Electromagnetic signature of Glucose in Aqueous Solutions and Human Blood

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Abstract:

This article proposes an Electromagnetic characterization of aqueous solutions containing glucose in various concentrations. Results concerning blood are also presented. Novelty of this work relies in its high frequency measurements together with its broadband character. Indeed, measurements from 100 MHz up to 50 Ghz are shown and detailed (up to 20 GHz for blood). Results are discussed and a possible application is detailed.

I-Introduction

Nowadays, electromagnetic (EM) waves at centimetre and millimetre wavelengths are increasingly used and penetrate our lives. Either from exploitation or prevention point of view, knowing effects and impact of these EM waves over biological material is of great interest. In this paper, focus is made over a particular component existing within blood: glucose. Aim of this paper is to evidence the particular EM response of this component over the whole frequency spectrum from 100 MHz to 20 GHz. To reach that aim, direct electromagnetical characterization of glycaemic aqueous solutions were performed.

II-Aqueous Solutions Measurement

The measurement set-up is compounded of a vectorial network analyser Agilent E8364A and an Agilent 85070E dielectric probe directly soaked into solutions.
Several basic solutions composed of distilled fresh water (D. water labelled), glucose in various concentrations (5 and 10% volume concentration- G5 & G10 labelled) and sodium chloride (NaCl labelled) have been processed.
For each of these formulas, the broadband real and imaginary relative dielectric permittivities have been plotted between 100 MHz and 50 GHz, measurement results are shown on Figure 1.

