# DESIGN OF A DIELECTRIC SPECTROSCOPY SENSOR FOR CONTINUOUS AND NON-INVASIVE BLOOD GLUCOSE MONITORING

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#### **ABSTRACT**

In this paper we propose a new architecture of a non-invasive, continuous blood glucose monitoring system, based on dielectric spectroscopy. In particular we design the electrical circuit, the schematic and the PCB of a mixed signal system working in a frequency range 1 MHz – 160 MHz, where the best performances in terms of electrical changes in the blood can be achieved. The proposed architecture allows to acquire easily the dependence on frequency for both amplitude and phase of the dielectric constant from which the glucose levels in blood is estimated.

**KEYWORDS:** Biosensors, Bioelectronics, Non-invasive Continuous Glucose Monitoring Systems, Glucose Sensor, Dielectric Spectroscopy, Electronic Interfaces and Data Processing, Microcontroller, Prototyping and Testing.

# I. INTRODUCTION

Diabetes Mellitus is a chronic disease which consists of various metabolic disorders. It is characterized by high levels of blood glucose (hyperglycaemia) and it is the result of a deficiency of insulin secretion or of resistance to the action of insulin or a combination of these [1]. In the long term, diabetes can lead to severe complications affecting many body tissues and organs. Diabetes therapy must maintain near normal glycaemia values (60 - 120 mg/dl) in diabetic patients but this is so difficult that there is a need for a blood glucose monitoring system that can provide information throughout the day.

Generally diabetic patients use self-monitoring of blood glucose to achieve tight metabolic control, but this is inefficient in detecting hyper and hypoglycaemic events due to glucose fluctuations. Therefore a continuous system for blood glucose monitoring is required to provides sound alarms for rapid variations of blood glucose levels in order to reduce the risk of hyper and hypoglycaemic events. Nowadays a number of alternative strategies are available including implanted glucose sensors, semi-invasive and non-invasive technologies but the most attractive methods are those non-invasive since diabetic patients can run measurements without any pain.

One of the most interesting non-invasive techniques is the dielectric spectroscopy, which allows, as compared with other methods, to detect glycaemic fluctuations in blood and not in the interstitial tissue.

A number of reports describe the use of dielectric spectroscopy for non-invasive blood glucose monitoring [2] [3] [4]. In fact dielectric properties of cells, blood and tissue, changing with glucose levels, exhibit a significant  $\beta$ -dispersion in the radio frequency range [5] due to the polarization at the interface between the intra- or extracellular solution and the phospholipid membrane, known as Maxwell-Wagner effect. However, it is well known [6] that changes within glucose levels do not affect directly the dielectric spectrum of skin and underlying tissue in the MHz frequency range so

glucose concentration can be measured using dielectric spectroscopy only through the change of tissue permittivity.

In order to develop a glucose sensor based on impedance spectroscopy that can be sensitive to the electrical changes in the blood, the working frequency must be not greater than 200 MHz to maintain sensitivity to the  $\beta$ -dispersion. At the same time, the working frequency must not be too low (> 100 kHz) in order to avoid problems with electrode polarization.

In this paper we propose a new architecture of a non-invasive, continuous blood glucose monitoring sensor, based on dielectric spectroscopy, working in the frequency range 1 MHz – 160 MHz, where the best performances in terms of electrical changes in the blood can be achieved.

In particular we have designed the electrical circuit, the schematic and the PCB of a mixed signal system. The device prototype is constituted by a commercial integrated circuit and it is compact, light and easily transportable.

In Section 2 we have described the main feature of the dielectric spectroscopy, while in Section 3 the proposed architecture has been analyzed, In Section 4 we have discussed the results, highlighting the main goals obtained by our design. Finally the conclusions and future developments have been illustrated in Section 5.

## II. DIELECTRIC SPECTROSCOPY

One of the most promising non-invasive approach for blood glucose monitoring is the dielectric spectroscopy, which can investigate the relaxation processes of complex systems in an extremely wide range of characteristic times from  $10^{-12}$  s to  $10^4$  s. In particular, the dielectric spectroscopy is sensitive to intermolecular interactions and can monitor collective processes.

