

Impedance Modulation by Pulsed Ultrasound

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ABSTRACT: The propagation of an acoustic wave in an electrolyte solution produces local and periodic conductivity changes. This acousto-electrical interaction is due to the variations of the parameters controlling ionic conductivity against pressure and temperature. The overall effect is about $10^{-7} \text{ \% Pa}^{-1}$ for solutions of physiological ions and is practically independent of the ionic species involved. The bulk compressibility of the medium is responsible for about 47% of the effect, the change in viscosity due to pressure changes is responsible for about 18%, and the changes of ionic mobility against temperature are responsible for about 35%. Detectable impedance changes were produced in the focal zone of a 500-kHz focused transducer using moderate intensity ultrasound (peak pressure < 1 MPa). This technique potentially enables the association of the spatial resolution of pulsed ultrasound and impedance measurement, although technical improvements and feasibility studies are still needed prior to practical applications.

INTRODUCTION

The spatial resolution of impedance techniques is intrinsically limited by the properties of the state equation governing the potential within a conductor (Laplace equation in a not charged conductor of isotropic and homogeneous conductivity). The current injected using two electrodes spreads within the conductor and, at a given point, the current density, J , depends on the distribution of the conductivity within the medium and the boundary conditions (shape of the conducting body, size, and locations of injection electrodes). The ratio of the voltage difference between two measuring electrodes, $\psi_A - \psi_B$, to the current, I_ϕ , injected using another pair of electrodes, ϕ_C and ϕ_D , is termed the mutual impedance of the object and is denoted Z . When the conductivity of a volume element, ΔV , is uniformly changed by $\Delta\sigma$, the potential, ϕ , created by the source electrodes becomes $\phi + \Delta\phi$, and the impedance is changed by ΔZ , according to equation 1, derived by Geselowitz¹ using Green's theorem:

$$\Delta Z = \Delta\sigma \int_{\Delta v} \frac{\nabla(\phi + \Delta\phi) \cdot \nabla(\psi)}{I_\phi I_\psi} dv = \Delta\sigma \int_{\Delta v} s(x, y, z) dv \quad (1)$$

where ψ is the potential distribution that would be created if the measuring electrodes were used to pass a current I_ψ . The quantity $s(x, y, z)$ is the sensitivity per unit volume at point $M(x, y, z)$ for the electrode system used. Hence, the local and periodic conductivity changes produced by an acoustic wave propagating in a body result in corresponding changes in this body's impedance. The purpose of the present study was to investigate the origin and the magnitude of this interaction effect.

THEORY

Experimental Evidence

It can be experimentally observed that pressure affects the conductivity of electrolyte solutions. For instance, a decrease in the resistance of samples of a range of electrolytes submitted to isothermal compression has been reported by Körber.² At constant temperature, the conductivity of seawater increases with static pressure.³ It can therefore be expected that the periodic pressure changes due to the propagation of an acoustic wave through a given volume element would also affect the conductivity of the medium. However, the compression resulting from the propagation of an acoustic wave is not isothermal and the associated temperature changes also affect the conductivity of the medium.⁴ As appreciable effects can be expected, certain authors have considered the possible application of the dc signal resulting from the interaction between an electric current and a sound wave at the same frequency for the transcutaneous stimulation of brain.^{5,6} In the present study, a constant current was used.

The Propagation of Ultrasound in an Aqueous Solution

Aqueous solutions of electrolytes were taken as conduction models of biological substances. In such solutions, the attenuation of ultrasound waves is negligible, which canceled, in the present study, the influence of the absorption of ultrasound by the medium. The propagation of an acoustic wave consists of pressure changes traveling in the medium at velocity c . A given volume element submitted to such a wave experiences a periodic displacement, ξ , and a periodic compression/expansion cycle.⁷ Assuming that the wave propagates along the z -axis, the propagation equation is written under the form of equation 2:

$$\frac{\partial^2 \xi}{\partial t^2} = \frac{1}{\rho \beta_s} \frac{\partial^2 \xi}{\partial z^2} \quad \text{with} \quad c^2 = \frac{1}{\beta_s \rho} \quad (2)$$

where ρ is the density (kg m^{-3}) of the medium and β_s is its adiabatic compressibility (reciprocal of its adiabatic bulk compressibility modulus, E).