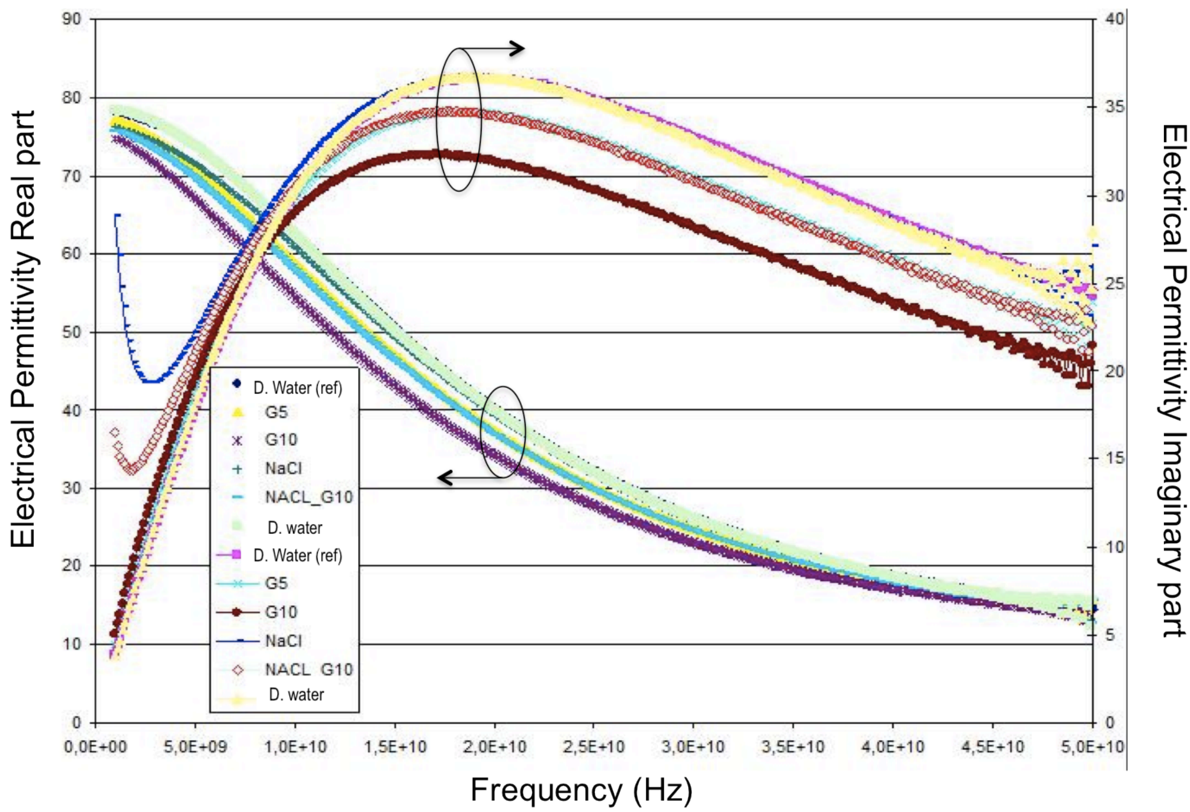


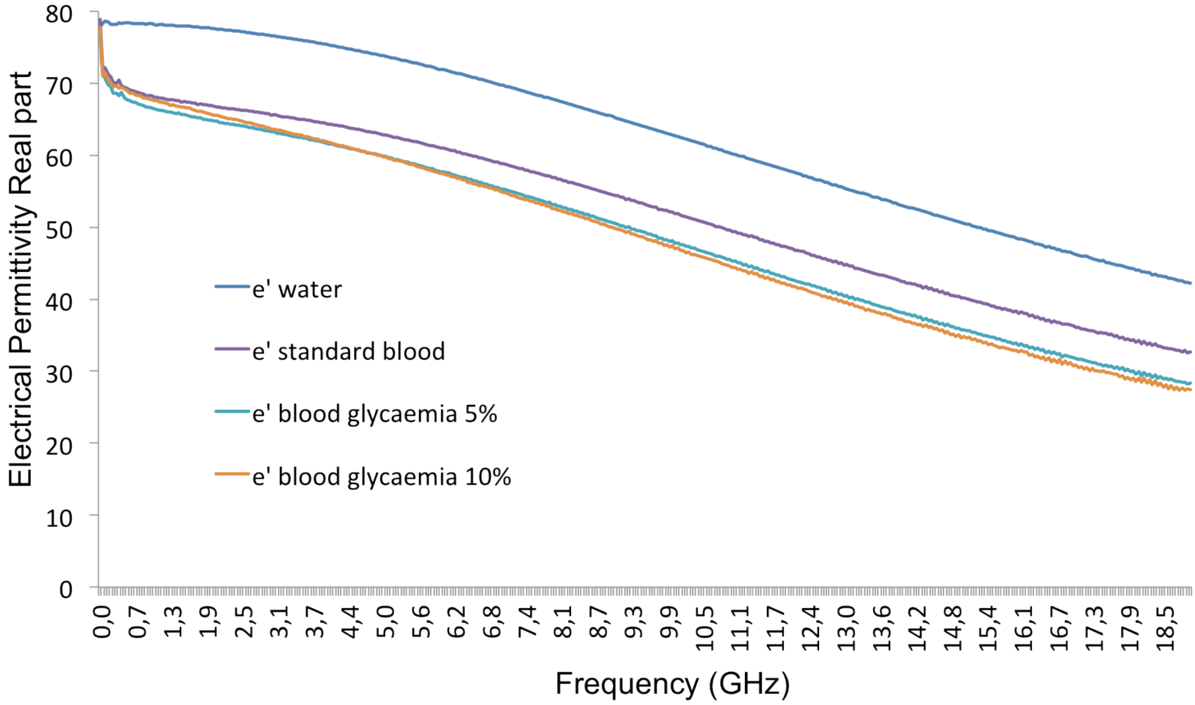
Fig. 1: measured relative dielectric permittivity
of aqueous glycaemic solutions

One can notice that imaginary part of the relative dielectric permittivity is linked to the glucose rate of the samples. Furthermore, these changes of the imaginary part of the relative dielectric permittivity are related to frequency.
At very low frequencies, the sodium chloride has a notable effect.
Then, for low frequencies *i.e.* under 8 GHz, the lower the glucose rate, the lower the imaginary relative dielectric permittivity.
Then, around 10 GHz, it seems that there is an inflection point, the effects of glucose concentration is weak.
Further to high frequencies, the higher the glucose rate, the lower the imaginary dielectric permittivity.

