Medical & Biological Engineering & Computing (2019) 57:2389–2405
https://doi.org/10.1007/s11517-019-02030-w

ORIGINAL ARTICLE

# Feasibility study of portable microwave microstrip open-loop resonator for non-invasive blood glucose level sensing: proof of concept

Carlos G. Juan[1] · Héctor García[2] · Ernesto Ávila-Navarro[2] · Enrique Bronchalo[3] · Vicente Galiano[4] · Óscar Moreno[5] · Domingo Orozco[5] · José María Sabater-Navarro[1]

Received: 25 March 2019 / Accepted: 10 August 2019 / Published online: 31 August 2019


## Abstract
Self-management of blood glucose level is part and parcel of diabetes treatment, which involves invasive, painful, and uncomfortable methods. A proper non-invasive blood glucose monitor (NIBGM) is therefore desirable to deal better with it. Microwave resonators can potentially be used for such a purpose. Following the positive results from an in vitro previous work, a portable device based upon a microwave resonator was developed and assessed in a multicenter proof of concept. Its electrical response was analyzed when an individual's tongue was placed onto it. The study was performed with 352 individuals during their oral glucose tolerance tests, having four measurements per individual. The findings revealed that the accuracy must be improved before the diabetes community can make real use of the device. However, the relationship between the measuring parameter and the individual's blood glucose level is coherent with that from previous works, although with higher data dispersion. This is reflected in correlation coefficients between glycemia and the measuring magnitude consistently negative, although small, for the different datasets analyzed. Further research is proposed, focused on system improvements, individual calibration, and multitechnology approach. The study of the influence of other blood components different to glucose is also advised.

**Keywords** Blood glucose · Microwaves · Portable device · Proof of concept · Quality factor

## 1 Introduction

The pursue of a non-invasive blood glucose monitor (NIBGM) has led to considerable research and development of different technologies during the last years. The benefits that such a system would bring to treatment of diabetes are evident and numerous. Diabetes has a remarkable, fast-growing presence nowadays, as it was estimated that in

✉ José María Sabater-Navarro
j.sabater@umh.es

Carlos G. Juan
carlos.juan01@umh.es

Héctor García
mhector@umh.es

Ernesto Ávila-Navarro
eavila@umh.es

Enrique Bronchalo
ebronchalo@umh.es

Vicente Galiano
vgaliano@umh.es

Óscar Moreno
omoreno@umh.es

Domingo Orozco
dorozco@umh.es

1 Department of Systems Engineering and Automation, Miguel Hernández University, Elche, Spain

2 Department of Materials Science, Optics and Electronic Technology, Miguel Hernández University, Elche, Spain

3 Department of Communications Engineering, Miguel Hernández University, Elche, Spain

4 Department of Computer Engineering, Miguel Hernández University, Elche, Spain

5 Department of Clinical Medicine, Miguel Hernández University, Elche, Spain

2014, there were 422 million adult people with diabetes worldwide, a figure which almost quadrupled since 1980 [1]. Self-management plays a crucial role in dealing with this disease, since a suitable glycemic (blood glucose level) control is required. Frequent glucose measurements are needed, on a daily basis, to make possible such a control. Currently, the blood glucose tests by finger pricking are the standard measurement method for self-management, which are invasive, painful, and uncomfortable [2] and often lead to an undesired decrement of the measurement frequency. Consequently, NIBGM technology could enhance diabetes treatment and management, and hence contribute reducing this burden which is threatening the global population.

In addition to the benefits concerning comfortability and ease in self-management, a suitable NIBGM could lead to efficient continuous glucose monitoring (CGM). This is highly desirable since it would enhance diabetes treatment, allowing to track almost immediately all the significant events (hyper and hypoglycemia) and making the right actuations at the moment. Currently, there are several CGM systems available, but they remain invasive, depending on disposable stuff, and have not been suitable for use throughout long periods of time, chiefly because of the inflammation of the skin in the surroundings of the sensor placing. In addition, current CGM has not fully met the expectations of diabetes community regarding hypoglycemia [3]. Furthermore, recent researches have shown that current blood glucose monitoring systems have a clear economic impact for health institutions, which is related to their measurement inaccuracy and the outcoming complications [4]. In addition, it has been proved that diabetes treatment costs are strongly lower with CGM than without it [5]. Thus, the necessity of a reliable NIBGM for CGM is evident.

Some attempts have been made to obtain such a technology, based upon different principles. On the one hand, models and algorithms to predict the glycemia evolution, requiring a lower amount of measurements, have been investigated ([6–12], for example). However, none of them has been fully successful for use by the general population due to the need of sophisticated models for realistic patient-oriented conditions [13]. Nevertheless, the considerable amount of references found in this regard, most of them based on machine learning techniques, shows the intense activity of this field of study and its potential. These techniques require large experimental measurements to feed the algorithms, and thus the development of reliable sensors must constantly be faced.

On the other hand, research on physical sensors has been undertaken through various approaches. Electrochemical CGM systems (although being invasive) have been studied [14], but they keep showing significant errors [15]. The measurements are made in interstitial fluid, not directly in blood, and there is a variable time delay between interstitial and blood glucose concentration that must be dealt with [16]. Research involving some other methods has been carried out, like CGM with on-chip disposable sensor measuring from saliva [17], hypoglycemia detection from electroencephalogram signal [18], or even NIBGM measuring from the individual's gingival crevicular fluid [19], breath [20], or tears [21, 22]; none of them reaching conclusive results, though. The study of optical technology for such a purpose is also active currently, mainly involving mid- and near-infrared spectroscopy [23–26], although some difficulties must be faced before real application [27].

However, if non-invasive measurement is required, sensors based on radio frequency and microwave techniques are often concerned thanks to their penetration capabilities and sensitivity to dielectric properties of the environment [28]. The use of the dielectric properties for biological markers monitoring has already been successfully applied to several fields (a couple of recent ones are [29, 30], for instance). In this regard, some investigations have shown the variation of the dielectric properties of glucose-containing solutions when the glucose level varies [31–33], and the dielectric properties for most of biological tissues were identified and modeled [34]. Consequently, systems sensitive to the dielectric changes of the environment should be suitable for tracking the glucose level variations.

The study of the dielectric behavior of blood has also pointed out the feasibility of using non-invasive microwave glucose sensors [35], and more specifically methods based on resonators [36]. Therefore, the application of techniques based upon microwave resonators has been put forward in this regard in the recent years, given that their electrical response can be highly sensitive to the dielectric permittivity of the surrounding media. Several authors have analyzed and evaluated different kinds of microwave resonators with various configurations [37–41], generally showing promising in vitro results, although not existing comprehensive in vivo studies in real scenarios yet.

In this sense, a step forward is now taken by testing the sensor developed in a previous work (based on microwave resonator techniques) [37] in a multicenter proof. In the light of the positive previous results, a portable version of the NIBGM candidate device was prepared, in order to be tested in two hospitals with real volunteers, as a proof of concept for this technology. This paper shows the development of the whole device, as well as the experimental procedure, the study of the results, and the conclusions. This study represents a novelty in this research since it provides reliable information about the behavior of these devices in real scenarios, and it could help to identify the suitable approach. This could contribute not only to enhance this kind of sensors, but also to improve other techniques, like those involving machine learning algorithms.

## 2 Methods

### 2.1 Measuring device

This work presents and assesses a portable device for measuring the blood glucose level (BGL) of an individual in a non-invasive way, i.e., without any direct contact with blood. The working principle relies on the idea that the presence of glucose in blood makes its dielectric properties vary, and this affects the electrical response of the devices nearby [42]. Therefore, as explained next, the device measures the electrical response of a microstrip resonator when an individual's tongue is placed onto it, and the changes in the response are evaluated.

The tongue has been selected as the approaching body area due to several reasons. The blood-tissue ratio (the relative content of blood in the tissue) is an essential parameter that should be as constant as possible to ensure that the measurements are always made in the same conditions. In this sense, the tongue is a relatively stable area where there are no substantial changes (in the general case) due to blood pressure or heart rate variations. In addition, it is convenient that the blood-tissue ratio is high, so that there is a considerable presence of blood in the measuring area. The thermal stability of the tongue is a desirable feature, too.

The dielectric properties of the tongue, as well as those of many biological tissues, were comprehensively characterized in [34]. These properties are of the utmost importance for the proper working of microwave sensors. The relative dielectric permittivity ($\varepsilon_r$) of the tissues is expected to be sensitive to the BGL. This is a complex parameter defined as $\varepsilon_r = \varepsilon_r' - j\varepsilon_r''$, with $j = \sqrt{-1}$, where the imaginary part is related to dielectric losses. Previous studies with the sensor used in this work showed that the main contribution of glucose to the dielectric behavior of aqueous solutions comes in the form of losses in the 1–7 GHz frequency range [37]. These losses are commonly expressed by means of the loss tangent (tan δ), which is defined as (neglecting the low-frequency conductivity):

$$\tan\delta = \frac{\varepsilon_r''}{\varepsilon_r'} \qquad (1)$$

Therefore, it is convenient that the measurement place shows relatively low values of the loss tangent, so that the variations due to the BGL changes become more noticeable. According to the data reported in [34], the loss tangent of a human tongue is plotted in Fig. 1 for the frequency range of interest. As it can be seen, the tongue has relatively low tan δ values between 1 and 5 GHz. Due to the above-mentioned reasons, the tongue was selected as the measurement area.