Dielectric spectroscopy has been used to study various material, liquid and solids, and it could be considered as an extent of the optical spectroscopy to the low frequency side of the infrared spectra.

In particular, the application of the dielectric spectroscopy for blood glucose monitoring requires the use a capacitive fringing field sensor to sense first the first layers of the body, in order to monitor electrical properties of the skin and underlying tissue.

A typical capacitive fringing field sensor is shown in Fig. 1.

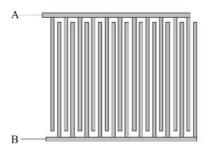


Figure 1. Capacitive fringing field sensor.

Sensor impedance, at various frequencies, depends on the sensor shape but also on the dielectric properties sensed by the fringe field, so it depends on dielectric susceptibility of blood, human skin and underling tissue. This shows that dielectric spectroscopy consists of an impedance measurement and therefore dielectric spectroscopy is also called impedance spectroscopy.

A simple equivalent circuit of the sensor mounted on the skin of a diabetic patient is shown in Fig. 2, in which, in a simplified approach, L is the inductance of the coil, C is the capacitance of the sensor attached to the skin and R is the average resistance of the skin and underling tissue.

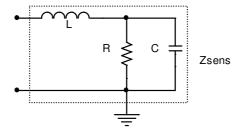


Figure 2. A simple equivalent circuit of the sensor mounted on the skin.

While usually the RF impedance can be measured by means of a VNA (Vector Network Analyser), we implement the basic method of the voltage divider, as shown in Fig. 3, where Zsens is the impedance of the sensor and Rs is a reference resistor connected in series with Zsens.

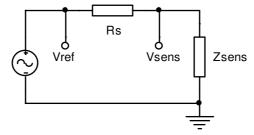


Figure 3. Impedance measurement with voltage divider.

A sinusoidal voltage signal, with low amplitude (< 0.3 V) and with frequency in the range 1 MHz – 160 MHz, is applied to the voltage divider (see). From the measurement of Vref and Vsens voltages we obtain the sensor impedance as:

$$Z_{sens} = R_s \frac{V_{sens}}{V_{ref} - V_{sens}} \tag{1}$$

Moreover, to compare Vref and Vsens voltages, we use a gain and phase measurement system, as shown in Fig. 4, whose outputs are proportional to magnitude ratio |G| and phase difference  $\theta$  of the input voltages:



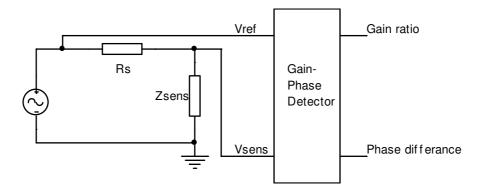


Figure 4. Impedance measurement with voltage divider and Gain-Phase Detector.

In this case Zsens can be obtained as:

$$|Z_{sens}| = R_s \frac{1}{|G| - 1} \tag{3}$$

Then we tune the signal generator to scan a band of frequencies to determine the minimum value of impedance (|Zmin|) and the corresponding frequency fmin, since these values give good statistical result in the estimation of the glucose content in the blood.

#### III. THE PROPOSED ARCHITECTURE

The blocks diagram of the blood glucose sensor based on dielectric spectroscopy, that we propose, is shown in Fig. 5.

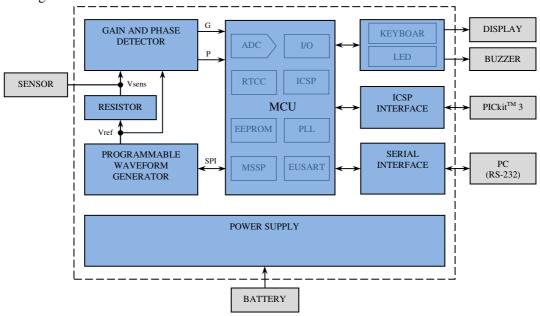


Figure 5. Proposed architecture of blood glucose sensor.