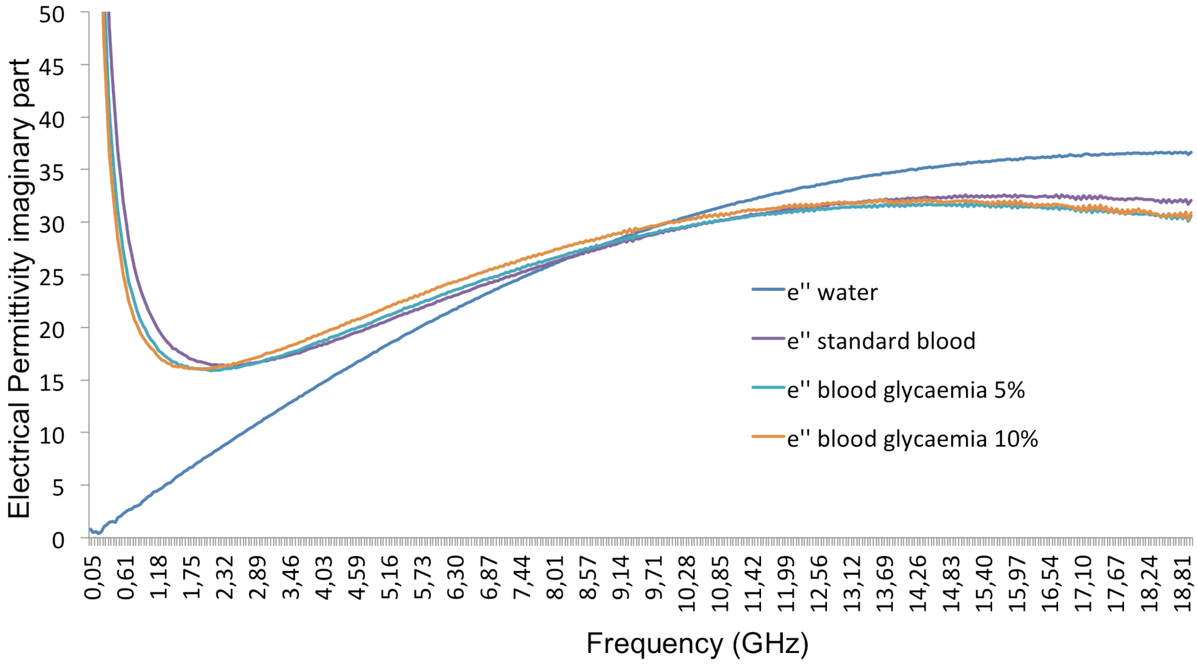
III-Blood Glycaemia Measurement

Further to these preliminary results, electromagnetical characterizations of a complex media, *i.e.* human blood, have been carried out. In order to try to, at first, make the problem as simple as possible, pooled human blood samples with artificially overdosed glycaemia rates have been used. Indeed, several samples of human bloods have been pooled. Then, the resulting equivalent blood has been divided into three parts: the first one has been overdosed with glucose in order to reach a glycaemia rate of 5%, the second one has been overdosed to reach a glycaemia rate of 10% and the last one was left unchanged, thus it presents an average human blood glycaemic rate.
These three samples were then characterized thanks to the method previously described. However, due to technical problems we were able to perform measurement under 20 GHz exclusively. The results are given in figure 2. As reported in the literature [1], [2], magnetization of human blood shows diamagnetic behavior leading to

magnetic susceptibility in scale of 10-6. This value is small enough so that permeability of blood can be approximated to 1 in our measurement setup.



a/ Relative dielectrical permittivity Real part



b/ Relative dielectrical permittivity Imaginary part

Fig. 2: measured relative dielectric permittivity
of pooled blood samples with various glycaemia rates

In order to have a clear idea of the reproducibility of the measurement and thus the intrinsic error of the characterization, we have measured twice the same samples with the same measurement set-up. Two measures are plotted into figure 3: one corresponds to the characterization of blood made before measuring any sample and the other one represents the blood characterization made after all the measurements. One can notice that the changes are weak, consequently, the measure could be considered as highly reproducible.