#### 2.1.1 Microwave resonator

In the light of the results of the previously proposed microwave sensors for glucose concentration identification in aqueous solutions [37], in this work, a portable version of the sensor at the lowest frequency was developed, aimed to in vivo research. Three identical units of the device were made, thus allowing conducting an experimental study in two different clinical scenarios, and having one extra reserve unit in case any of the other units needed to be replaced. Each device is composed of an ad hoc case, a microwave resonator, the data acquisition electronics, a tactile screen serving as user interface, the driving and data storing electronics, a memory card for storage, and the mechanical structure to ensure that

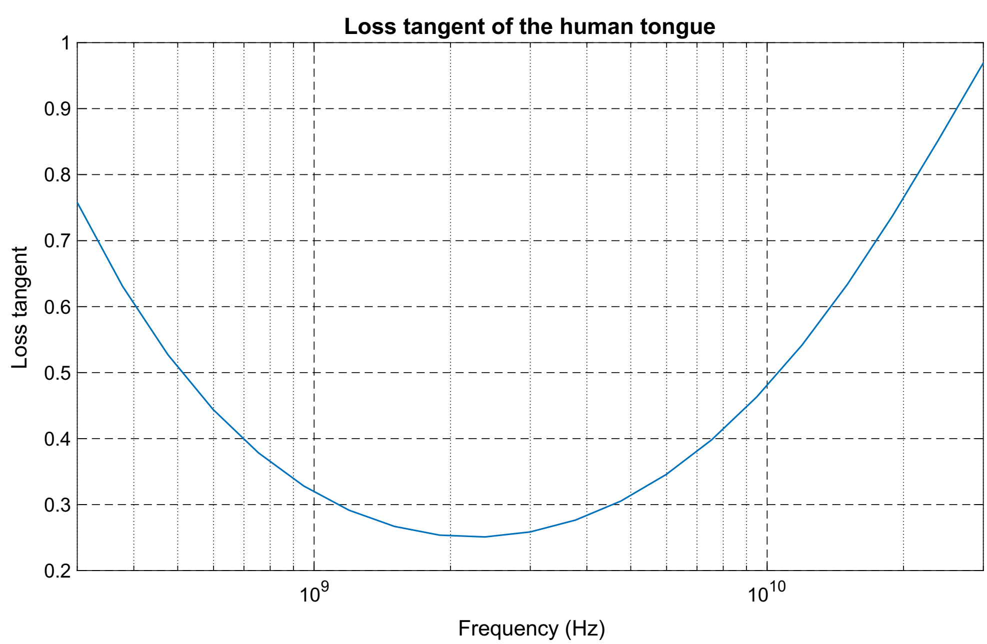



**Fig. 1** Loss tangent of human tongue tissue according to the data reported in [34]

the measurements were made always in the same position. Their purpose was to measure the electrical response of the resonator (in terms of the scattering parameters) when an individual's tongue was placed onto it, and check if there is any relationship with the BGL, as suggested in previous studies [38]. Figure 2 shows a picture of the three sensor units. All the elements not labeled were inside the case.

The key element of the system was the resonator, which was designed following the conclusions reached in previous in vitro studies [32, 37]. Hence, an open-loop microstrip resonator was developed, so that it acts as a glucose concentration sensor. This circuit presents a well-defined frequency peak around the resonant frequency which allows to easily track the changes. This response can be seen near the resonant frequency in Fig. 3 for an empty measurement, i.e., with no user, concerning the S21 parameter. To simplify the driving electronics and ensure the feasibility of the implementation, low frequency (i.e., up to 2.5 GHz) was considered. According to the positive previous results [37], which showed good sensitivity even for low frequency, and following the design basis discussed in that study, the resonator was developed at roughly 2.44 GHz, since the electrical response was expected to move only towards lower frequencies. As previously mentioned, this is a convenient frequency according to the tan δ data for the human tongue plotted in Fig. 1. This resonant frequency ($f_r$) is given by

$$f_r = \frac{c}{2l\sqrt{\varepsilon_{\mathrm{ref}}}} \tag{2}$$

where $c$ is the speed of light in vacuum, $\varepsilon_{\mathrm{ref}}$ is the effective relative permittivity, and $l$ is the length of the resonant line. The maximum amplitude of the S21 parameter was − 9.51 dB for empty measurement, as shown in Fig. 3.

Therefore, with sensing purposes, open-loop configuration was selected in order to have the sensor as sensitive as possible to the changes in the dielectric characteristics of the surrounding media. This concept exploits the high electric field generated between the open ends for the first resonant mode, having voltage maxima of opposite signs at resonance. This is therefore the place where the maximum electric interaction with the environment will be given. For this reason, the gap between the open ends was selected as the measuring area, the place where the individual's tongue should be placed for sensing. This gap was thus accurately designed to provide enough electric field intensity for having considerable interaction with the tissue. The gap length was finally set to 1.6 mm.

Also, high characteristic impedance was selected for the resonator, with the aim of increasing the field intensity at the open ends. For this purpose, a relatively narrow strip width of 600 μm was chosen, resulting in a characteristic impedance close to 120 Ω. Besides, Taconic TLX-8 low-loss, low-permittivity substrate ($\varepsilon_r = 2.55$, $\tan\delta = 0.0017$) was selected, with a considerable thickness of 1200 μm, to prevent it from influencing the measurements. This way, the fields are not heavily confined into the substrate and they can be more affected by the upper environment. Finally, 50 Ω I/O lines (with 3.2 mm width) were coupled to the resonator by means of coupled-line sections. The coupling strength was designed as a trade-off between too strong coupling (which would worsen the resolution of the electrical response) and too weak coupling (which would lead to considerable influence of noise). Coaxial connectors were soldered at the end of these lines to provide for electrical response measurement. The design is shown in Fig. 4.

### 2.1.2 Measurement setup

The 1.6-mm gap between the ends of the open-loop resonator was the region of interest for sensing purposes, where the changes in the dielectric permittivity of the medium were expected to highly affect the electric response. In this sense, the individual's tongue should be placed exactly onto this gap and always in the same position. Hence, while designing the case, a special structure was incorporated whose purpose was to guide the individual's tongue and ensure that the posture and the placement were the same during every single measurement. This was achieved by a silicone mouthpiece with a small hole in the middle, which fitted in the structure always in the same position, so that the hole was always on the gap of the resonator, and the tongue was guided through it. This way,

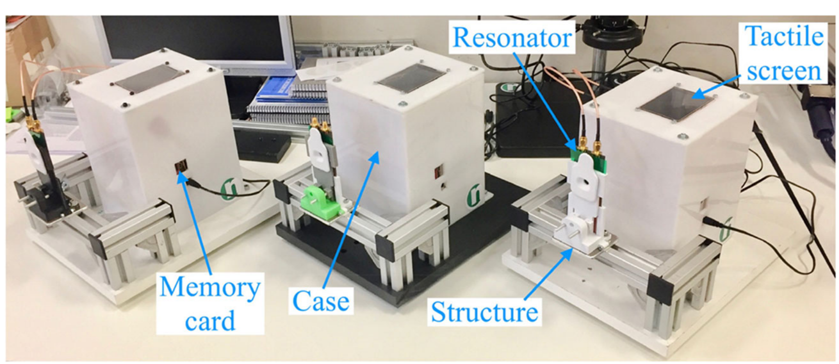
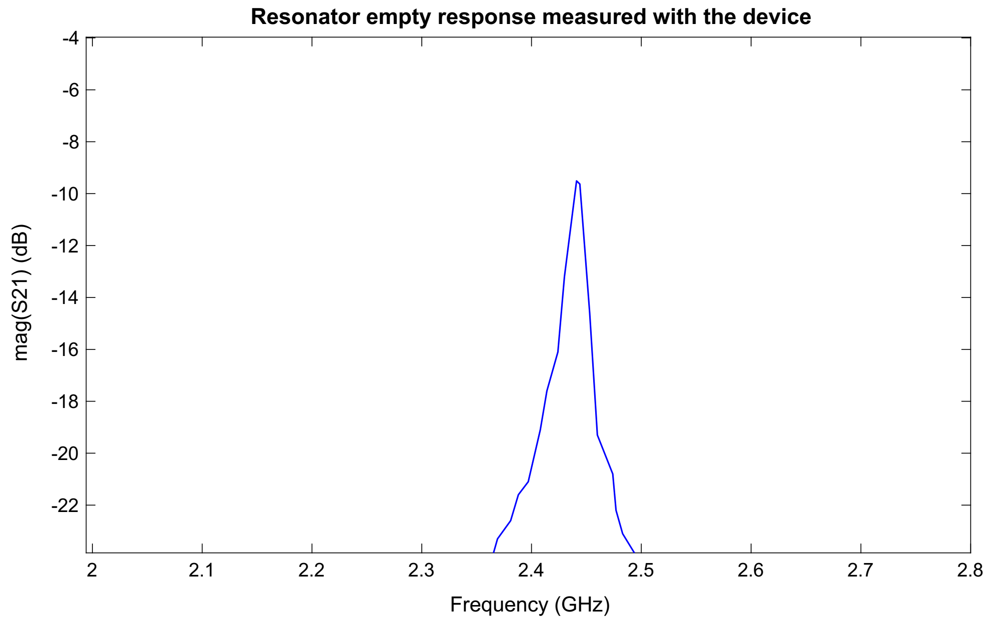



**Fig. 2** Three units of the device developed

**Fig. 3** Frequency response of the microwave resonator measured with the device with no user




both the repeatability and the reproducibility of the measurements were ensured, and the comparison between different measurements was allowed. Figure 5 shows some sketches of the mouthpiece, in which the absolute dimensions are 60.25 × 35.90 × 5.80 mm.

So that every measurement was aseptic, a new thin (180 μm) disposable plastic square was placed between the resonator and the mouthpiece, which had been previously proved not to alter the frequency response. Raw data of the same measurement with and without this plastic square can be obtained in [43]. Also, a big set of mouthpieces was provided so that a different one could be used in each measurement throughout the day, and they all could be sterilized before the next session. These two pieces (plastic square and mouthpiece) fitted perfectly into a third solid plastic piece, a movable holder, which could be slightly removed (thanks to two aluminum handles) to prepare the set, and then put back to the proper position. Finally, two grippers were applied always in the same position in order to make sure there was always the same pressure. A picture of the structure is shown in Fig. 6.

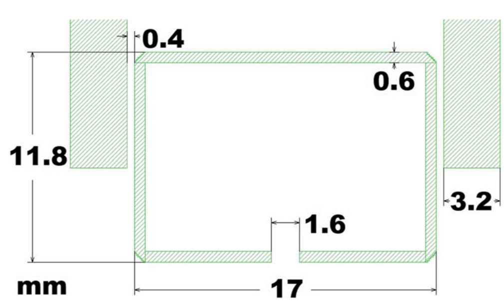



**Fig. 4** Design of the open-loop microstrip resonator acting as sensor

### 2.1.3 Microwave electronics system

Once the user and the setup were in the right position, the measurement was made. The sensor driving electronics consisted of a low-cost scalar network analyzer, which allowed obtaining the magnitude of the transmitted signal between the input and output of any microwave device under test (DUT) within the 1.6–2.7 GHz range. The elements involved in the design of the device are listed in Table 1. The schematic is shown in Fig. 7a, and the implemented scalar network analyzer in Fig. 7b.

