon_{s} - \varepsilon_{2s}}{\varepsilon_{s} + x \varepsilon_{2s}} = \frac{\varepsilon_{1s} - \varepsilon_{2s}}{\varepsilon_{1s} + x \varepsilon_{2s}} \phi \quad \text{Shape factor} - x$$



The factor x is a function of the axial ratio of the ellipsoids and the ratio of the static permittivities of the two phases.



Maxwell (1881) also derived the dielectric mixture model for a shell-covered sphere:



- Core radius R

- Equivalent shell permittivity  $\varepsilon_s^s$

This model can be applied to the case of a dilute suspension of spheres surrounded by multiple membranes.



#### Mixture models:





For tissues calling for dense concentration of randomly distributed inclusions, the electrical interactions among the inclusions are not negligible and, therefore, mutual polarization must be considered. This is not straightforward at all since, in these media, the particles are polarized under the influence of both the applied macroscopic field and the local field of the neighbouring particles.

Bruggeman (1935) proposed an integral procedure which consisted of building up the spherical dispersion medium by successive additions of infinitesimal amounts of the dispersive phase.



- At a given state, the static permittivity of the medium is  $\varepsilon_s$  with volume fraction  $\phi'$ ;
- A further addition of the sparse phase  $\delta \phi'$  produces a permittivity variation  $\delta \epsilon_s$ .
- The new permittivity value  $\epsilon_s^+$  is expressed by the Maxwell mixture model where:
- $\succ \epsilon_{\rm s}$  is replaced by  $\epsilon_{\rm s} + \delta \epsilon_{\rm s}$
- $\succ$   $\epsilon_{2s}$  is replaced by  $\epsilon_{s}$
- $\Rightarrow \phi \text{ is replaced by } \frac{\delta \phi'}{(1-\phi)}$



$$\frac{2\varepsilon_{s} + \varepsilon_{1s}}{3\varepsilon_{s} (\varepsilon_{s} - \varepsilon_{1s})} \delta \varepsilon_{s} = \frac{\delta \phi'}{1 - \phi'}$$





Integrating from  $\epsilon_{2s}$  (the continuum permittivity) to  $\epsilon_s$  and from 0 to  $\phi$  yields the Bruggeman equation:

$$\left\{\frac{\varepsilon_{1s} - \varepsilon_{2s}}{\varepsilon_{1s} - \varepsilon_{s}}\right\}^{3} \frac{\varepsilon_{s}}{\varepsilon_{2s}} = \frac{1}{(1 - \phi)^{3}}$$

The Bruggeman equation can be solved analytically and can be extended to allow for complex permittivities and to the case of spheres covered by multiple membranes (compound model).







In heterogeneous dielectric tissues with at least one conducting component, interfacial polarization typically occurs and, hence, any theoretical mixture formula that provides the complex permittivity of such kinds of media may be shown to give rise to a dielectric relaxation which may be expressed by any of the previous relaxation models, e.g., the Maxwell one:

$$\varepsilon^* = \varepsilon_2^* \quad \frac{\varepsilon_1^* + 2\varepsilon_2^* + 2\phi(\varepsilon_1^* - \varepsilon_2^*)}{\varepsilon_1^* + 2\varepsilon_2^* - \phi(\varepsilon_1^* - \varepsilon_2^*)} \qquad \qquad \varepsilon_1^* = \varepsilon_{1s} - j\frac{\sigma_1}{\omega\varepsilon_0}$$

$$\varepsilon_2^* = \varepsilon_{2s} - j\frac{\sigma_2}{\omega\varepsilon_0}$$

Assuming that no intrinsic dielectric relaxation is exhibited by either component.



The latter can be be transformed into a Debye type equation with an ohmic term:



In respect of the Debye model:





# Showcase: Tinga-Voss-Blossey mixture dielectric model



The TVB mixture model (1973) regards randomly dispersed confocal ellipsoids consisting of an inner ellipsoid ( $\epsilon_i$ ) surrounded by a shell of another material ( $\epsilon_h$ ).

The two-phase mixture ( $\varepsilon_m$ ) is compelled to take on the geometry of two confocal ellipsoids with an inner ellipsoid (inclusion) and a "fictitious" outer ellipsoidal shell (host material).