During a period of the acoustic wave, the mechanical work applied to a given volume element is converted into heat. As the time constant of heat transfer between a given volume element and the surrounding medium is generally much longer than an acoustic wave's period, no appreciable heat transfer can take place and the compression/expansion cycle is adiabatic. The following sections describe how the conductivity of an electrolyte solution is affected by these pressure and temperature changes.

Involved Phenomena

The phenomena involved in the acousto-electric interaction are summarized in FIGURE 1. The conductivity of an electrolyte solution essentially depends on the concentration of dissolved ions and their mobilities. The conductivity, σ , of a binary electrolyte is given by equation 3:

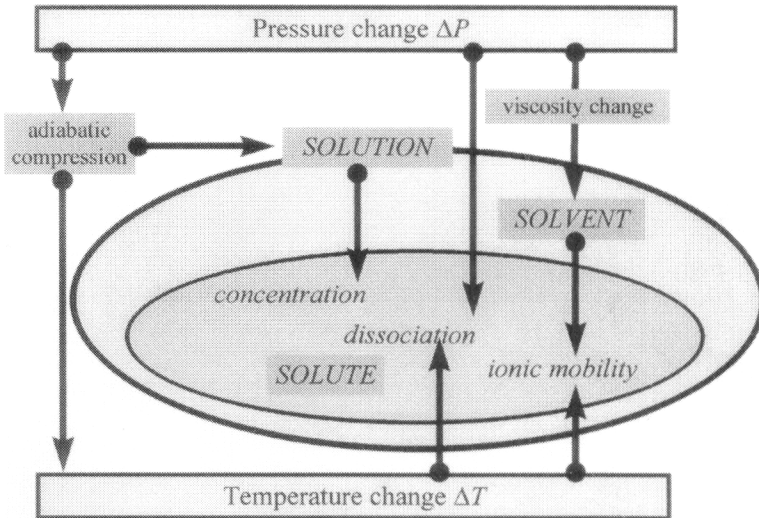


FIGURE 1. The phenomena responsible for the modulation of conductivity by an acoustic wave in an aqueous solution of electrolyte. These phenomena affect the solution (bulk compressibility), the solvent (viscosity), and the solute (dissociation). The changes in the solvent mobility affect the mobilities of the dissolved ions.

$$\sigma = Fk_{\pm}\alpha C(z_{+}u_{+} + z_{-}u_{-}) \quad (3)$$

where

σ : conductivity of the solution (S m^{-1}),
 F : faraday ($\approx 96,487 \text{ C mol}^{-1}$),
 k_{\pm} : mean ionic activity ($\gamma_{\pm} \leq 1$),
 α : dissociation coefficient,
 C : volume concentration (mol m^{-3}),
 z_{+} , z_{-} : number of charges of the cation and anion, respectively,
 u_{+} , u_{-} : mobilities of the cation and anion, respectively ($\text{m}^2 \text{ volt}^{-1} \text{ s}^{-1}$).

The pressure and temperature affect differently the variables in equation 3. The activity coefficient, k_{\pm} , accounts for the conductivity deficiency as ionic concentration increases. This is due to the coulombic forces exerted by all the ions dissolved in the solution on each of them. This coefficient differs appreciably from 1 for high values of ionic concentration. It can be seen that γ_{\pm} is not affected by the propagation of an acoustic wave in a solution as the effect is intrinsically small at usual concentrations ($k_{\pm} \approx 1$) and only a limited region of the solution is modified by the pressure burst at a given time,⁸ so the total influence exerted is practically unchanged. Therefore, the changes in conductivity are only due to the effect of pressure and temperature upon the molality (volume concentration) C , the dissociation coefficient α , and the ionic mobilities u_{+} and u_{-} .