This architecture consists of a Micro Controller Unit (MCU), that controls via SPI a programmable wave form generator; this one generates a sinusoidal voltage signal witch supplies the voltage divider Sensor-Resistor. A gain and phase detector compares the two signals Vref and Vsens on the voltage divider and outputs two analog voltage signals proportional to gain and phase difference of the input voltages. These two analog signals are converted in digital data by MCU's ADC. Data are elaborated through a specific algorithm and then they can be stored on the MCU's EEPROM, or can be sent to external peripherals like displays. Alarms are signalled using led and buzzer. Serial interface allows uploading data to PC via RS-232 serial port and ICSP (In-Circuit Serial Programming) interface and allows also circuit connecting with PICkit<sup>TM</sup> 3 programmer for programming and debugging. Power supply block feeds all various supply voltages need by each component.

#### 3.1. Programmable waveform generator

As programmable waveform generator we have chosen the AD9954 [7], a direct digital synthesizer (DDS) from Analog Devices that uses digital technology, coupled with an internal high speed, high performance DAC to form a complete high frequency synthesizer capable of producing sinusoidal waveform at up to 160 MHz. The AD9954 allows fine tuning of both frequency (0.01 Hz or better) and phase (0.022° granularity) and is digitally programmable via a 3-wire SPI interface connected to the microcontroller. The in-band spurious component has amplitudes below -50 dB.

The main advantages of this device are power-down modes (hardware or software controlled) and easy software frequency tuning using specific 32 bit register.

This device is characterized by differential current outputs to reduce the amount of common-mode noise present at the DAC output resulting in a better signal-to-noise ratio.

To obtain a single mode voltage output, we have used the TT1-6-KK81, a balun working in 0.004 MHz - 300 MHz frequency range. Besides, in order to reduce out band noise at output, after the balun, we have placed a low pass filter [7], with a cut-off frequency of 170 MHz.

## 3.2. Gain-phase detector

As gain-phase detector we have used the AD8302 [8], a fully integrated system from Analog Devices for measuring either gain or loss over a ±30 dB range and phase over 0° to 180°.

The ac-coupled input signals can range from -60 dBm to 0 dBm in a  $50\,\Omega$  system, from low frequencies up to 2.7 GHz [8]. Low frequency cut off is determined by the input coupling capacitor and the internal resistance of 3 k $\Omega$ . AD8302 is based on two matched logarithmic amplifiers and a phase detector (Fig. 6) [9]. Moreover, the main advantage of this device is the accuracy and the simplicity of use.

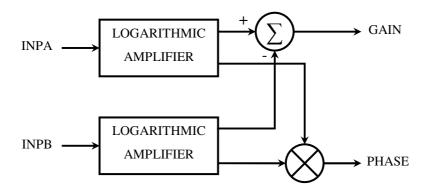


Figure 6. Blocks diagram of AD8302.

Both input signal are passed to two similar logarithmic amplifier which have two output, the first being linear function of the logarithm of the input signal, the second being an amplitude-normalized replica of the input signal.

Applying two signals of similar waveforms at INPA INPB inputs, AD8302 outputs give the difference of amplitude signals coming out from the logarithmic amplifiers. Since subtraction in the logarithmic domain corresponds to a ratio in the linear domain, the resulting output becomes:

$$V_{MAG} = V_{SLP} \cdot 20 \log_{10} \left( \frac{V_{INPA}}{V_{INPB}} \right) \tag{4}$$

where  $V_{MAG}$  is the output corresponding to the difference of the signals amplitude,  $V_{SLP}$  is the magnitude slope (+ 30 mV/dB) and  $V_{INPA}$  and  $V_{INPA}$  are the input voltages in our system connected to Vref and Vsens nodes of the voltage divider.

The phase difference of the signals at input is obtained comparing the amplitude-normalized signals coming from the logarithmic amplifiers. The phase is then transformed in a voltage at output pin according the formula:

$$V_{PHS} = V_{\oplus} \cdot \Phi(V_{INPA}, V_{INPB}) \tag{5}$$

where  $V_{\Phi}$  is the phase slope (± 10 mV/degree) and  $\Phi(V_{INPA}, V_{INPB})$  is the difference phase between the two input signals.

#### 3.3. Microcontroller

Now there are several duties to consider: the hardware control for the measurement, the elaboration of the measurement data, the log management, the alarm activation.