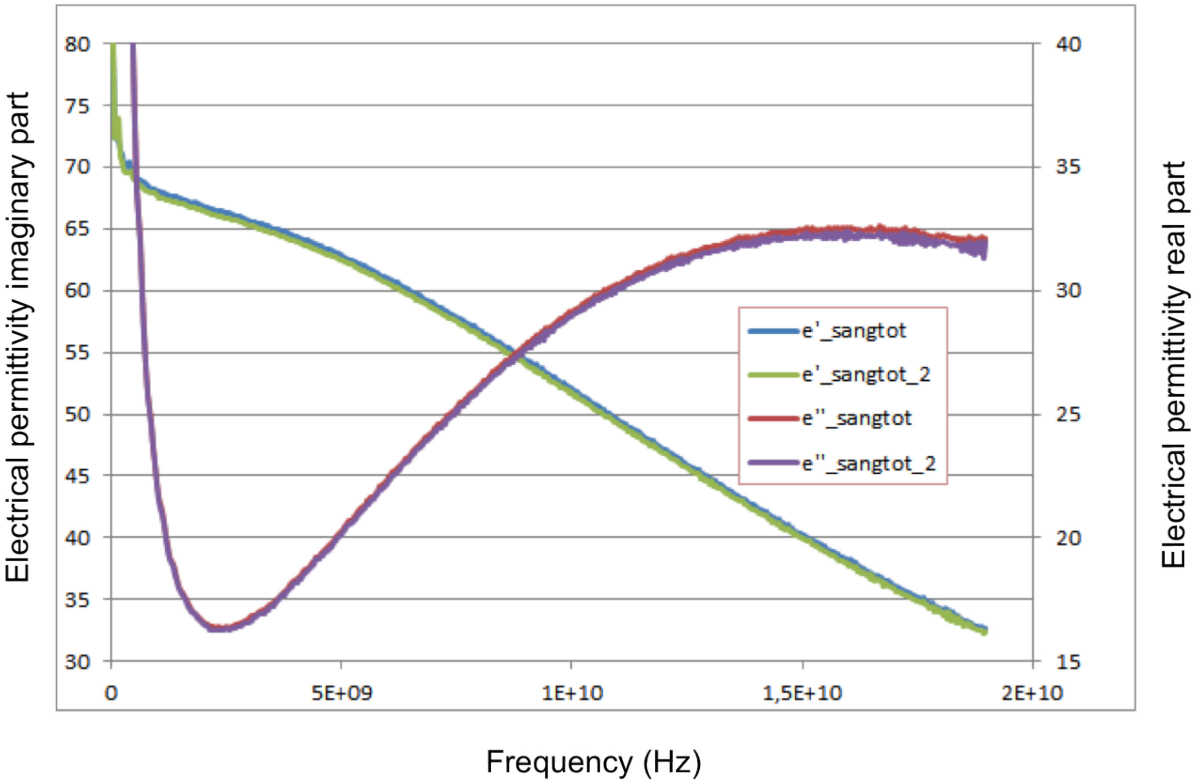


Fig.3: measured characteristics of blood made at two different moments
before the samples measurement (sangtot label)
after the samples measurement (sangtot_2 label)

All these measurement results clearly show that there is a link between the sugar blood rate and its electromagnetical behaviour and it opens numerous ways for exploitation of this particular behaviour.

IV- Conclusions and perspectives

In this paper, several characterizations of glucose solved into aqueous solutions have been performed over a wide frequency band (1 to 50 GHz) and shows that glucose rate has an effect over the relative electrical permittivity of the solution. These observations have then been extended to glucose rates into pooled human blood. Although these measurements have been carried out on overdosed pooled blood samples (around 10 times the pathological glycaemia rates), these results seem of great interest for the development of medical glycaemia sensors, and in particular for non-invasive devices.
Indeed, today, Diabetes Mellitus-affected patients still use blood sample glucose reader. A small drop of blood, obtained by pricking the skin with a sterile lancet (small needle), is placed on a disposable test strip that the meter reads and uses to calculate the blood glucose level through an electro-enzymatic process.
Other measurement techniques exist, optical ones being the most investigated. In particular, methods based on Near InfraRed light scattering measurement [3]-[8], Ultra-

Violet light Fluorescence [9], PhotoAcoustic spectroscopy [10]-[11], or Optical Coherence Tomography [12]-[13] have been widely examined. Non-optical techniques such as temperature measurement [14]-[15] or electrical measurement based on skin impedances [16]-[17] have also been investigated but none of these techniques have lead to a widely spread sensor because of the difficulty to de-correlate glucose-related effects from other in vivo phenomena.

Efforts to improve sensors based on these techniques are still on-going and generates an intense interest from major electronic companies such as Google™ or Microsoft™ [18] - [19].

Electromagnetic-based glucose detection appears as a serious candidate to challenge these techniques as they could allow a non-invasive testing [20]-[25].

References

1 M. E. Cano, A. Gil-Villegas, M. a. Sosa, J. C. Villagómez, and O. Baffa, "Computer simulation of magnetic properties of human blood," Chem. Phys. Lett., vol. 432, no. 4–6, pp. 548–552, Dec. 2006

2 L. Sakhnini and R. Khuzaie, "Magnetic behavior of human erythrocytes at different hemoglobin states," Eur. Biophys. J., vol. 30, no. 6, pp. 467–470, Oct. 2001

3 Omar S. Khalil « Non-Invasive Glucose Measurement Technologies: An Update from 1999 to the Dawn of the New Millennium » Diabetes Technology & Therapeutics Vol. 6, n° 5, 2004

4 Gabriely I, Wozniak R, Mevorach M, Kaplan J, Aharon Y, Shamoon H « Transcutaneous glucose measurement using near infrared spectroscopy during hypoglycemia » Diabetes Care 1999, 22:2026–2032.