The voltage-controlled oscillator (VCO) was able to generate a linear frequency range between 1600 and 3200 MHz for a sweep 0.5–20 V voltage input. This oscillator provided a frequency transition of 5 ms, which yields a whole measuring time for our device of about 3.5 s. After the VCO's output, a low pass filter was implemented with microstrip stubs techniques [44] to prevent the harmonics from the oscillator tuning from interfering in the rest of the system. Then, the directional coupler was used for dividing the filtered signal from the oscillator into two new alike signals: on the one hand, the signal employed for characterizing the DUT (in this case, the microstrip resonator); on the other hand, the reference signal for obtaining the magnitude response of the DUT. A 50 Ω resistance (0.1% precision from Vishay) was used to load its isolated port with the coupler characteristic impedance.

The RF signal detection after the transmission through the DUT was made with the detector, which provides in its output the magnitude difference between the reference signal (from the coupler) and the signal obtained from the DUT (after the transmission). Hence, the magnitude S21 parameter, or transmission signal of the DUT, is obtained after the detector. To do

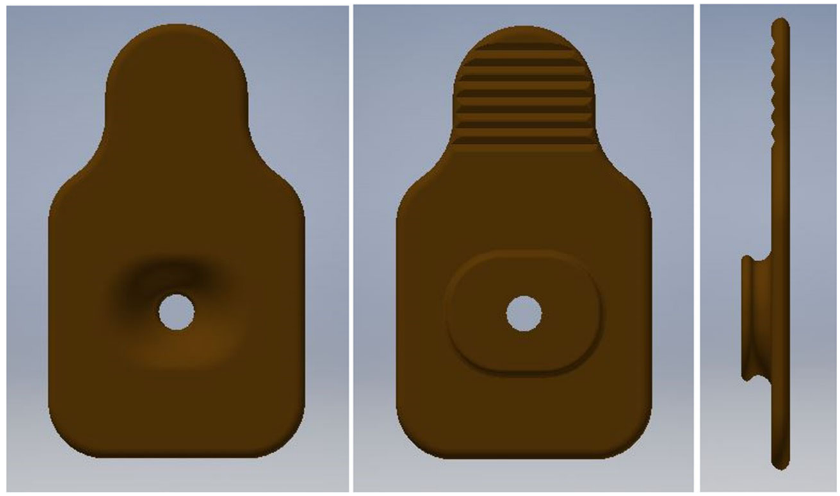


**Fig. 5** Mouthpiece to ensure that the tongue was always guided to the right position

that, the power reference level required by the detector is − 30 dBm, whereas the DUT signal can be represented as an amplitude ranging from 0 to − 60 dBm. Therefore, two attenuators were suitably used to adapt the VCO's and DUT's output power levels to the RF detector input requirements and get the greatest detection range. The whole RF circuit (Fig. 7a) was finally implemented (Fig. 7b) in fiberglass substrate ABC16 (FR-4) from CIF ($\varepsilon_r = 4.4$), 600 μm thick. Two coaxial connectors were also added to the circuit to provide for connection to the DUT (Fig. 7b). The ground connections were drilled and filled with 800-μm-diameter copper wire, welded to both faces of the circuit. Further explanation and discussion about this microwave system can be found in [45].

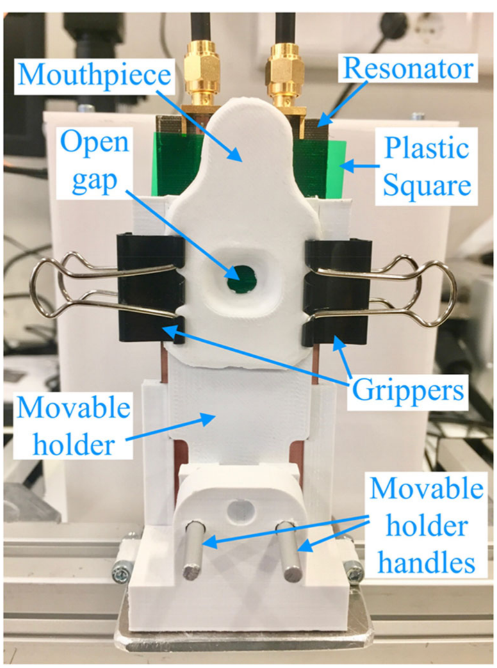



**Fig. 6** Structure of the sensor holding setup

### 2.1.4 Data processing and graphical interface

The voltage sweep signal required by the VCO is generated by the microcontroller unit, which has capabilities for data storage in an extern memory card. This signal is a voltage stepped ramp from 0.5 to 9.5 V with a period of roughly 2 s, driven from a digital output of the microcontroller unit (MCU) to V_Tune line in the oscillator (see Fig. 7b). The signal was always the same, to ensure that all the measurements were made in the same conditions. Then, as the frequency sweep is generated in the VCO, all the gain voltage (V_Gain) values provided by the detector are saved in a data array in the MCU. These voltage data are converted to dB using a calibration file saved in the memory card, which contains the previously measured relationships between the voltages and decibels for the different generated frequencies. Thus, after the conversion, the final data are stored in a new S2P file in the memory card. The global powering of the device is made with the power supply SW4307 from PowerPax directly connected to the MCU. Then, the feeding voltages are driven to the different circuits from the MCU.

In addition, a tactile screen was incorporated to provide for graphical user interface, which was connected to the MCU with a communication bus UART. This screen allowed the users to introduce the individual data and to make the measurement, as well as to see the final graph. A picture of an individual making a measurement is shown in Fig. 8, and some pictures of the screen showing the measurements can be seen in Fig. 9. Finally, a methacrylate case for protecting the electronics was designed, with dimensions 210 × 145 × 160 mm (as it can be seen in Figs. 2 and 6). The screen was embedded on the top of it, and two side holes provided for the coaxial connection of the resonator to the driving electronics.

## 2.2 Measurements and experimental study

Once the devices were developed, their performance was initially assessed in laboratory with some volunteers. The three

**Table 1** Electronic components used in the design of the device

| | Component | Model | Manufacturer |
|---|---|---|---|
| Analog | Voltage-controlled oscillator | CVCO55BE-1600-3200 | Crystek |
| | Directional coupler | X3C19E2-20S | Anaren |
| | RF Gain detector | AD8302 | Analog devices |
| | Attenuators | PAT1220 | Susumu |
| | Low pass filter | 4th order, microstrip line | home-made |
| Digital | Microcontroller unit | PIC32-PINGUINO-OTG | Olimex |
| | Tactile screen | SK-gen4-32PT | 4D systems |

units developed were equally tested, yielding similar results, thus accounting for the reproducibility of the device designed. These tests consisted in the volunteers making a measurement with the device at the beginning (after 8-h fasting), then drinking a sugared drink, and then making more measurements every few minutes. At the same time of each device measurement, the individual's BGL was measured with a commercial glucometer (Accu-Chek® Aviva) for reference, thus having several couples of experimental and reference measurement values for each volunteer at the end of each test. After finishing, the raw data of all the experimental measurements were retrieved from the memory card and analyzed.

As tracking parameter, unloaded quality factor ($Q$) of the obtained resonant S21 peaks (as shown in Fig. 9) was used, due to its previously proved convenience [37]. To get it, loaded quality factor ($Q_L$) was previously computed from the resonant frequency $f_r$ (i.e., the frequency of the maximum S21 parameter) and the bandwidth at 3 dB ($BW_{3dB}$, the frequency range between the two S21 points at which the amplitude falls 3 dB from the maximum) as shown next:

$$Q_L = \frac{f_r}{BW_{3dB}} \quad (3)$$

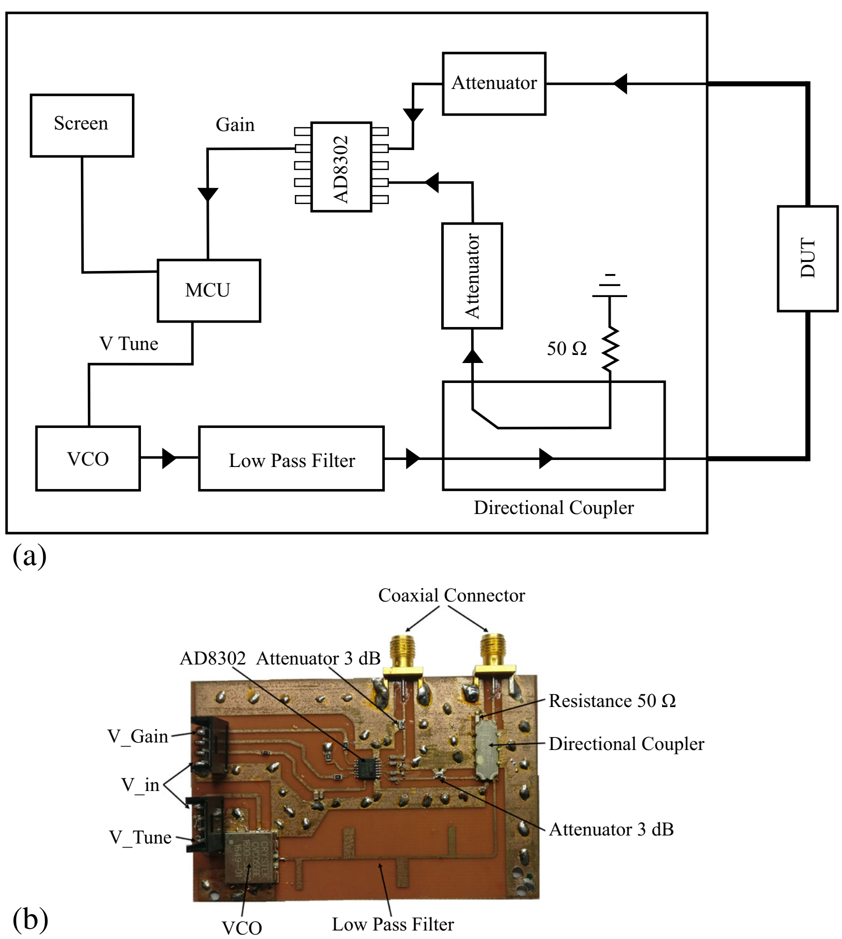



**Fig. 7** Scalar network analyzer. **a** Schematic. **b** Implementation

**Fig. 8** Individual making a measurement

Then, unloaded $Q$ factor was obtained as discussed in [46] using the following expression, where $S21_0$ is the maximum amplitude in the S21 resonant peak in linear scale (converted from the dB raw data):

$$Q = \frac{Q_L}{1-S21_0} \tag{4}$$

Finally, each obtained unloaded $Q$ factor was assigned its corresponding reference BGL from the commercial glucometer and labeled according to its corresponding individual. For comprehensive discussion about $Q$ factor measurement, see [47]. This parameter gives an estimation of the total amount of energy stored in the resonator, and it is hence closely related to the losses in the system. Thus, its use as tracking parameter is motivated form the belief that the major contribution of glucose to the dielectric properties of the environment comes in the form of losses [37].