To these aims the used microcontroller is PIC18F67K22 of Microchip Technology Inc. [10] with operating speed up to 64 MHz, 12-bit A/D, a 128 kB on-chip flash memory and 4 kB data memory.

The microcontroller schedules the measurement operation using its real time clock, since glycaemia measurement should be repeated from time to time, on regular basis. This has an important impact on battery life, since during the idle time all the circuits are off, and the microcontroller is placed in a sleep mode controlled by its real time clock and push buttons. In this status the current request is negligible, about 2  $\mu$ A, depending on various settings and chip production variability, while current request for the full running is not easy to be determined, depending on program activity. The power supply was planned to feed 500 mA at 3.3 V, leaving a large margin for the digital current spikes.

During the measurement phase, the microcontroller powers all useful devices, programs the DDS using a SPI channel and digitalizes, using its ADC, the output of the gain-phase detector. The microcontroller repeats this on various frequencies seeking for impendence minimum, and then it switches off all unused devices. Subsequently the microcontroller converts this measurement in a glycaemic value, presents it on an LCD display and then stores this value in compressed form in an internal memory, along with the time. Moreover the microcontroller checks if the measured value is out bounds, and eventually activates the buzzer and the leds.

Furthermore the microcontroller reacts to the button pushing to show the log and status, and, via the serial line, transmits the data log to a connected pc.

#### 3.4. EUSART interface

EUSART interface allows uploading data to PC via RS-232 serial port.

In particular we have used the MAX3222 transceiver of Maxim [11] with a 1  $\mu$ A shutdown mode current to reduce power consumption and to extend battery life in portable systems like this. The device requires only four small 0.1  $\mu$ F external charge pump capacitors. This interface will be used for developing purposes since for the production we foresee the use of an USB interface for data downloading.

# 3.5. Power supply system

Since devices require different analog and digital voltage supplies, we have chosen to obtain each power supply from different voltage regulators. For developing purposes we use linear regulators, but, before the commercial phase, we plan to develop a compact switching power supply since it would be much more efficient, but we will check the noise induced in the measurement. At the moment we have several linear regulators which provide separated analog circuit supply and digital circuit supply. This split reduces the noise coming from digital components that disturbs the analog components through the power supply lines. Furthermore this configuration is useful to reduce power consumptions during idle time since each voltage regulator has a shutdown pin that can be used to switch off the power supply and all connected devices.

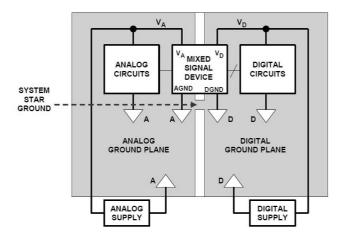
The present power supply uses an external 9 V power supply, and, in order to feed various chips, this voltage is reduced to 5 V, 3.3 V and 1.8 V, with evident energetic waste.

We have used the LT3024 dual voltage regulator from Linear Technology [12] to supply both analog and digital power supplies for the microcontroller. We used LT1762 [13] to provide power supply to the digital part of the DDS and the LT3010 We used LT1762 [13] to provide power supply to the digital part of the DDS and the LT3010 [13] to provide power supply for other analog circuits. Another LT3010 voltage regulator has been used to feed the MAX3222. The LT3010-5 [14], instead, has a fixed voltage output of 5 V, so it provides power supply to AD8302.

The shift from linear to switching power supply shall be necessary to greatly enhance the energetic efficiency of the power supply block. The battery selection would done when more precise data about energy request would be more clear, the length of the measurement time and the pause between two measurement are key parameters in the determination of daily energy request. Furthermore the power request of the microprocessor will be optimized choosing the most energetically efficient clock frequency compatible with the measurement. Our aim is a system requiring minimum battery care, the best would be a rechargeable batteries system using batteries commercially available at the corner shop. If we assume a pessimistic situation, supposing all chip involved in measurement running at full power, with a current request of 300 mA, for a measurement time of 30 seconds every 5 minutes, we have an average of 30 mA and a daily (24 hours) request of 0.72 Ah, which could be feed even with a couple of AA sized NiMH rechargeable battery with an a capacity of 0.9 Ah.