5 Heise HM, Bittner A, Marbach R « Clinical chemistry and near infrared spectroscopy: technology for non- invasive glucose monitoring » J Infrared Spectrosc 1998;6:349–359.

6 Heise HM, Bittner A, Marbach R « Near-infrared reflectance spectroscopy for noninvasive monitoring of metabolites » Clin Chem Lab Med 2000;38:137–145

7 Blank TB, Ruchti TL, Lorenz AD, Monfre SL, Makarewicz MR, Mattu M, Hazen KH « Clinical results from non-invasive blood glucose monitor » Proc SPIE 2002;4624:1–10.

8 Maruo K, Chin J, Tamura M « Non-invasive blood glucose monitoring by novel fiber optical probe » Proc SPIE 2001;4264:20–27.

9 Evans ND, Gnudi L, Rolinski OJ, Birch DJ, Pickup JC « Non-invasive glucose monitoring by NAD(P)H autofluorescence spectroscopy in fibroblasts and adipocytes: a model for skin glucose sensing. Diabetes » Technol Ther 2003;5:807–816.

10 MacKenzie HA, Ashton HS, Spiers S, Shen Y, Free- born SS, Hannigan J, Lindberg J, Rae P: « Advances in photoacoustic noninvasive glucose testing. » Clin Chem 1999;45:1587–1595.

11 Fainchtein R, Stoyanov BJ, Murphy JC, Wilson DA, Hanley DF « Local determination of hemoglobin concentration and degree of oxygenation in tissue by pulsed photoacoustic spectroscopy » Proc SPIE 2000; 3916:19–33.

12 Larin KV, Eledrisi MS, Motamedi M, Esenaliev RO « Noninvasive blood glucose monitoring with optical coherence tomography: a pilot study in human subjects. » Diabetes Care 2002;25:2263–2267.

13 E. senaliev RO, Larin KV , Larina IV , Motamedi M « Noninvasive monitoring of glucose concentration with optical coherence tomography ». Opt Lett 2001; 26:992–994.
14 Malchoff CD, Shoukri K, Landau JI, Buchert JM: « A novel noninvasive blood glucose monitor » Diabetes Care 2002;25:2268–2275.
15 Zheng P, Kramer CE, Barnes CW, Braig JR, Sterling BB: Noninvasive glucose determination by oscillat- ing thermal gradient spectrometry. Diabetes Tech- nol Ther 2000;2:17–25.
16 A. Caduff, E. Hirt, Y. Feldman, Z. Ali, L. Heinemann « First human experiments with a novel non-invasive, non optical continuous glucose monitoring system » Biosensors and Bioelectronics N° 19, pp.209-217, 2003
17 A. Caduff, Y. Feldman "Device for the measurement of glucose concentrations" U.S.Patent 7,534,208 B2, 19 May 2009
18 http://googleblog.blogspot.fr/2014/01/introducing-our-smart-contact-lens.html
19 http://www.gizmag.com/microsoft-electronic-diabetic-contact-lens/20987/
20 Orna Amir, Daphna Weinstein, Silviu Zilberman, Malka Less, Daniele Perl-Treves, Harel Primack, Aharon Weinstein, Efi Gabis, Boris Fikhte, and Avraham Karasik « Continuous Noninvasive Glucose Monitoring Technology Based on "Occlusion Spectroscopy" » Journal of Diabetes Science and Technology Vol. 1, n° 4, July 2007
21 Hanlon EB, Manoharan R, Koo TW, Shafer KE, Motz JT, Fitzmaurice M, Kramer JR, Itzkan I, Dasari RR, Feld MS « Prospects for in vivo Raman spectroscopy » Phys Med Biol 2000;45:R1–R59.
22 Steffes PG « Laser-based measurement of glucose in the ocular aqueous humor: an efficacious portal for determination of serum glucose levels » Diabetes Technol Ther 1999;1:129–133.
23 M Gourzi, A Rouane, R Guelaz, M S Alavi, M B McHugh, M Nadi, P Roth « Non-invasive glycaemia blood measurements by electromagnetic sensor: study in static and dynamic blood circulation » Journal of Med Eng Technol. ;29 (1):22-6 15764378
24 O.C Kulkarni, P. Mandal, S.S. Das, S.A. Banerjee « Feasibility Study on Noninvasive Blood Glucose Measurement Using Photoacoustic Method »
4th International Conference on Bioinformatics and Biomedical Engineering (iCBBE), 2010
25 Eric C Green « Design of microwave sensor for non invasive determination of blood glucose concentration » MS thesis dissertation Baylor University. Dept. of Electrical and Computer Engineering, 2005