The results of the first laboratory assessment showed an acceptable behavior of the device as BGL measuring system in some users. However, the same behavior was not seen in all the users, since it is expected to be sensitive to the user, and thus individual calibration will be required. Notwithstanding, as a first, explorative assessment, some cases could be identified with interesting results. Although not appearing in all the tests, these specific cases allowed identifying a relationship with certain linearity between the measured unloaded $Q$ factor and the reference BGL, as it can be seen in session 1 in Fig. 10a, and in session 2 in Fig. 10b. These graphs show the results for two volunteers in three different measurement sessions (during different days) concerning the absolute change in the unloaded $Q$ factor of the resonator with respect to the first fasting measurement, against the time since the glucose intake (in minutes). Each $Q$ factor point is labeled with the volunteer's BGL (in mg/dL) obtained with the commercial glucometer.

Therefore, to further study the behavior of the device, a comprehensive experimentation in a real clinical scenario was made. The need to study the device responses both at individual and collective level with a considerable amount of measurements, in addition to the positive results of previous in vitro studies with the proposed sensor [37], as well as the objective to identify differences from the expected behavior and possible improvement aspects of the device, suggested its use for making measurements with volunteers in a clinical context, as a proof of concept.

The portable devices were set up in two different hospitals in Alicante region (Spain): Hospital General Universitario de Alicante (hereinafter referred to as hospital 1) and Hospital Universitario San Juan de Alicante (hereinafter referred to as hospital 2), to provide for a proof of concept of this technology in a real context. Hospital 2 device was set up in a fixed table and with a stable position, to ensure that the individuals were always in the same posture and the measurements were made in the same conditions. However, due to facility constraints, hospital 1 device had to be set up in a moving table, which was taken to

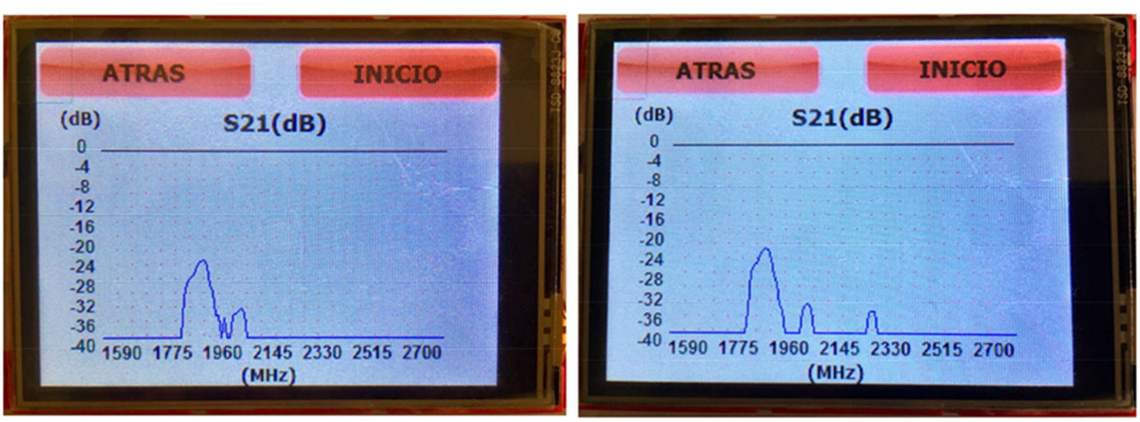



**Fig. 9** Pictures of the graph screen during two volunteers' measurements

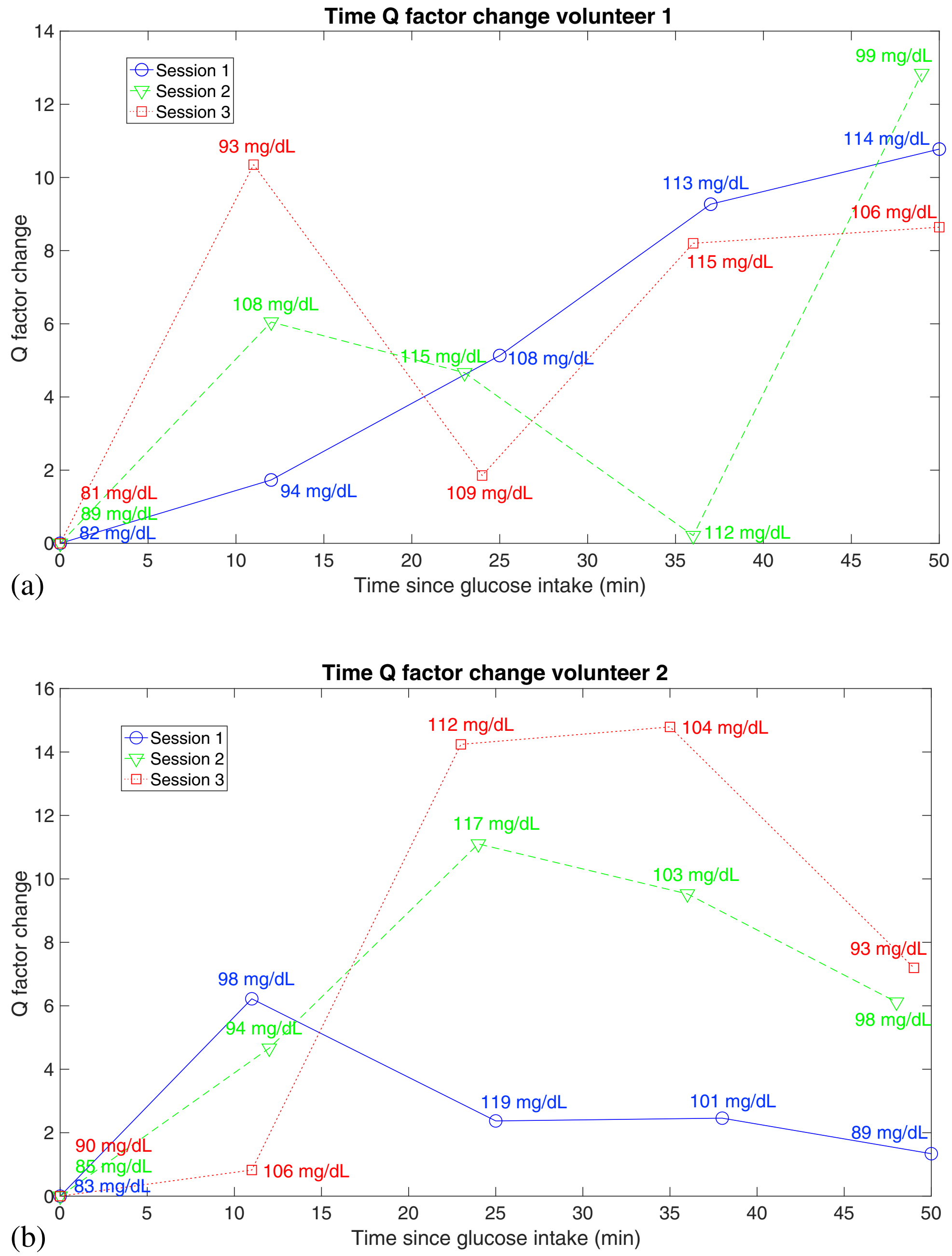



**Fig. 10** Selection of results of the laboratory assessment of the device with two volunteers: volunteer 1 (**a**) and volunteer 2 (**b**)

the volunteer for each measurement, and hence, the same position and conditions for everyone could not be ensured. This circumstance allows assessing the repeatability and the dependence of the measurements on other factors such as device position or user posture.

The experiment consisted in measuring the electrical response of the resonator when a volunteer's tongue was placed onto it, as described previously. The volunteers were pregnant women who went to the hospital to be checked for the OGTT (oral glucose tolerance test) in their scheduled periodical clinical revisions. This medical test consists in the ingestion of a certain amount of liquid glucose after 8-h fasting and having blood extraction for clinical analysis just before the ingestion, as well as after 1, 2 and 3 h. Therefore, this test was a convenient opportunity to evaluate the devices, as the volunteers made one measurement at the same time that each blood extraction and comparison with clinical analysis was possible, in addition to the fact that a wide range of BGL took place during the tests.

Given that the measurements were made during the scheduled revisions of the volunteers, they supposed no additional inconvenience for the volunteers. Also, since the experiment was carried out during clinical OGTTs, it was performed under the supervision of Ethics Committee of Hospital General

Universitario de Alicante and Ethics Committee of Hospital Universitario San Juan de Alicante. The experiment was carried out during 5 months, having one dedicated nurse in each hospital. Data were backed up weekly, and the results were analyzed after the measurements were finished. In total, 352 volunteers participated during the time the devices were available, making four measurements each one in general (except a few exceptions), having a total amount of 1217 measurements. All the resulting data can be freely accessed in [48], as well as extensive anonymous clinical data of the volunteers. The basic physiological parameters of the volunteers are shown in Table 2. It should be noted that these parameters have no influence on the sensor behavior.

## 3 Results

After the above-mentioned experimentation, all the data were gathered and thoroughly analyzed. From each measurement, unloaded $Q$ factor was obtained as explained above. Thus, each measurement yielded to an unloaded $Q$ factor value, which could be associated to a plasma glucose level once the clinical results were available.

However, despite the above-mentioned measures taken to prevent the variations in the placement of the tongue, the individual's posture and the pressure applied, some unusual resonator responses were observed, not resembling the expected resonant peak, which may be attributed to changes in these conditions (for instance, differences in the volunteer posture in hospital 1). An extra parameter was therefore needed to discern the reliable measurements. During the analysis, each measurement was assigned an integer reliability factor based upon the similarity of the obtained electrical response with the expected shape, ranging 0 (not reliable to any extent) to 4 (completely reliable), so that the truly trustable measurements could be concerned in the study. For instance, Fig. 11 plots all the obtained trustworthy unloaded $Q$ factor values (reliability = 4, referred to as "reliable") against their corresponding plasma glucose levels for hospital 1 (a) and hospital 2 (b).