Both temperature and pressure affect the dissociation constant, α , in partially dissociated weak electrolytes. In the present study, only strong (totally dissociated) electrolytes were used. The dissociation coefficient was thus equal to unity and independent of pressure and temperature. Hence, the remaining relevant variables in equation 3 were molality C and the ionic mobilities u_+ and u_- . The differentiation of equation 3 with these variables gives equation 4:

$$\frac{\Delta\sigma}{\sigma} \approx \frac{\Delta C}{C} + \frac{\Delta(z_+u_+ + z_-u_-)}{z_+u_+ + z_-u_-}. \quad (4)$$

Effect of Pressure and Temperature upon the Molality

As the total number of ions present in the solution is constant, the molality (volume concentration) of the solution is affected by changes in the solution's specific volume, V , against pressure and temperature. Under adiabatic conditions, the compression and the thermal expansion of the medium take place simultaneously and have opposite effects. The adiabatic compressibility, β_s (Pa^{-1}), is defined by equation 5:

$$\beta_s = -\frac{1}{V} \frac{\partial V}{\partial P} \quad (5)$$

where P is the pressure and V is the specific volume of the medium ($\text{m}^3 \text{kg}^{-1}$). Finally, the changes in molality are expressed by equation 6:

$$\frac{\Delta C}{C} \approx \frac{1}{C} \frac{\partial C}{\partial P} dP = -\frac{1}{V} \frac{\partial V}{\partial P} = \beta_s \Delta P. \quad (6)$$

Effect on Ionic Mobility

Ion mobility is the limit speed reached by an ion in solution in the presence of a constant and uniform unity electric field. Assuming that ions are spheres and using Stokes' law for viscosity forces, ionic mobility can be expressed by equation 7:

$$u = \frac{z_i q_e}{6\pi\eta rR} \quad (7)$$

where q_e is the electron charge and R is the radius of the ion. Both temperature and pressure affect the viscosity, η , of the solvent. Above 4 °C, the viscosity of water decreases with pressure with a coefficient, H_p , of about $-17.3 \cdot 10^{-11} \text{ Pa}^{-1}$ at 20 °C according to Warburg and Sachs, reported by Partington.⁹ At a constant pressure, ionic mobilities increase with temperature by about 2% K^{-1} (TABLE 1). This effect is responsible for the $\approx 2\% \text{ K}^{-1}$ change in the conductivity of biological substances against temperature.¹⁰ Finally, the change in ionic mobility is given by equation 8:

$$du = \frac{\partial u}{\partial T} dT - H_p dP. \quad (8)$$

TABLE 1. Ion Mobilities^a

Ions	u ($10^{-8} \text{ m}^2 \text{ s}^{-1} \text{ V}^{-1}$)	m_T (% K^{-1})
Na^+	5.19	2.48
K^+	7.62	2.17
Ca^{2+}	6.2	2.55
Cl^-	7.91	2.48
I^-	7.7	2.17
F^-	5.4	2.55

^a Values of ionic mobilities, u , at 25 °C and thermal coefficients, m_T , for some physiological ions from Pethig¹⁰ and Kohlrausch.¹³

Adiabatic Temperature Changes

The volume changes during the adiabatic compression/expansion cycle can be considered as the sum of a volume change at a constant temperature under the effect of pressure change and a volume change due to the thermal effect. Using the isothermal compressibility β_T and the cubic thermal expansion coefficient θ (K^{-1}) yields equation 9:

$$\beta_T \Delta p + \theta \Delta T = \beta_S \Delta p. \tag{9}$$

Using thermodynamic equations [$\beta_S/\beta_T = \gamma = C_p/C_v$, $\Delta W = Pd(1/\rho)$], one may derive several equivalent expressions of the rate of the induced temperature change against pressure change:⁷

$$\Theta = \frac{\Delta T}{\Delta P} = \frac{T\theta}{\rho C_p} = \frac{\beta_S(1-\gamma)}{\theta} = \frac{(1-\gamma)}{\theta \rho c^2} \tag{10}$$

where T is the absolute temperature and C_p is the specific heat capacity of the solution ($\text{J kg}^{-1} \text{K}^{-1}$).