The dimensions of the fictitious outer ellipsoid are such that the volume of the shell surrounding the inner ellipsoid  $(v_i)$  is equal to the total volume of the host material in the mixture divided by the total number of ellipsoids.



#### Showcase: Tinga-Voss-Blossey mixture dielectric model



$$\mathbf{v}_i = \frac{V_2}{V_1}$$







# Showcase: Tinga-Voss-Blossey mixture dielectric model

For randomly oriented inclusions, the equivalent dielectric constant of the mixture is given by:

$$\varepsilon_{\rm m} = \varepsilon_{\rm h} + \frac{v_{\rm i}}{3} \left(\varepsilon_{\rm i} - \varepsilon_{\rm h}\right) \cdot \sum_{u=a,b,c} \frac{1}{1 + \left(A_{u2} - A_{u1}v_{\rm i}\right) \left(\frac{\varepsilon_{\rm i}}{\varepsilon_{\rm h}} - 1\right)}$$

Depolarization factor outer ellipsoid –  $A_{u1}$ Depolarization factor inner ellipsoid –  $A_{u2}$ 

Where: 
$$A_{u_j} = \frac{a_j b_j c_j}{2} \int_0^\infty \frac{ds}{(s+u_j^2)[(s+a_j^2)(s+b_j^2)(s+c_j^2)]^{1/2}} \quad u_j \in \{a_j, b_j, c_j\}$$





## Showcase: Tinga-Voss-Blossey mixture dielectric model

$$\blacktriangleright \text{ Thin circular disc inclusions: } \epsilon_{\rm m} = \epsilon_{\rm h} + \frac{v_{\rm i}}{3} \left(\epsilon_{\rm i} - \epsilon_{\rm h}\right) \left[\frac{2\epsilon_{\rm i}(1 - v_{\rm i}) + \epsilon_{\rm h}(1 + 2v_{\rm i})}{v_{\rm i}\epsilon_{\rm h} + (1 - v_{\rm i})\epsilon_{\rm i}}\right] \qquad \begin{array}{c} a_1 = b_1, a_2 = b_2, \\ c_1 \ll a_1, c_2 \ll a_2 \\ A_{a_1} = A_{a_2} = A_{b_1} = A_{b_2} = 0 \\ A_{c_1} = A_{c_2} = 1 \end{array}$$

$$\succ \text{ Spherical inclusions: } \boldsymbol{\varepsilon}_{\mathbf{m}} = \boldsymbol{\varepsilon}_{\mathbf{h}} + \frac{3\boldsymbol{v}_{\mathbf{i}}\boldsymbol{\varepsilon}_{\mathbf{h}}(\boldsymbol{\varepsilon}_{\mathbf{i}} - \boldsymbol{\varepsilon}_{\mathbf{h}})}{(2\boldsymbol{\varepsilon}_{\mathbf{h}} + \boldsymbol{\varepsilon}_{\mathbf{i}}) - \boldsymbol{v}_{\mathbf{i}}(\boldsymbol{\varepsilon}_{\mathbf{i}} - \boldsymbol{\varepsilon}_{\mathbf{h}})} \qquad A_{a_1} = A_{a_2} = A_{b_1} = A_{b_2} = A_{c_1} = A_{c_2} = \frac{1}{3}$$

$$\succ \text{ Long narrow needle inclusions: } \varepsilon_{m} = \varepsilon_{h} + \frac{v_{i}}{3} (\varepsilon_{i} - \varepsilon_{h}) \begin{bmatrix} \frac{\varepsilon_{h}(5 + v_{i}) + (1 - v_{i})\varepsilon_{i}}{\varepsilon_{h}(1 + v_{i}) + \varepsilon_{i}(1 - v_{i})} \end{bmatrix} \quad A_{a_{1}} = A_{a_{2}} = A_{b_{1}} = A_{b_{2}} = 0.5$$

$$A_{c_{1}} = A_{c_{2}} = 0$$
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#### Showcase: Tinga-Voss-Blossey mixture dielectric model