Furthermore, the device is expected to be sensitive to the individual, which means an extra variability factor. Thus, to reduce the variations between different volunteers and ease the global comparison, differential values were considered. These values were computed as the absolute value of the difference between the first, 0-h measurement and the rest of measurements (while keeping the reliability = 4 in all the measurements), the same way as in Fig. 10. The results are shown in Fig. 12, again for hospital 1 (a) and hospital 2 (b). In these graphs, Diff1 = abs(Qunload1 − Qunload0), Diff2 = abs(Qunload2 − Qunload0), and Diff3 = abs(Qunload3 − Qunload0), being Qunload0, Qunload1, Qunload2, and Qunload3 those from Fig. 11. It should be noted that the number of available points in these graphs is reduced because (a) at least one point per volunteer is eliminated (Qunload0, which acts as reference) and (b) at least two points satisfying reliability = 4 are needed per patient (being one of them Qunload0 mandatorily), which is a restrictive criterion.

Finally, with the aim of seeing the information linked to each volunteer (given the individual sensitivity of the device), the graphs in Figs. 13 (hospital 1) and 14 (hospital 2) were plotted, assigning bluish tones for the low values and purplish tones for the large ones. These graphs provide a volunteer-based classification of the measurements, being the volunteers anonymously labeled by the measurement number, and they therefore allow identifying the individual behavior of the device for each person. In order to obtain these graphs, a less restrictive criterion had to be applied for the reliability factor filtering (reliability $\geq 3$, referred to as "semi-reliable"), inasmuch as this time, it was needed to obtain available measurements for the whole study of each individual plotted, a too restrictive criterion if only reliability = 4 was concerned.

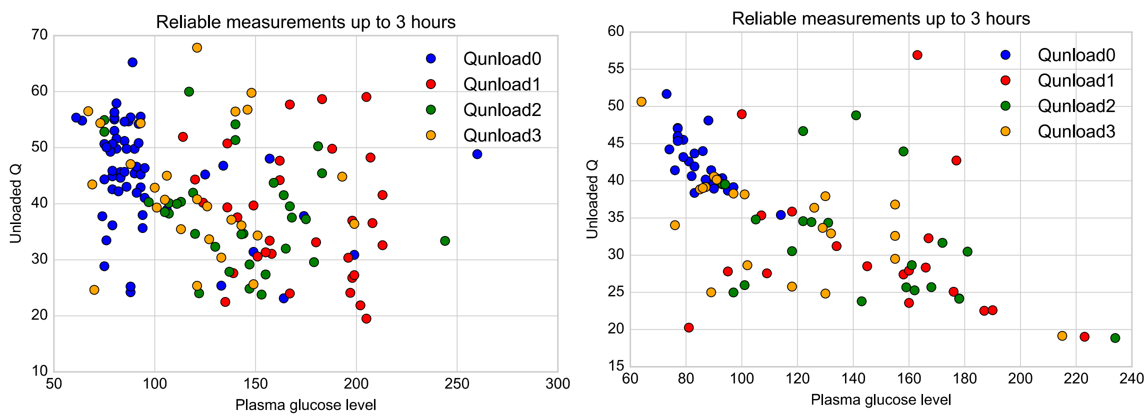
## 4 Discussion

According to the raw measurements, as it can be seen in Figs. 11 and 12, the results do not show a perfect correspondence between the measurement magnitude (unloaded $Q$ factor) and the target magnitude (plasma glucose level). Notwithstanding, results for hospital 2 (Figs. 11b and 12b) are better than results for hospital 1 (Figs. 11a and 12a). Hospital 2 absolute results (Fig. 11b) show an inverse correlation between the unloaded $Q$ factors and plasma glucose levels considering the point density, although with some dispersion. This is an expected result given the lossy properties of glucose [31, 35]. In addition, in these results, it can be seen falls in $Q$ of up to 60% for increments of the plasma glucose level of roughly 140 mg/dL, a usual rise for an individual with diabetes. This is a promising result in terms of sensitivity.

Unfortunately, after all the processing, very few data were available for hospital 2 differential results (Fig. 12b). This is because it is a smaller hospital and thus less volunteers made the measurements. Besides, the requirements for obtaining one point in this graph are too restrictive (both Qunload0 and any other Qunload measurements for the same volunteer must have the highest reliability factor value). However, although lacking the right amount of points to state it, it might seem that a positive

**Table 2** Physiological parameters of the volunteers

| Parameter | Mean | Min–max | Standard deviation |
|---|---|---|---|
| Age (years) | 33.47 | 19–49 | 5.55 |
| Gestational age (weeks) | 26.73 | 6–39 | 6.56 |
| Weight (kg) | 77.61 | 43–125 | 14.75 |
| Height (cm) | 163.33 | 139–185 | 6.42 |



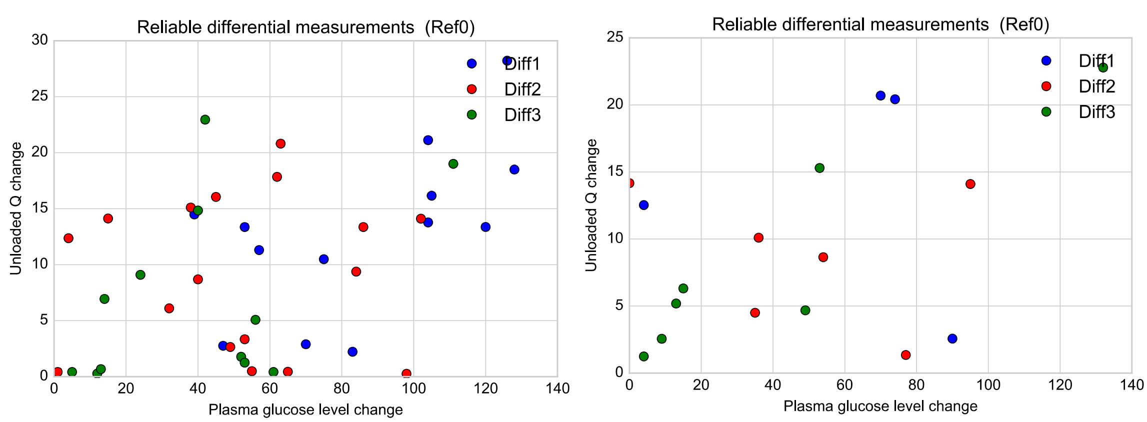

(a) (b)

**Fig. 11** Reliable unloaded $Q$ factor values against plasma glucose level for measurements before glucose intake (Qunload0, blue circles), and after 1 h (Qunload1, red circles), 2 h (Qunload2, green circles), and 3 h (Qunload3, yellow circles): Hospital 1 (**a**) and hospital 2 (**b**)

correlation (due to the absolute differential character of the processing) exists between the unloaded $Q$ factor change and the plasma glucose level, with some dispersion though. This is a logical result, coherent with previous works [37], and the magnitudes of the changes (up to 20 points change in $Q$ for 80–100 mg/dL rise) really show promise.

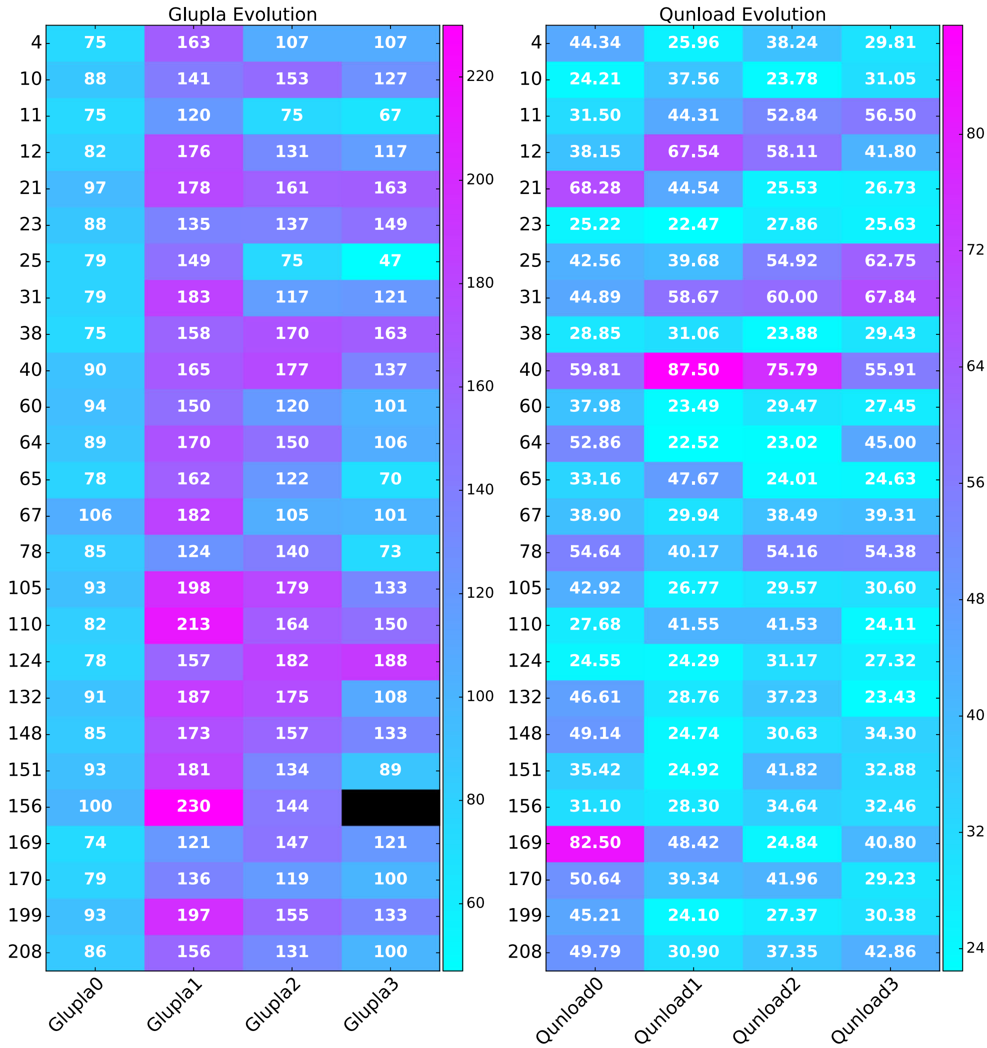
Regarding hospital 1, no good raw results have been seen (Figs. 11a and 12a), despite that the same sensor was used. This difference might be due to the lack of a fixed location to place the device (as there was in hospital 2), which prevents the individual's tongue placement and pressure from being always the same. It might be also put down to the driving and data acquisition electronics, which were implemented with a low-cost philosophy to ease the reproducibility of the experiment, and hence the desired accuracy and reliability could not be achieved. This circumstance could also explain the dispersion seen in hospital 2 results, as well as the need to use a reliability factor for each measurement and the difficulty of obtaining high reliability factor values.