Finally, the conductivity change can be expressed by equation 11, which defines the interaction coefficient K_I :

$$\Delta \sigma = \sigma \left[\beta_S - H_p + \Theta \frac{(z_+ u_+ m_{T+} + z_- u_- m_{T-})}{z_+ u_+ + z_- u_-} \right] \Delta P = \sigma K_I \Delta P. \tag{11}$$

At a given time, the change ΔZ of the measured impedance results from the conductivity changes produced in the whole medium by the pressure field:

$$\Delta Z(t) \approx \iiint_{\text{medium}} s(x, y, z) K_I \sigma \Delta P(t) dv. \tag{12}$$

If focused ultrasound is used, the pressure appreciably varies only within the acoustic beam, of width $w(z)$, and the influence of the medium not passed by the wave can be neglected. Assuming that the interaction coefficient K_I is constant in the medium, equation 12 can be transformed into equation 13:

$$\Delta Z(t) \approx K_I \int \int_{\text{path width}} s(x, y, z) \sigma(x, y, z) \Delta P(t) dv. \quad (13)$$

If pulsed ultrasound is used, only a limited portion of the path is submitted to pressure changes at a given time. The length of this portion is the product of the burst length and the velocity of ultrasound in the considered medium. This gives the longitudinal spatial resolution of the acousto-electric modulation effect. The transverse spatial resolution is determined by the width of the sound beam and thus depends on the characteristics of the acoustic transducer used.

NUMERICAL APPLICATION

The purpose of this section is to give values illustrating the magnitude of the effects. The temperature change associated with the adiabatic pressure change was calculated using equation 10. With the numerical values given in TABLE 2, one obtains about $1.4 \cdot 10^{-8}$ KPa⁻¹. The interaction coefficient K_I is the sum of three terms (terms in brackets in equation 11). The first term is the bulk compressibility, the value of which is about $46 \cdot 10^{-11}$ Pa⁻¹ (TABLE 2). The second term is the pressure coefficient of the solvent viscosity. The numerical value is about $17.3 \cdot 10^{-11}$ Pa⁻¹ (cf. subsection entitled "Effect on Ionic Mobility"). The last term, the change of ionic mobility against temperature, was calculated using the values found in TABLE 1. The values of the three terms of the interaction coefficient calculated for NaCl, KCl, and CaCl₂ solutions are given in TABLE 3.

EXPERIMENTAL MEASUREMENT

Experimental Setup

The detectability of the interaction effect was checked in saline. The measurements were carried out in a measurement chamber, consisting of a 20-mm-long Lucite cylinder

TABLE 2. Thermodynamic Data Used in the Present Study

Parameter	Value	Units
Density ⁷	998.2	kg m ⁻³ (water)
Density ⁷	1004.6	kg m ⁻³ (saline)
Compressibility β_T ⁷	$45.86 \cdot 10^{-11}$	Pa ⁻¹ (water)
Cubic expansion θ ¹²	$20.7 \cdot 10^{-5}$	K ⁻¹ (water)
Cubic expansion θ ⁷	23.9	K ⁻¹ (saline)
Specific heat C_p ¹⁴	4181.8	J kg ⁻¹ K ⁻¹ (water)
$\gamma = C_p/C_v$ ⁷	1.00656	(water)
Sound velocity ¹⁵	1480	ms ⁻¹ (water)