# Mixture models: remarks

- The presented mixture equations have been developed for two-phase media, whereas biological tissues are very much more complex. Hence, they just represent a qualitative guide to the tissue structure.
- At microwaves, the main contribution to the permittivity is expected to be from water which exhibits dipolar relaxation in the GHz region. The other components of the tissue are expected to be less important, since most other biological content show dispersions at lower frequencies.
- Attempts to get detailed info on tissue structure cannot be made using single-frequency measurements: only by sorting out the different dispersion mechanisms over a very wide range of frequencies can be useful.
- At a single microwave frequency, nevertheless, useful information may be still derived, e.g., the comparison of total water content with that expected from models may give information about bound water and may also indicate which models are most useful for a specific biological applications.









At microwaves, the methods to characterize the dielectric properties of tissues fall within two main categories:

- **NON-RESONANT METHODS**: they are often used to make measurements over a broad frequency range.
- **RESONANT METHODS**: they are usually adopted to perform single-frequency measurements or measurements at a set of several discrete frequencies.

To combine both methods allows getting a general picture of the dielectric properties of the tissue under test.

One of the main problems to be faced by those who make *in vitro* tissue dielectric measurements is that samples available from surgery are often very small. Thus, there is need to design measurement techniques which are able to probe samples consisting of small volumes of tissue.

Another major challenge is that most biological tissues are very lossy due to their high water content. This presents difficulties in the measurement of sample conductivity: often, the higher the conductivity of a lossy sample, the lower is the measurement accuracy of both permittivity and conductivity.





- In non-resonant methods, the dielectric properties are derived from wave impedance and velocity measurements. Measurements of reflection and transmission coefficients at the interface can provide information on the permittivity and permeability relationships between the media.
- Accordingly, non-resonant approaches are grouped as reflection and transmission/reflection methods.
- All types of transmission lines can be used to carry the probing wave, including coaxial line (RF), hollow metallic waveguide (MW), dielectric waveguide (OF), planar transmission line (MW) and free space.







In non-resonant reflection methods, a single parameter (either permittivity or permeability) can be estimated by measuring reflection coefficient at a defined the reference plane. They are classified as:

- **Open-reflection method**
- Shorted reflection method

Coaxial lines well fit the need of broad-band measurements during reflection methods.







Sample

In non-resonant transmission/reflection methods, the sample under test is inserted in a piece of transmission line and its dielectric properties are estimated by evaluating the reflection and transmission coefficients.

This method is widely used to measure dielectric properties (both permittivity and permeability) of low-conductivity tissues or to measure surface impedance of high-conductivity thin films (thickness <  $\delta$ ).

Coaxial transmission/reflection





Resonant methods usually call for higher accuracies and finer sensitivities than nonresonant methods, and they are the most suitable approach for low-loss biological tissues. They are classified as:

- **Resonator (dielectric resonator) method**
- **Resonant-perturbation (cavity-perturbation )method**



Dielectric cylinder (TE<sub>011</sub> mode) sandwiched between two conducting plates



Cylindrical cavity ( $TM_{010}$  mode) for permittivity (A) and permeability (B) measurements





The resonator method relies on the dependance of resonant frequency and quality factor of a dielectric resonator (of given size) from its permittivity and permeability. This approach is widely adopted to measure low-loss non-magnetic tissues. This method can be used to measure high dielectric constant and to characterize anisotropic samples (e. g., brain and myocardial tissues).

The resonant-perturbation method is based on the fact that, for a resonator with given electromagnetic boundaries, partial changes in the EM boundaries induced by introducing the sample under test result in changes of its resonant frequency and quality factor. This method is suitable to characterize low-loss materials.





#### Data Review:

The earliest recorded measurements of bulk dielectric properties of tissue were made by Peltier (1834), who discovered capacitive properties of animal bodies. A significant pulse to dielectric properties measurements was given by technological advancements in the 1950's. Measurements on human tissues were first reported by England, Sharples and Cook (1949-1951).

Most available dielectric data on human and animal tissues cover the frequency range from 100 MHz – 10 GHz, therefore covering the  $\delta$ - and  $\gamma$ -dispersion ranges. They were largely collected during *in vitro* measurements.