Therefore, it seems evident that some enhancements should be performed concerning the structure and the driving electronics, to avoid these problems. The driving and data acquisition electronics should provide more accurate and reliable electrical responses, using a more sophisticated microwave system, similar to those in commercial network analyzers, to avoid the need of considering reliability factors. In addition to the structure for guiding the tongue, the use of pressure sensors should be considered to ensure always the same pressure of the tongue against the resonator. Also, in the context of clinical use, a special table should also be provided to ensure the installation of the device in a fixed and stable location. A reduction in the total size of the device could ease this aspect, which is also related to the electronics and the needed case. All these aspects would increase the production cost but would likely provide for considerably more accurate and reliable device performing. Furthermore, it should be noticed that no complaint was placed, nor negative reaction was found in any volunteer for using the tongue as the body sensing area




(a) (b)

**Fig. 12** Reliable unloaded $Q$ factor differential values (with respect to the first measurement) against plasma glucose level for measurements at 1 h (Diff1, blue circles), 2 h (Diff2, red circles), and 3 h (Diff3, green circles) after liquid glucose intake: hospital 1 (**a**) and hospital 2 (**b**)




(a) (b)

**Fig. 13** Hospital 1 semi-reliable measurements ordered according to the volunteer. **a** Plasma glucose (Glupla) evolution for the four blood extractions (Glupla0, Glupla1, Glupla2, and Glupla3), **b** Unloaded $Q$ factor evolution for the four measurements (Qunload0, Qunload1, Qunload2, and Qunload3). Bluish tones are given for low values and purplish tones for large values

throughout the whole study, since the measurement is made in a fast, comfortable way.

Considering the volunteer-based results (Figs. 13 and 14), as it can be noticed, weakening the criterion for the reliability factor filtering provides noisier and more random results. This is a consequence of accepting lower quality measurements, but it provides useful information about the potential of this technology. Notwithstanding, specific cases may be identified which produced good results, that is, showed an inverse correlation between the plasma glucose evolution and the unloaded $Q$ evolution. This can be easily noticed by seeing the color contrasts between plots (a) and (b) in Figs. 13 and 14. According to these results, Table 3 shows the individuals that had good results throughout the whole test, as well as those that had good results in at least two measurements, the total number of remarkable individuals (number of individuals in the previous two categories altogether), and the total number of good measurements.

This means that there were 35 users matching the reliability factor in both hospitals (the total amount of individuals considered in Figs. 13 and 14), 9.95% of the total study. Of them, 15 had a complete good measurement set, having 27 individuals at least two good measurements, with 91 good measurements out of 139. Hence, inside this selection according to the reliability factor, there was an individual success rate of 42.86%, with 77.14% of them having two or more good measurements, and a measurement success rate of 65.57%. It seems evident that an individual calibration with reference BGL measurements would enhance the performance of the device. However, it must be noted that this is only a selection of the measurements based upon a reliability factor, and it represents a small part of the whole study (approximately a tenth fraction).

Concerning the reliable measurements during the whole experiment, there were a total of 229 measurements with reliability = 4, out of 1217, a logical result given that this was the most restrictive criterion. With these measurements, and

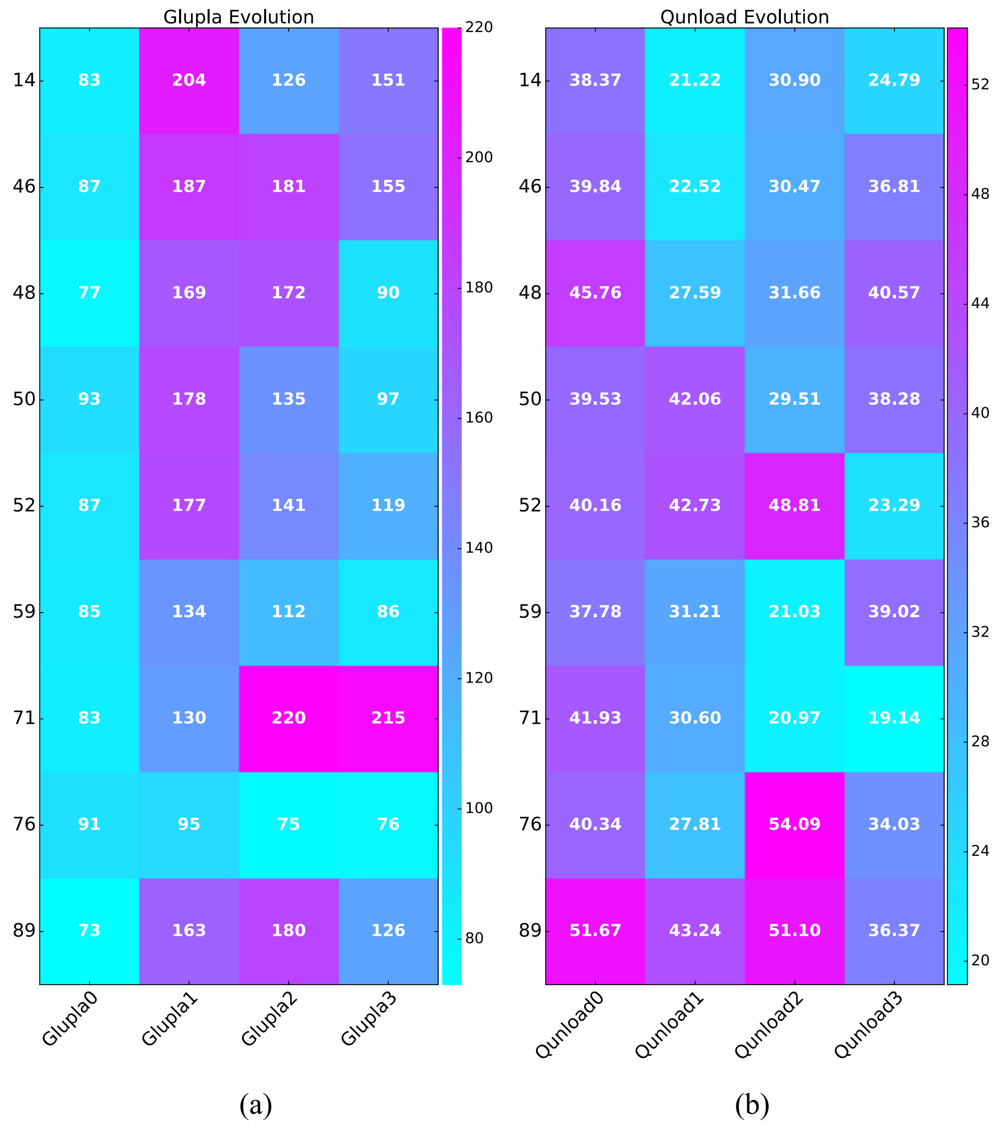



**Fig. 14** Hospital 2 semi-reliable measurements ordered according to the volunteer. **a** Plasma glucose (Glupla) evolution for the four blood extractions (Glupla0, Glupla1, Glupla2, and Glupla3). **b** Unloaded $Q$ factor evolution for the four measurements (Qunload0, Qunload1, Qunload2, and Qunload3). Bluish tones are given for low values and purplish tones for large values

considering a linear correlation between the measured unloaded $Q$ and the user's plasma glucose level, Table 4 shows the correlation coefficients for each measurement time (at 0, 1, 2, and 3 h after the glucose intake) for the two hospitals. It should be noted that the real correlation between the unloaded $Q$ and the user's plasma glucose is likely to be non-linear, and a parametric relationship between them should be investigated. However, the current data are too dispersed in a statistical sense to provide for such an analysis in a reliable way. Also, these results come from a general analysis by merging measurements from all the individuals. Since the device is sensitive to the user, different correlations may be found for each one, and hence, these results should not be taken as strict indicators of the overall device performance.

As it can be seen, all the correlation coefficients for all the cases are negative, which is in accordance with the discussion of the results plotted in Figs. 11, 13, and 14. The results do not show high enough correlation coefficients to propose this system for

**Table 3** Summary of the semi-reliable results

| | Individuals with good results throughout the test | Individuals with good results in at least two measurements | Total remarkable individuals | Total good measurements |
|---|---|---|---|---|
| Hospital 1 | 4, 21, 25, 60, 64, 67, 105, 148, 169, 199, 208 | 11, 23, 38, 65, 78, 132, 170 | 18 | 63 |
| Hospital 2 | 14, 48, 59, 71 | 46, 50, 52, 76, 89 | 9 | 28 |
| *TOTAL* | *15* | *12* | *27* | *91* |

**Table 4** Correlation coefficients obtained for the reliable measurements at each measurement time in each hospital

| Hospital | Measurement time | | | |
|---|---|---|---|---|
| | 0 h | 1 h | 2 h | 3 h |
| Hospital 1 | -0.283 | -0.102 | -0.297 | -0.126 |
| Hospital 2 | -0.748 | -0.226 | -0.434 | -0.627 |

real application, since many enhancements should be applied, as discussed above. However, the consistency found between the different data groups (always negative correlation) suggests that the measuring principle, although needing for improvements, has a trustable basis, and it therefore seems exploitable. These results indicate that this technique is worthy of further research.

The difference between the correlations obtained in both hospitals is evident, having better results in hospital 2, which can be due to the differences in the device setup, as explained in Sect. 2.2. Another remarkable fact is that the best correlations (and hence the best sensor results) are given for the first measurement (at 0 h) in both hospitals. This could be explained by a less relaxed posture or attitude of the volunteers towards the device in their first experience with it, having a slightly lower pressure of their tongues against the resonator, and providing for a better measurement. This may mean that a pressure control could enhance the functioning of these devices, and therefore pressure sensors should be incorporated, as it has been recently proposed [49].