TABLE 3. Calculated Values^a

	Bulk Compressibility	Water Viscosity against Pressure	Ionic Mobility against Temperature	Total
NaCl	46.2	17.3	33.5	$97.0 \cdot 10^{-11} \text{ Pa}^{-1}$
KCl	46.2	17.3	31.7	$95.2 \cdot 10^{-11} \text{ Pa}^{-1}$
CaCl ₂	46.2	17.3	35.0	$98.5 \cdot 10^{-11} \text{ Pa}^{-1}$

^aCalculated contributions of the bulk compressibility, the pressure effect on viscosity, and the temperature effect upon ion mobility to the conductivity changes produced the propagation of an acoustic wave in aqueous solutions of physiological ions.

of 85-mm inner diameter, closed by two acoustically transparent membranes perpendicular to the beam axis. This chamber was immersed in a larger tank filled with degassed water and was positioned using three orthogonal micromanipulators.

In the present study, a single pair of electrodes, located inside the above chamber, was used to inject the current and to measure the interaction signal. The electrodes consisted of two vertical, parallel, 1-mm-in-diameter stainless steel rods covered by an insulating sheath, so only a 3-mm-long portion was active in the middle of each electrode (Fig. 2).

The ultrasonic field was generated by a focused transducer, 50 mm in diameter, and fed with 20-μs-long bursts (10 periods of a 500-kHz sine wave) at a repetition frequency of 10 Hz, synchronized with the current (Fig. 3). The maximum peak pressure was 1 MPa in the focal zone, where the electrodes were placed. The current was injected using a purpose-built balanced voltage-to-current convertor of less than 0.1 mS output conductance. The

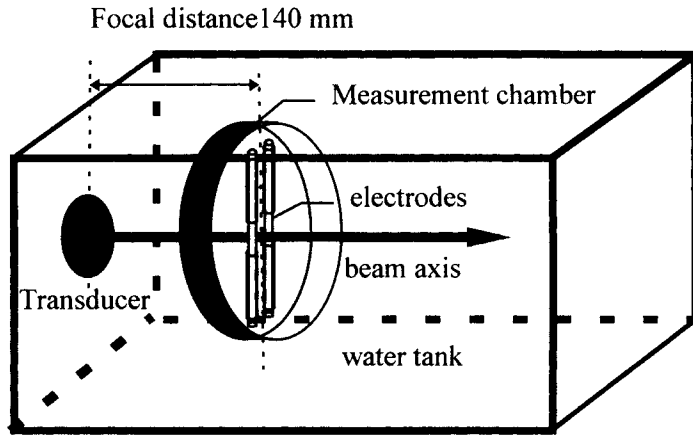


FIGURE 2. Representation of the experimental setup. The positioning system is not drawn for clarity. An acoustically transparent membrane was pasted on each side of the measurement chamber, so only a limited quantity of the tested liquid was used for each experiment.

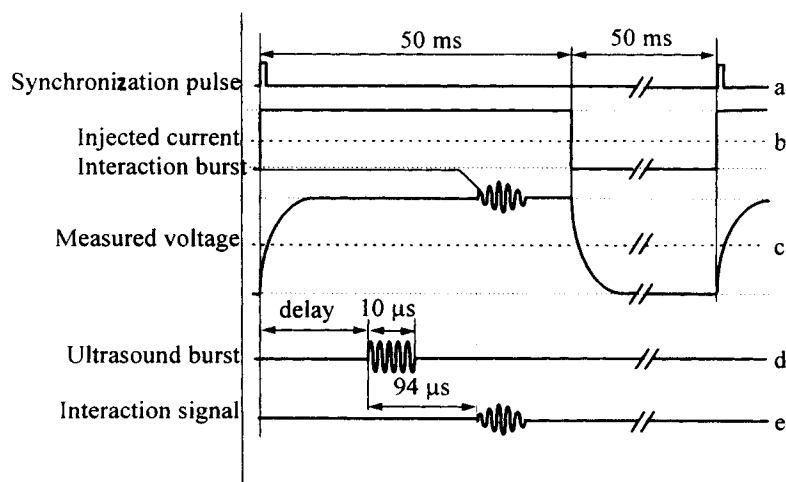


FIGURE 3. Signal timing. For clarity, the time scales are distorted. The injected current (b) and the acoustic burst (d) were synchronized. The electric signal (c) was sensed by the electrode after 94 μ s, representing the propagation time of the acoustic wave from the transducer to the focal zone, where the electrodes were placed. According to the settings, the acoustic burst could be sent on either the positive or negative half-wave of the injected current.

