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Comment on experimental methods and conclusions of impedance spectroscopy of solutions at physiological glucose concentrations by A. Tura, S. Sbrignadello, S. Barison, S. Conti, G. Pacini

A. Caduff [a,*], M.S. Talary [a], Yu. Feldman [b]

[a] *Solianis Monitoring AG., 8050 Zürich, Switzerland*

[b] *Department of Applied Physics, The Hebrew University of Jerusalem, Jerusalem 91904, Israel*

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The recent paper [1] discussed the possibility of using impedance spectroscopy (IS) in the frequency range 10^{-1} Hz to 10 MHz for the direct monitoring of physiological concentrations of glucose in aqueous solutions and in blood suspensions. The main conclusion of this paper was that glucose concentration changes could be most effectively measured using IS in the frequency range below 1 MHz than at higher frequencies.

First of all in this comment we would like to point out that the experimental results of IS measurements presented in the paper are confusing. The values of the phase shift discussed are not realistic. The phase of impedance for any RC sensor can vary between $-\pi/2$ to $\pi/2$, but not in the range shown in Fig. 2, 3 and 4. The authors have used the standard 4-electrode combined conductivity/temperature probe (SP06T) designed for conductivity measurements with the help of a conductivity and pH meter (HD3456.2). This electrode is not suitable for broad band impedance measurements with the Solartron 1260 analyser. This is the reason that it is not clear what actually the authors have measured in their experiments. Clearly they are using a fringing field, but with no discussion on how the impedance can be obtained from the resulting non-uniform fields in a broad frequency range, it is difficult to interpret the presented results.

If we assume however that they took these points into consideration and under a strong assumption that impedance measurements were provided correctly, it has to be clear that any difference in the measured values of the impedance (modulus and phase shift) versus physiological glucose concentrations presented in the paper simply reflect the different values of small conductivity variations of the glucose dissolved in water. As a first course in dielectric spectroscopy would point out, such conductivity changes induce significant changes in electrode polarization phenomena. Therefore, without an understanding of this double layer formed on the stimulation electrodes it is doubtful the voltage across the probing electrodes was accurately measured.

Let us consider our statement in more detail:

It is well known that aqueous solutions of glucose and other sugars only provide noticeable dielectric responses at quite high concentrations of the soluble molecules (>1 mol/L) and even then only at high frequencies (>100 MHz). These dielectric changes are widely accepted as being due to the degree of hydration of the sugar molecules and significant broadening of dielectric spectra [2–7]. It is also true that a low frequency dispersion for non physiological, highly concentrated sugar/water mixtures (including glucose) can be observed at frequencies <1 MHz additional to the one at the high frequencies mentioned above, and at a low temperature interval due to relaxation processes associated with their glass forming properties [8]. However these mechanisms are unlikely to be within the scope of the paper [1]. The existing extensive literature related to relaxation processes associated with dielectric materials in the given frequency range should provide sufficient confidence to assume that no dielectric response can be directly assigned to any variations of dielectric permittivity or impedance in the frequency range <1 MHz at room temperatures due to variations of glucose within physiological concentrations. Using dielectric spectroscopy techniques (DS), the precise dielectric measurements of D-glucose aqueous solutions in the frequency range 300 kHz to 100 GHz shows very clearly that the dielectric decrement and other relaxation parameters even for 1 mol/L do not exceed 5–7% (see Table 1). Moreover, no additional low frequency dispersion due to the D-glucose was detected [4].

* Corresponding author.

E-mail address: andreas.caduff@solianis.com (A. Caduff).

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Table 1
Parameters of the Cole–Cole relaxation spectral function for aqueous solutions of D-glucose in comparison with pure water at 25 °C [4]

C, mol/L	ε_∞ ±0.4	ε_s±0.4	τ, ps±1%	α
0	4.0	78	10.0	0.098
1	3.0	74.7	10.7	0.097

The same comments can be related to paper [9], which the authors of paper [1] use to support their hypothesis. Here the authors make similar measurements with a two electrode needle-type sample cell with aqueous solutions of glucose where additional well known problems associated with electrode polarization effects exist that will affect their measurements in this frequency range, but are not adequately addressed by the authors [9].

In both papers, despite the different electrode configurations and the method of data presentation, the authors are confronted with the same phenomena of the electrode polarization that, in the frequency band lower than 1 MHz, is extremely sensitive to the small changes of dc conductivity. Definitely dc conductivity is varied with physiological glucose concentrations. Note that the statement of the authors that the platinum electrodes will decrease significantly the electrode polarization [1] is relevant only to the black platinum that is usually used to cover electrodes in order to decrease that harmful effect and to move to another frequency interval [10]. Thus, the statement of the authors that glucose can be detected directly due to its dielectric contribution in the low frequency interval and that this can be used for clinical applications is not correct when compared to commonly accepted dielectric theory and IS/DS measurement practice [11].

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