#### Data Review:

Tissue type	T	f(GHz)	: 0.1	0.2	0.5	1.0	2.0	3.0	4.0	10.0	Comments
Whole Blood	25	ε'	69	65	61	59	58	56	T		
		σ				9.2	17	27	1		
	27	ε'		67	64*	63^					*0.4 GHz, ^0.9 GHz
		σ		10	11	13			1		
	37	ε'			-	_		53		45*	*9.43 GHz
		σ	1				1	25	1	105	
	15	ε'		-				60		42*	*9.4 GHz
		σ					1	33		140	
	25	ε						58		46*	
		σ	1			1		29		120	
	35	ε'				1		56		48*	
		σ						27		100	
Bone	37	ε'	1			_	8.4*	8.4	7.8^		*1.8 GHz, ^3.6 GHz
		σ	1				1.5	2.2	3.3		mid-shalt tibia
	37	ε'				_				7.4*	*9.43 GHz
	1	σ						1		8.1	lemur
Bone Marrow	37	ε'								4.2	
		σ	1							11	
	37	ε'	1			4.3-7.3		4.2-5.8		4.4-5.4*	*8.5 GHz
		σ			1	0.4-1.0	1	1.2-2.3		1.7-4.7	· · · · · · · · · · · · · · ·

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Comments



#### Data Review:

Tissue type	Т	f(GHz)	: 0.1	0.2	0.5	1.0	2.0	3.0	4.0	10.0	Comments
					_						
Brain	37	ε'					32*	32	^33		*2.45 GHz, ^3.9 GHz
		σ					21	29	34		
	23	ε'							1		
		σ	3.3-5.0								
Breast	37	ε'	80 (a)								Infiltrating ductal
Carcinoma	]	σ	9.3	1							carcinoma.
											(b)surrounding tissue
	37	ε'	60 (b)								(<6 mm from tumour)
		σ	11								(c)periprieral (25 mm from tumour)
	1										(d)central (mainly
	37	ε'	8.0 (c)			1					infiltrating tumour
		σ	0.62								cells)
											80-85% water
	37	ε'	23(2)								
		σ	1.0								
	37	ε'						62		42*, 38*	*9.4 GHz
	1	σ						25		95, 92	scionis
		Ι.									
	37	ε΄						57		42*, 41*	
		σ						30		106, 110	
		1.									
	37	ε.						Į		38*	
		σ								92	
	127									204	
	''	3								20	
	1	σ				1	1	1	1	89	



#### Data Review:

Tissue type	T	f(GHz):	0.1	0.2	0.5	1.0	2.0	3.0	14.0	10.0	Comments
Breast-	37	ε'	6.5								
normal	1	σ	0.41								
Fat		ε'			6.0	6.2		6.0*			*2.5 GHz
		σ			1.1	1.2		2.3			<u>In VIVO</u>
	27	ε'	<u> </u>	4.5-7.5	4-7 *	3.2-6^		1			*0.4 GHz, ^0.9 GHz
		σ		0.20-0.67	0.25-0.77	0.29-0.91					
	37	ε'					4.2* (a)	3.9 (a)	4.1^ (a)		•1.8 GHz, ^4.6 GHz
		σ	1		{		1.1	1.5	1.9		(a)breast
			1						1		(b)abdominal wall
	37	ε΄						4.9 (b)	4.2 ** (b)		(c)near laecal fistula (d)sole of foot
	)	σ		1				2.4	2.0		(0,000 01 000
			1	}				1		1	
	37	ε		1			7.2* (c)	7.0 (c)	5.8^ (c)		
		σ					2.3	2.9	4.8		
	1	Ι.			Į					l	
	131	3					11• (d)	12 (d)	7.7~ (d)		
		σ					3.0	3.8	2.3		
	37	ε						5.2 (a)		4.0* (a)	*9.43 GHz
		σ			Į	1		2.6		5.3	(b) leg
									1		
	37	ε		1				7.2 (a)	1	4.1 <b>▼</b> (b)	1
	ļ	σ						2.9		4.7	
	37	ε΄	8-13			5.3-7.5	5.8*	3.9-7.2	4.7^	3.5-4.5**	*2.45 GHz, ^5 GHz
		σ	0.67			0.83-1.5	1.1	1.1-2.3	1.9	2.7-4.2	- 0.3 Onz