The above-mentioned electronics and setup improvements would presumably increase the valid measurement ratio. Also, the need for individual calibration suggests that there are more phenomena to track. In this sense, a sensor like the one proposed could be integrated into a multitechnology approach with measurements based on different physical principles, which would help to increase the success ratio and, more importantly, the selectivity. This could eventually lead to a reliable NIBGM system, in which different measurement processes would provide enough information to feed sophisticated machine learning algorithms able to build accurate electromagnetic models of the real biological environment. These systems should be capable of characterizing the models and solving them for the measured data, obtaining all the needed parameters, like the BGL.

## 5 Conclusions

A portable version of a non-invasive BGL sensor based upon a microwave resonator has been presented and assessed in a multicenter proof of concept. The results shown in this document have pointed out some cases in which the proposed device shows promise as a NIBGM, although this conclusion cannot be applied to the general case. One of the main conclusions highlights the high sentivity of the device to some parameters related to the measuring procedure, such as the position of the individual or the pressure at placing the tongue. These results sugest as well that the device could be sentitive to other parameters related to each individual, given the observed differences between volunteers. However, it has been shown that when these conditions do not vary, the evolution of the electrical response of the device is generally linked to the evolution of the BGL of the individual, and hence this technology is worthwhile investigating.

Further research is therefore advisable, having as future scope the development of a better, more comfortable and more stable structure to make sure the same position in every measurement, and the use of pressure sensors to ensure the same pressure always. These aspects, besides providing for individual calibration, would lead to more reliable measurements of the sensor. In this sense, the experimentation with the proposed technology in real contexts is essential to provide useful data for developing calibration and postprocessing algorithms able to provide individually adapted processing of the measurements. Such a feature is expected to remarkably enhance the performance of these devices.

Also, the results shown in this paper allow to expect a good sensitivity of the device once the above-mentioned enhancements are applied, but the same reasoning cannot be inferred for the selectivity, given the differences found between volunteers with similar glucose level values. It seems evident that there are more components in blood affecting the measurement process, in addition to glucose, and hence all the different behaviors should be characterized. Thus, a multisensor approach, combining different technologies able to track several physical principles would be desireable. A sensor fusion system able to model and characerize the full environment, taking into account all the affecting parameters and phenomena, and applying machine learning techniques to build the model for each individual would doubtlessly provide for a more accurate performance as NIBGM. A sensor like the one presented in this work may potentially be an essential part of such a system.

**Acknowledgments** The authors would like to sincerely thank the nursing work carried out by María de los Ángeles Vicedo García and Ana Laura Morote Castellanos throughout the measurements and data acquisition process.

**Funding information** Carlos G. Juan's work was funded by the Spanish Ministry of Education, Culture, and Sport through the Research and Doctorate Supporting Program FPU under Grant FPU14/00401. This work was partially funded by the Foundation for the Promotion of Health and Biomedical Research of Valencia Region (FISABIO) through Project UGP-15-202, and by Spanish Research State Agency and European Regional Development Fund through "Craneeal" Project (DPI2106-80391-C3-2-R).

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of Hospital General Universitario de Alicante and Ethics Committee of Hospital Universitatio San Juan de Alicante, as well as with the 1964 Declaration of Helsinki and its later amendments.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References


1. World Health Organization (2016) Global report on diabetes. Switzerland, Geneva
2. Heinemann L (2008) Finger pricking and pain: a never ending story. J Diabetes Sci Technol 2(5):919–921. https://doi.org/10.1177/193229680800200526
3. van Beers CAJ, DeVries JH (2016) Continuous glucose monitoring: impact on hypoglycemia. J Diabetes Sci Technol 10(6):251–1258. https://doi.org/10.1177/1932296816653411
4. Fortwaengler K, Campos-Náñez E, Parkin CG, Breton MD (2018) The financial impact of inaccurate blood glucose monitoring systems. J Diabetes Sci Technol 12(2):318–324. https://doi.org/10.1177/1932296817731423
5. Gill M, Zhu C, Shah M, Chhabra H (2018) Health care costs, hospital admissions, and glycemic control using a standalone, real-time, continuous glucose monitoring system in commercially insured patients with type 1 diabetes. J Diabetes Sci Technol 12(4):800–807. https://doi.org/10.1177/1932296818777265
6. Zarkogianni K, Mitsis K, Litsa E, Arredondo M-T, Fico G, Fioravanti A, Nikita KS (2015) Comparative assessment of glucose prediction models for patients with type 1 diabetes mellitus applying sensors for glucose and physical activity monitoring. Med Biol Eng Comput 53(12):1333–1343. https://doi.org/10.1007/s11517-015-1320-9
7. Zhao C, Yu C (2015) Rapid model identification for online subcutaneous glucose concentration prediction for new subjects with type 1 diabetes. IEEE Trans Biomed Eng 57(8):1333–1344. https://doi.org/10.1109/TBME.2014.2387293
8. Georga EI, Protopappas VC, Polyzos D, Fotiadis DI (2015) Evaluation of short-term predictors of glucose concentration in type 1 diabetes combining feature ranking with regression models. Med Biol Eng Comput 53(12):1305–1318. https://doi.org/10.1007/s11517-015-1263-1
9. Lee JB, Dassau E, Gondhalekar R, Seborg DE, Pinsker JE, Doyle FJ III (2016) Enhanced model predictive control (empc) strategy for automated glucose control. Ind Eng Chem Res 55:11857–11868. https://doi.org/10.1021/acs.iecr.6b02718
10. Abraham MB, Nicholas JA, Smith GJ, Fairchild JM, King BR, Ambler GR, Cameron FJ, Davis EA, Jones TW (2018) Reduction in hypoglycemia with the predictive low-glucose management system: a long-term randomized controlled trial in adolescents with type 1 diabetes. Diabetes Care 41:303–310. https://doi.org/10.2337/dc17-1604
11. Georga EI, Príncipe JC, Fotiadis DI (2019) Short-term prediction of glucose in type 1 diabetes using kernel adaptive filters. Med Biol Eng Comput 57(1):27–46. https://doi.org/10.1007/s11517-018-1859-3
12. Abu-Rmileh A, Garcia-Gabin W (2010) Feedforward–feedback multiple predictive controllers for glucose regulation in type 1 diabetes. Comput Methods Prog Biomed 99(1):113–123. https://doi.org/10.1016/j.cmpb.2010.02.010
13. Lunze K, Singh T, Walter M, Brendel MD, Leonhardt S (2013) Blood glucose control algorithms for type 1 diabetic patients: a methodological review. Biomed Signal Process Control 8(2):107–119. https://doi.org/10.1016/j.bspc.2012.09.003
14. Nichols SP, Koh A, Storm WL, Shin JH, Schoenfisch H (2013) Biocompatible materials for continuous glucose monitoring devices. Chem Rev 113(4):2528–2549. https://doi.org/10.1021/cr300387j
15. Facchinetti A, Del Favero S, Sparacino G, Castle JR, Ward WK, Cobelli C (2014) Modeling the glucose sensor error. IEEE Trans Biomed Eng 61(3):620–629. https://doi.org/10.1109/TBME.2013.2284023
16. Reiterer F, Polterauer P, Freckmann G, del Re L (2016) Identification of CGM time delays and implications for BG control in T1DM. In IFMBE Proc. XIV Mediterranean Conf on Med and Biol Eng Comp 2016, Paphos, Cyprus, pp 190–195. https://doi.org/10.1007/978-3-319-32703-7_39
17. Du Y, Zhang W, Wang ML (2016) An on-chip disposable salivary glucose sensor for diabetes control. J Diabetes Sci Technol 10(6):1344–1352. https://doi.org/10.1177/1932296816642251
18. Laione F, Marques JLB (2005) Methodology for hypoglycaemia detection based on the processing, analysis and classification of the electroencephalogram. Med Biol Eng Comput 43(4):501–507. https://doi.org/10.1007/BF02344732
19. Yamaguchi M, Kawabata Y, Kambe S, Wårdell K, Nystrom FH, Naitoh K, Yoshida H (2004) Non-invasive monitoring of gingival crevicular fluid for estimation of blood glucose level. Med Biol Eng Comput 42(3):322–327. https://doi.org/10.1007/BF02344706
20. Yan K, Zhang D, Wu D, Wei H, Lu G (2014) Design of a breath analysis system for diabetes screening and blood glucose level prediction. IEEE Trans Biomed Eng 61(11):2787–2795. https://doi.org/10.1109/TBME.2014.2329753
21. Liao Y-T, Yao H, Lingley A, Parviz B, Otis BP (2012) A 3-μW CMOS glucose sensor for wireless contact-lens tear glucose monitoring. IEEE J Solid State Circuits 47(1):335–344. https://doi.org/10.1109/JSSC.2011.2170633
22. Chen L, Tse WH, Chen Y, McDonald MW, Melling J, Zhang J (2017) Nanostructured biosensor for detecting glucose in tear by applying fluorescence resonance energy transfer quenching mechanism. Biosens Bioelectron 91:393–399. https://doi.org/10.1016/j.bios.2016.12.044
23. Novais S, Ferreira CIA, Ferreira MS, Pinto JL (2018) Optical fiber tip sensor for the measurement of glucose aqueous solutions. IEEE Photonics J 10(5):6803609–6803609. https://doi.org/10.1109/JPHOT.2018.2869944
24. Pleitez MA, Lieblein T, Bauer A, Hertzberg O, Lilienfeld-Toal H, Mäntele W (2013) In vivo noninvasive monitoring of glucose concentration in human epidermis by mid-infrared pulsed photoacoustic spectroscopy. Anal Chem 85:1013–1020. https://doi.org/10.1021/ac302841f
25. Ghazaryan A, Ovsepian SV, Ntziachristos V (2018) Extended near-infrared optoacoustic spectrometry for sensing physiological concentrations of glucose. Front Endocrinol 9(112). https://doi.org/10.3389/fendo.2018.00112
26. Vahlsing T, Delbeck S, Leonhardt S, Michael Heise H (2018) Noninvasive monitoring of blood glucose using color-coded photoplethysmographic images of the illuminated fingertip within the visible and near-infrared range: opportunities and questions. J Diabetes Sci Technol 12(6):1169–1177. https://doi.org/10.1177/1932296818798347
27. Yadav J, Rani A, Singh V, Murari BM (2015) Prospects and limitations of non-invasive blood glucose monitoring using near-infrared spectroscopy. Biomed Signal Process Control 18:214–227. https://doi.org/10.1016/j.bspc.2015.01.005
28. Yilmaz T, Foster R, Hao Y (2019) Radio-frequency and microwave techniques for non-invasive measurement of blood glucose levels. Diagnostics 9(6):1–34. https://doi.org/10.3390/diagnostics9010006