## 3.6. PCB design

In order to design system PCB, we have used OrCAD Layout Plus from the Cadence's suite. We have chosen to design a double side board: top layer for placing components and for routing and bottom layer for grounding. In a mixed signal system like this, it is important to physically separate sensitive analog components from noisy digital components [15], so we have split the board in two halves for the analog and the digital circuitry. Each half has its own ground plane, connected at a common system "star" ground located near in the power area, as shown in Fig. 7.



**Figure 7.** Grounding mixed signal double side board systems (from [15]).

We have also placed all mixed signal devices (like microcontroller and the DDS) bridging between the analog and the digital part.

In Fig. 8 we have reported the PCB layout of the designed system, which is, for the moment, a test prototype. In fact we keep some space for easy handling during measurement on the board, so the board is 10 cm times 11 cm, but this surface could be squeezed by a factor two.

We have in mind to check the noise and trying to identify noise problem to develop an eventual second version of the layout.

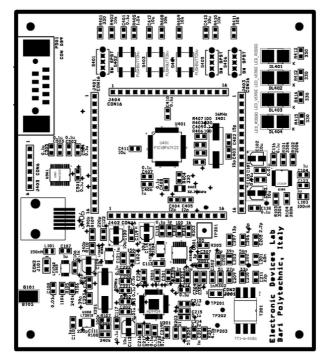


Figure 8. Layout of the proposed system.

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## IV. RESULTS AND DISCUSSION

This study can be considered the first step to verify whether our proposed sensor might be adequate as the basis for an approach for non-invasive monitoring of glycaemia, within the framework of the approaches based on the measurement of the dielectric properties of human tissues [16] [17] [18].

The proposed architecture consists of a MCU, that controls via SPI a programmable wave form generator; this one generates a sinusoidal voltage signal witch supplies the voltage divider Sensor-Resistor.

A gain and phase detector compares two signals on the voltage divider and outputs two analog voltage signals proportional to gain and phase difference of the input voltages. These two analog signals are converted in digital data by MCU's ADC. Data are elaborated through a specific algorithm and then they can be stored on the MCU's EEPROM, or can be sent to external peripherals like displays. Alarms are signalled using led and buzzer.

Serial interface allows uploading data to PC via RS-232 serial port and ICSP (In-Circuit Serial Programming) interface and allows also circuit connecting with PICkit<sup>TM</sup> 3 programmer for programming and debugging. Power supply block feeds all various supply voltages need by each component.

The proposed design allowed us to obtain some improvements compared to state of the art [16-18].

In particular our programmable generator allows fine tuning of both frequency (0.01 Hz or better) and phase (0.022° granularity) and is digitally programmable via a 3-wire SPI interface connected to the microcontroller. In this way the in-band spurious component has amplitudes below -50 dB.

The proposed gain-phase detector allows to measure either gain or loss over a  $\pm 30$  dB range and phase over  $0^{\circ}$  to  $180^{\circ}$  and its main advantage is the accuracy and the simplicity of use.

The used microcontroller, with operating speed up to 64 MHz, 12-bit A/D, a 128 kB on-chip flash memory and 4 kB data memory, allows the hardware control for the measurement, the elaboration of the measurement data, the log management and the alarm activation. Moreover the microcontroller schedules the measurement operation using its real time clock. This has an important impact on battery life, since during the idle time all the circuits are off, and the microcontroller is placed in a sleep mode controlled by its real time clock and push buttons.

The device prototype consists of integrated electronic components which provide compact circuitry and small power consumption thanks to the controlled power off. These characteristics make the designed device compact, light and easily transportable.

# V. CONCLUSIONS AND FUTURE DEVELOPMENTS

In this paper we have proposed a new architecture of a non-invasive, continuous blood glucose monitoring system, based on dielectric spectroscopy and we have designed its schematics and PCB. The presented method measures, on a wide range of frequencies, the impendence of a sensor placed on the skin and frequencies are scanned until the minimum impedance is found.

The proposed system has been planned to work in frequency range 1 MHz - 160 MHz, in which the best sensibility in terms of dielectric changes in the blood can be obtained.

Currently many clinical measurements are under development in order to prove the applicability of the proposed approach.

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