#### Data Review:

Tissue type	T	f(GHz) :	10.1	0.2	0.5	1.0	12.0	10.0	1.10		
110000 .71											
Kidney	37	E'	80 (84)		1	1	T		1		Data at 16±7 hours after death. Bracketed
Ridiicy		σ	11 (12)			}			}		values transformed to 1-2 hours after death.
	1	1	1	1	1	1	1	1			83.9% water
	127	<u> </u>	+	62	55-57*	53-56^					*0.4 GHz, ^0.9 GHz
	121	ε		9.6	10	12			1		
	L	0			+		+				
]	23	ε	1	1						Į –	
	1	σ	0.5-10	1	1	+	+			<u> </u>	Data at 16 ±7 hours
Liver	37	ε	71 (74)		{	1	1		1		after death. Bracketed
		σ	5.8 (7.0)			(					values transformed to
	1	1	}	1		1				1	77.3 % water
				50.56	46.53*	44-52^	+			1	*0.4 GHz, ^0.9 GHz
	27	ε ·	1	50-50	67.83	8 3-11			1		
		σ	1	5.9-8.0	0.7-0.5						
	23	ε	-		1	1	1				
[		σ	5.1-6.7			1.00		42.43		34-38*	*8.5 GHz
	37	ε'			43-51	40-47		20		50-57	
	1	σ		1		9.5-10		- 20	<u> </u>		A CHA MA CHA
Lung	27	ε'		35	36*	35^					104 GHZ, 10.9 GHZ
	1	σ		5.3	6.1	7.3					D. C. Harris
1	23	ε'									Deflated lung
4	}	σ	7.1-10	1	1						
Musala	+	- c'	+		49	49		49*			*2.5 GHz in vivo
Muscie	1				8.6	9.5		13	1		Sartonus muscle
1	122	1	172	+	+		+				Cardiac muscle, Data
	131	ε	8.0		1	1	1		1		taken 16±7 hours after
		σ	0.5								78.9% water

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10.0 Comments

14.0

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Data Review:

Tissue type	T	f(GHz) :	0.1	0.2	0.5	1.0	2.0	3.0	4.0	10.0	Comments
Muscle	27	ε'		56	54-56 *	53-55^	1			Т	*0.4 GHz, ^0.9 GHz
		σ		8.3-9.1	9.5-10	12					(a) cardiac muscle
	27	ε'		59-63 (a)	54-58* (a)	53-57^ (a)					
		σ		7.7-9.1	8.7-10	10-12					
	37	ε'	<u> </u>	<u> </u>	<u> </u>	$\vdash$	51* (a)	51 (a)	47^ (a)	+	*1.8 GHz, '4.6GHz
	ſ ′	σ			'		24	30	52	[	(a) soleus
	,	1 - /					-				(b) pectoralis major
	37	ε'			1		50* (b)	50 (b)	47^ (b)		
	/	σ					23	29	42		
		'									
	37	ε'					52* (b)	52 (b)	494 (b)		
		σ					21	32 (0)	50		
	37	<u>↓'</u>	<b>├</b> ────┘	<del> </del>	───′	<b> </b>				24*	10 (CH-
		ε .			/					70	*9.4GHz
	'	σ	1		1 /	'				/9	skeletal
	37		'		/	'				1	
	1	, č	'		/		1			337	
		ļ'	<b>└───</b> ′	<b> </b> '	ļ/		L			84	
	23	ε΄			/						(a)skeletai
	'	σ	6.5-7.7(a)		!	1					(b)cardiac
	/	1	'		!						
	23	ε			/						
		σ	6.0-7.4(b)								
	37	ε'				49-52	48*	45-48	44^	40-52**	*2.45 GHz, ^5 GHz
		σ		1 1	1 1	13	18	22-23	39	71	**8.5 GHz