29. Greene J, Abdullah B, Cullen J, Korostynska O, Louis J, Mason A (2019) Non-invasive monitoring of glycogen in real-time using an electromagnetic sensor. In: Mukhopadhyay S, Jayasundera K, Postolache O (eds) Modern sensing technologies. smart sensors, measurement and instrumentation, vol 29, Springer, pp. 1–15. ISBN: 978-3-319-99539-7. https://doi.org/10.1007/978-3-319-99540-3_1
30. Amin B, Elahi MA, Shahzad A, Porter E, McDermott B, O'Halloran M (2019) Dielectric properties of bones for the monitoring of osteoporosis. Med Biol Eng Comput 57(1):1–13. https://doi.org/10.1007/s11517-018-1887-z
31. Potelon B, Quendo C, Carré J-L, Chevalier A, Person C, Queffelec P (2014) Electromagnetic signature of glucose in aqueous solutions and human blood. In Proc MEMSWAVE Conf 2014, La Rochelle, France, pp. 4–7
32. Juan CG, Bronchalo E, Torregrosa G, Ávila E, García N, Sabater-Navarro JM (2017) Dielectric characterization of water glucose solutions using a transmission/reflection line method. Biomed Signal Process Control 31(1):139–147. https://doi.org/10.1016/j.bspc.2016.07.011
33. Lin T, Gu S, Lasri T (2017) Highly sensitive characterization of glucose aqueous solution with low concentration: application to broadband dielectric spectroscopy. Sensors Actuators A Phys 267: 318–326. https://doi.org/10.1016/j.sna.2017.10.029
34. Gabriel S, Lau RW, Gabriel C (1996) The dielectric properties of biological tissues: III. Parametric models for the dielectric spectrum of tissues. Phys Med Biol 41(11):2271–2293
35. Costanzo S, Cioffi V, Raffo A (2018) Complex permittivity effect on the performances of non-invasive microwave blood glucose sensing: enhanced model and preliminary results. In Proc WorldCIST'18 2018: Trends and advances in information systems and technologies, Naples, Italy, pp 1505–1511. https://doi.org/10.1007/978-3-319-77712-2_146,
36. Parkhomenko MP, Savel'ev SV, von Gratovski SV (2017) Analysis of dielectric properties of blood and development of a resonator method for noninvasive measuring of glucose content in blood. J Commun Technol Electron 62(3):267–281. https://doi.org/10.1134/S1064226917030159
37. Juan CG, Bronchalo E, Potelon B, Quendo C, Ávila-Navarro E, Sabater-Navarro JM (2019) Concentration measurement of microliter-volume water–glucose solutions using *Q* factor of microwave sensors. IEEE Trans Instrum Meas 68(7):2621–2634. https://doi.org/10.1109/TIM.2018.2866743
38. Juan CG, Bronchalo E, Torregrosa G, Garcia A, Sabater-Navarro JM (2015) Microwave microstrip resonator for developing a non-invasive glucose sensor. Int J Comput Assist Radiol Surg (CARS) 10(1):172–173. https://doi.org/10.1007/s11548-015-1213-2
39. Jean BR, Green EC, McClung MJ (2008) A microwave frequency sensor for non-invasive blood-glucose measurement. In Proc IEEE Sensors Appl Symp (SAS) 2008, Atlanta, GA, USA https://doi.org/10.1109/SAS.2008.4472932
40. Yilmaz T, Foster R, Hao Y (2014) Towards accurate dielectric property retrieval of biological tissues for blood glucose monitoring. IEEE Trans Microw Theory Tech 62(12):3193–3204. https://doi.org/10.1109/TMTT.2014.2365019
41. Choi H, Naylon J, Luzio S, Beutler J, Birchall J, Martin C, Porch A (2015) Design and in vitro interference test of microwave noninvasive blood glucose monitoring sensor. IEEE Trans Microw Theory Tech 63(10):3016–3025. https://doi.org/10.1109/TMTT.2015.2472019
42. Raicu V, Feldman Y (2015) Dielectric relaxation in biological systems: physical principles, methods and applications. Oxford Univ. Press. ISBN: 9780199686513, Oxford. https://doi.org/10.1093/acprof:oso/9780199686513.001.0001
43. nBio Research Group (2019) File with_without_plastic.zip. In: Glucolate nBio. Available via http://nbio.umh.es/glucolate/. Accessed 11 July 2019
44. Pozar D (1998) Microwave filters. In Pozar D (ed.) Microwave engineering, 2nd edn. John Wiley & Sons, pp. 422–498. ISBN: 0–471–17096-8
45. García H, Juan CG, Ávila-Navarro E, Bronchalo E, Sabater-Navarro JM (2019) Portable device based on microwave resonator for noninvasive blood glucose monitoring. In 2019 41st Annual Int Conf of the IEEE Eng Med Biol Society (EMBC), Berlin, Germay
46. Bray JR, Roy L (2004) Measuring the unloaded, loaded, and external quality factors of one- and two-port resonators using scattering-parameter magnitudes at fractional power levels. IEE Proc-Microw Antennas Propag 151(4):345–350. https://doi.org/10.1049/ip-map:20040521
47. Kajfez D (2011) *Q* factor measurements using Matlab. Norwood: Artech House. ISBN: 9781608071616
48. nBio Research Group (2019) File all_data.zip. In: Glucolate nBio. Available via http://nbio.umh.es/glucolate/. Accessed 11 July 2019
49. Turgul V, Kale I (2016) A novel pressure sensing circuit for non-invasive RF/microwave blood glucose sensors. In 16th Mediterranean Microwave Symposium (MMS), Abu Dhabi, United Arab Emirates. https://doi.org/10.1109/MMS.2016.7803818




**Carlos G. Juan** received the M.Sc. degree in Telecommunication Engineering from Miguel Hernández University, Elche, Spain, in 2014. He is currently a Teaching and Research Assistant at the Department of Systems Engineering and Automation, where he is currently pursuing the Ph.D. degree in Industrial and Telecommunication Technologies at nBio Research Group, with a scholarship funded by the Spanish Government. Google Scholar: https://scholar.google.es/citations?user=P13I358AAAAJ&hl=es

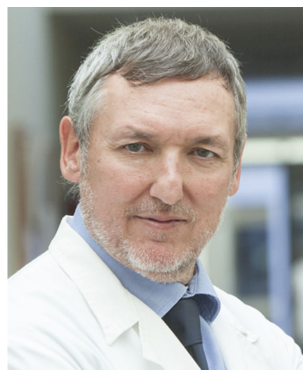
**Héctor García** received the M.Sc. degree in Telecommunication Engineering from Miguel Hernández University, Elche, Spain, in 2016. He is currently an Associate Professor at the Department of Materials Science, Optics and Electronic Technology, and a researcher of Radiofrequency System Group.

**Ernesto Ávila** received the M.Sc. degree in Telecommunication Engineering from Polytechnic University of Valencia, Valencia, Spain, in 1998, and the Ph.D. degree from Miguel Hernández University, Elche, Spain, in 2008. In 2000, he joined Miguel Hernández University, where he is an Associate Professor with the Department of Materials Science, Optics and Electronic Technology. Nowadays, he is Vice-Dean of the School of Engineering of Elche.

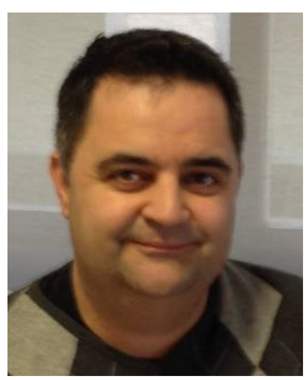
**Enrique Bronchalo** received the Physics degree from Universidad Complutense de Madrid, and the Ph.D. in Physics from Universidad de Alcalá. He is currently an Associate Professor at the Department of Communications Engineering, Miguel Hernández University, Elche, Spain.

**Vicente Galiano** received the M.Sc. degree in Telecommunication engineering from the Polytechnic University of Valencia, Spain, in 1999, and the Ph.D. degree in computer science from the University Miguel Hernandez of Elche, Alicante, Spain, in 2007. He is currently an Associate Professor with the Department of Physics and Computer Architecture, Miguel Hernandez University in Elche, Alicante, Spain. His main research interests include high-level interfaces design in parallel libraries, parallel simulations for modeling biological systems.

**Óscar Moreno** , M.D., is coordinator of the reference Diabetes Unit at Hospital General Universitario de Alicante, Alicante, Spain, since 2013. He is a member of the diabetes working group at Endocrinology and Nutrition Spanish Society (SEEN), and he was the main coordinator between 2011 and 2014. Since 2011, he is Associate Professor of the Department of Clinical Medicine at Miguel Hernández University, Elche, Spain. He is coordinator of Diabetes and Associated Metabolic Diseases Research Group at Alicante Health and Biomedical Research Institute (ISABIAL-FISABIO). He has been coordinator, researcher, and principal investigator of numerous research projects.



**Domingo Orozco** , M.D., is a specialist in Family Medicine and Associate Professor with the Department of Clinical Medicine at Miguel Hernández University, Elche, Spain. He joined Miguel Hernández University at the moment it was founded, and he is Director of the Master on Health Management and coordinator of Cardiometabolic Study Valencian Research Group. He is coordinator of Non Communicable Diseases Group at World Organization of Family Doctors (WONCA). He is a member of the Coordinating Group of the Chronicity Approach Strategy at the Ministry of Health, Consumption and Social Welfare of Spain, and former President of its Family Medicine National Commission. He is an academic of the Royal Academy of Medicine in Valencia Region, coordinator of Telemedicine VALCRONIC Project, and former manager of the Foundation for the Promotion of Health and Biomedical Research (FISABIO).



**José María Sabater-Navarro** received the M.Sc. degree in Industrial Engineering from Polytechnic University of Valencia, Valencia, Spain, in 1998, where he received a Young Researchers grant at the Chemical Institute (ITQ) CSIC-UPV, and he received the Ph.D. degree from Miguel Hernández University, Elche, Spain, in 2003. He is currently a Full Professor at the Department of Systems Engineering and Automation, and a researcher of nBio Research Group. Since 2009, he is Vice-Dean of the School of Engineering of Elche, and since 2012, he is Director of the Master on Industrial Engineering degree. Google Scholar: https://scholar.google.es/citations?hl=es&user=2BFSa4sAAAAJ