current consisted of symmetrical square waves (up to ± 12 mA) to ensure a constant current during the propagation of the sound burst and to avoid dc electrode polarization.

The voltage difference between the electrodes was amplified by a differential amplifier with a 670-k Ω input impedance, a gain of 100, and a passband from 20 kHz to 2 MHz. A Tektronix 2430 digital oscilloscope was used to display, digitalize, and transmit the data to a PC-compatible microcomputer.

Results

Measurements were carried out in various electrolyte solutions, especially in isotonic saline for the purpose of the present study. A voltage difference was observed when the sound wave was passing near the electrodes. The signal consisted of bursts at the ultrasound frequency. A signal of smaller magnitude, denoted V_0 , was also observed in the absence of any injected current. The signal—so-called “Ultrasonic Vibrational Potential” (UVP)—is due to the Debye effect.¹¹ UVP results from the displacement of the ions in the solution by the frictional forces produced by the periodic displacement of the surrounding liquid. As the masses and frictional coefficients of the positive and negative ions are not equal, this results in a periodic separation of charges. In the present study, the relevant signal was obtained by systematically subtracting V_0 from the signal measured in the presence of an injected current. A sample of the interaction signal is shown in FIGURE 4.

The peak value, V_X , of the signal was automatically calculated from the recorded waveforms. The results obtained in physiological saline are shown in FIGURE 5. The measured signal was an increasing function of the applied acoustic peak pressure and current. How-

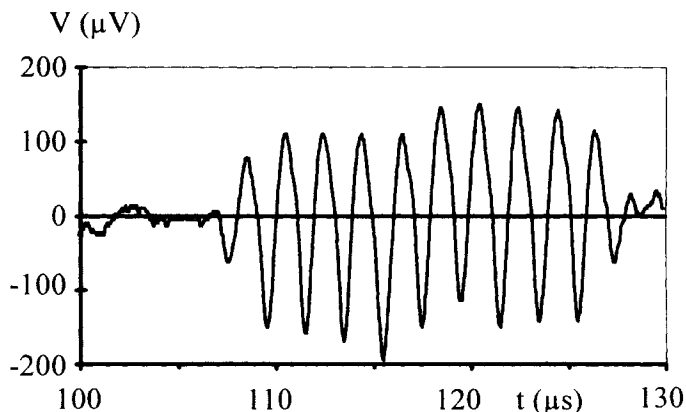


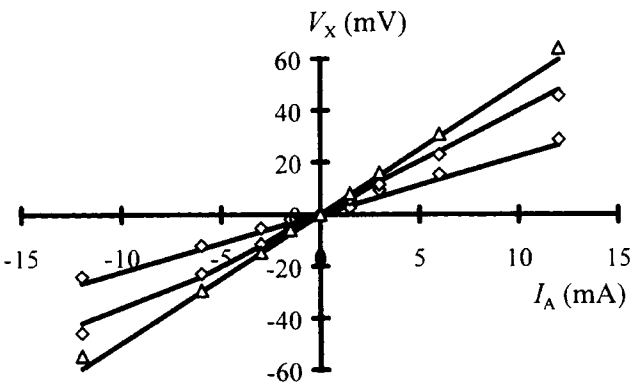
FIGURE 4. Typical interaction signal (after subtraction of V_0) at the output of the $G = 100$ amplifier.

ever, it was not possible to relate the value of the measured signal to the theoretically expected magnitude of the interaction signal. The reasons were (i) the use of the two-electrode technique in which the medium impedance and the electrode contact impedances add, (ii) the nonuniform sensitivity distribution of a pair of electrodes, and (iii) the production of conductivity changes of opposite polarities (thus tending to cancel each other) by the used sinusoidal acoustic wave. Thus, the measured signal was presumably much smaller than the theoretical value.