#### Data Review:

Tissue	type	T	f(GHz) :	0.1	0.2	0.5	1.0	2.0	13.0	4.0	10.0	Comments
Ocular	Tissue	37	ε΄	48	44	39	36	33	31	29*		**0.53 GHz for ε',
Lens	nuclear		σ	3.2	4.1	5.6	7.4	13^	19^^	28		0.56 GHz for o.
		1				1		1	1			^2.2GHz for σ,
	cortical	37	ε'	62	58	50**	47	44	41	38*		^3.2 GHz for o.
		l	σ	6.0	7.1	5.4	10	15	21	32	ļ	*4.3 GHz for E'.
												4.7 GHz for σ.
Skin			ε'					40	44*		37	*2.5 GHz
			σ					21	27		76	in vivo
			ε΄								22	in_vivo
			σ								98	
			ε'				42	40*	38^	37**		*1.8 GHz, ^3.2 GHz
			σ			1	6.1	13	22	30		**3.8 GHz
												In the
!			ε΄		51*, 53*	47^, 48^	43, 48 **					*0.25 GHz, ^0.4 GHz
			σ		7.1 6.9	7.4, 8.6	9.2,11					**0.9 GHz (both measurements)
		37	ε'					52* (a)	51 (a)	46^(a)		*1.8 GHz, ^4.6 GHz
			σ				1	21	25	41		(a)near faecal fistula
								{	1		Į	(c)instep sole
		37	ε΄				1	40* (a)	40 (b)	39^(b)	í	•
			σ	1			1	18	21	34		
			ļ	ł								
		37	ε						42 (c)	40^ (c)		
			σ	1					22	32		



#### Data Review:

Tissue type	Ť	f(GHz) :	0.1	0.2	0.5	1.0	2.0	3.0	4.0	10.0	Comments
Skin	37	ε'						41		36* (a)	*9.4 GHz
		σ						28		86	(a)breast (b)leg
	37	ε						50		34* (b)	
		σ						25		81	
	37	ε'						52			
		σ		[				28			
	37	ε'	65	57	47	43-46	43•	40-45	41	36^	*2.45 GHz, ^8.5 GHz
	_	σ	7.2-8.3	8.0	7.4	9.1-11	19	20-27	39	71	
Spleen	37	ε΄	73 (76)								Data at 16±7 hours
	}	σ	11 (10)								after death. Bracketed
											hours after death. 79.0% water
	23	ε'									
		σ	7.1-9.1								



Data Review: FAT



26/10/23

## Data Review: BRAIN



Variability is related to water content. Grey brain tissue calls for larger water content than white brain tissue.

Data Review: SKIN



Prof. A. Buono

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Frequency (GHz)



26/10/23

### Data Review:

Tissue	Water content (% by weight)	Water content (% by volume)		
Whole blood	78.5	83		
Blood plasma	91	93		
Blood corpuscles	68-72	73-77		
Muscle	70-80	75-84		
Skin	62-76	68-80		
Fat	5-20	4-18		
Liver	71-77	76-81		
Lung	79-84	83-87		
Slpeen	75-80	80-84		
Kidney	78-84	82-87		
Whole Brain	73-78	78-82		
Brain (grey )	80-85	84-88		
Brain (white)	68-73	73-78		



*f* = 3 GHz

Water content by volume calculated assuming a density of  $1.3 \text{ g/cm}^3$  for the non-water content of tissue, except for fat where a density of  $0.86 \text{ g/cm}^3$  was used.



Prof. A. Buono

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og(relative permittivity)

## Data Review:

Tissue	Water content (% by weight)	Water content (% by volume)			
Whole blood	78.5	83			
Blood plasma	91	93			
Blood corpuscles	68-72	73-77			
Muscle	70-80	75-84			
Skin	62-76	68-80			
Fat	5-20	4-18			
Liver	71-77	76-81			
Lung	79-84	83-87			
Slpeen	75-80	80-84			
Kidney	78-84	82-87			
Whole Brain	73-78	78-82			
Brain (grey )	80-85	84-88			
Brain (white)	68-73	73-78			



Dispersion of typical high water content tissue

Above 100 MHz, dielectric properties of most of *in vivo* and *in vitro* tissues do not show significant variations.