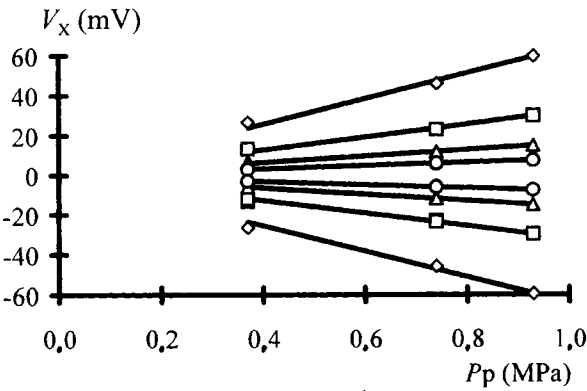
DISCUSSION

An appreciable interaction signal was observed in experimental conditions *in vitro*. A larger magnitude signal can be expected if the effect of a bipolar acoustic wave could be avoided. The advantage of the interaction signal is that it only exists where and when the pressure field affects a volume region passed by a current. Hence, there is no baseline at the frequency of the relevant signal, and the amplifier gain is only limited by the signal-to-noise ratio. Furthermore, with a constant current, the interaction signal is at the same frequency as the transmitted acoustic wave, which enables coherent demodulation. The volume producing the signal depends on the width of the beam and the length of the burst (30 mm for a 20- μ s burst and a sound velocity¹² of 1480 ms^{-1}). This resolution can be improved using shorter acoustic signals and, possibly, processing the signal using proper deconvolution techniques.

From equation 13, it can be seen that the impedance modulation is proportional to the conductivity and sensitivity at a given volume element. It can be observed in TABLE 3 that two of the three phenomena involved in the interaction only depend on the physical properties of the solvent (compressibility and effect of pressure upon the solvent viscosity). The effect of the induced temperature changes upon ionic mobilities (TABLE 3) depends on the ion species. However, the numerical values of ion mobilities and their temperature coefficients result in a relatively constant effect. This can be understood considering that



a



b

FIGURE 5. (a) Plots of the magnitude V_X of the interaction signal measured in isotonic saline against the injected current I_A for three values (0.37, 0.74, and 0.93 MPa) of the peak pressure. (b) The same data plotted against the peak pressure, P_p , for four pairs of symmetrical values of the injected current (± 1.5 , ± 3 , ± 6 , ± 12 mA).

(i) the major effect of temperature upon ion mobility is the change in solvent viscosity and
 (ii) the physical differences between ion species are relatively small. Finally, the values obtained for physiological ions (TABLE 3) show that the acousto-electric interaction effect depends very little on the ion species ensuring the conduction.

CONCLUSIONS

The present study enabled the theoretical calculation of the magnitude of the acousto-electric interaction. The experimental measurements showed that the signal produced by moderate intensity ultrasound is detectable in electrolyte solutions, at least in the focal zone of the transducer. Improved experimental setup is needed for practical applications of this signal. The major advantage is that only the region affected by the sound wave creates a signal at a given time, so this modality potentially enables impedance measurement with the spatial resolution of pulsed ultrasound. However, prior to practical applications, technical improvements and feasibility studies are still needed, including the design of hardware systems combining impedance measurement and time windowing techniques, the optimization of the acoustic signal, and measurements in absorbing (cellular) media.

ACKNOWLEDGMENTS

We acknowledge A. Matias and R. Jarry for the fabrication of the water tank, the measurement chamber, and the mechanical elements; and Y. Theillère for the construction of the voltage-to-current convertor and differential amplifier.

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