## **Review Microwave Resonant Glucose Sensors**

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The measurement of glucose concentration finds interesting potential applications in both industry and biomedical contexts. Among the proposed solutions, the use of microwave planar resonant sensors has led to remarkable scientific activity during the last years. These sensors rely on the changes in the dielectric properties of the medium due to variations in the glucose concentration. These devices show electrical responses dependent on the surrounding dielectric properties, and therefore the changes in their response can be related to variations in the glucose content. This work shows an up-to-date review of this sensing approach after more than one decade of research and development. The attempts involved are sorted by the sensing parameter, and the computation of a common relative sensitivity to glucose is proposed as general comparison tool. The manuscript also discusses the key points of each sensor category and the possible future lines and challenges of the sensing approach.

Keywords: glucose sensor ; insertion/return loss ; microwave ; phase measurement ; planar ; relative sensitivity ; resonant frequency ; resonator ; unloaded quality factor

## 1. Introduction

The use of microwave techniques for developing all sort of sensors has stirred an intense research field, which has been attracting increasing attention by the scientific community during the last decades. The efforts devoted to these techniques have generally paid off, leading to successful application to many contexts (e.g., <sup>[1][2][3][4][5]</sup>). Although many approaches can be taken, the common measurement principle of these sensors is the electromagnetic interaction between the sensor and the medium under test. The propagation of electromagnetic fields through the media depends, among other parameters, on the permittivity of the media, a frequency-dependent parameter unique for each material. Many microwave devices show responses strongly dependent on the permittivity of the surrounding media. This, in addition to their ease of integration and cost-effectiveness, explains why these devices are often used as permittivity sensors.

Several techniques can be used for this dielectric characterization purpose. Depending on the medium under test, application and frequency range, different methods are employed, such as wideband antennas <sup>[1]</sup>, coaxial lines <sup>[6]</sup>, planar capacitive techniques <sup>[2]</sup>, frequency synthesizer-based methods <sup>[8]</sup> or CMOS microwave sensors <sup>[9]</sup>, among others. Due to several interesting features, such as cost-effectiveness, ease of development and ease of integration, methods based on planar microwave resonators are frequently considered for applications requiring dielectric permittivity measurements <sup>[10]</sup> <sup>[11][12]</sup>, especially for characterization of lossy organic liquids <sup>[13]</sup>. It is in this context where the attention of a part of the microwave community was attracted towards glucose sensing.

Several measuring technologies have been proposed for different contexts, such as electrochemical <sup>[14]</sup>[15][16][17] or optoelectronic devices <sup>[18][19]</sup>, among others. However, microwave devices, and especially planar resonant ones, show some beneficial features such as ease of production and integration, reduced size, competitive cost and interesting penetration depths, especially for non-invasive measurements, generally with low tissue scattering <sup>[20]</sup>. Under these circumstances, the study of microwave planar resonant techniques for glucose concentration sensing has become an intense research field during the last years. As a matter of fact, searching the keywords "microwave", "resonator" and "glucose" in the Scopus database yields 127 results at the moment of writing this article, 70.16% of them being from the last 5 years. For such a highly specific technical topic, these numbers give a clear idea of the current interest raised within the scientific community.

This manuscript offers a systematic review of the available approaches to glucose sensing, regardless of the application scenario, with the specific focus on planar resonant methods. A new classification scheme based on the sensing parameter, suitably adapted for this sensing paradigm, is proposed, and the review is thereby organized accordingly. To ease the understanding and comparison of the different approaches involved, the computation of a normalized relative sensitivity to glucose is proposed, which is especially convenient for discussion involving different sensing parameters. The manuscript is organized as follows. Section 2 outlines the fundamentals of this sensing technique and its

development from the early stages to the current attempts. It also discusses the categorization possibilities and the finally proposed classification criterion, as well as the calculation of a general sensitivity. Section 3, Section 4, Section 5 and Section 6 review the different available works within each category, whereas Section 7 and Section 8 show the discussion of the current state of this technology and draw the main conclusions of the study.

## 2. Microwave Planar Resonant Glucose Sensors: Fundamentals and Classification

The utility of microwave techniques for the measurement of glucose concentration is due to the influence of this magnitude in the complex permittivity of water, blood and other aqueous solutions <sup>[21]</sup>. The presence of glucose affects the orientational polarization process of water, shifting the relaxation spectrum towards lower frequencies <sup>[22][23][24]</sup>. The influence of glucose concentration in the permittivity of water–glucose solutions has been reported for a wide variety of frequency ranges using different techniques (e.g., <sup>[25][26][27][28][29]</sup>). This dielectric signature of glucose can find applications in the industrial production of sugar-containing drinks. In the diabetes community, the effect of glucose on the permittivity of blood <sup>[30][31]</sup> and plasma <sup>[32]</sup> opens the way for the design of non-invasive glucose sensors <sup>[33]</sup>, although there remain serious technological problems to be solved in this field.

Within the common microwave techniques, planar devices have received the greatest attention for this concern. They are usually considered for many applications due to their cost-effectiveness and ease of integration. However, other approaches have also been studied, such as waveguide techniques <sup>[34][35]</sup>, although their bulky nature hinders their evolution towards feasible commercial devices. Among the possibilities of planar technology for glucose sensing, resonant sensors are the most frequently found in the scientific literature, although other approaches have been studied, such as microstrip lines in transmission/reflection modes <sup>[36]</sup> or planar antennas in transmission <sup>[37][38]</sup> or reflection modes <sup>[39]</sup>. Resonant planar sensors present the advantage of concentrating the electric field in a small volume at frequencies around the resonant frequency, thus intensifying the sensor–MUT (Material Under Test) interaction. Additionally, they require a narrow bandwidth due to their sharp electrical response, which facilitates the design of the associated electronics. Since the first proposals 30 years ago <sup>[40]</sup>, planar resonators have been widely used for dielectric permittivity measurements in a plethora of contexts.

Among the different possibilities for classification, in a wide application context, the working principle was proposed as the most convenient criterion <sup>[41]</sup>, especially to ease the comparison. This classification yields five kinds of sensors: frequency-variation sensors ( e.g., <sup>[42][43][44]</sup>), phase-variation sensors (e.g., <sup>[45][46]</sup>), frequency-splitting sensors (e.g., <sup>[42]</sup>), coupling-modulation sensors (e.g., <sup>[49][50][51]</sup>) and differential-mode sensors (e.g., <sup>[52][53][54]</sup>). This classification scheme, however, while interesting for a broad application view, might not be the most suitable one for the specific case of glucose sensing. Differentiating the sensors according to the operating principle, while coherent, might mask interesting complementary information that can be retrieved from different sensing parameters, which can be of interest for addressing sensitivity and, especially, selectivity issues.

In this sense, the focus seems to be put on the sensing parameter, i.e., the computed parameter from the sensor response which is eventually associated with the retrieved glucose concentration. The selected sensing parameter remarkably determines the sensing approach, even when remaining in the same sensing technique or working principle. In addition, several sensing parameters may be extracted from one single measurement. Accuracy enhancements by data fusion of several extracted and processed parameters from the same measured signal have been reported for other techniques <sup>[55]</sup>. Taking a brief look at the literature of microwave planar resonant glucose sensors, it is easy to see how several sensing parameters are considered in different references, such as f r , Q u , insertion/return loss or phase. However, the criteria for selecting them are not evident, and a consensus on which one (or ones) to use for each case does not seem to appear. All these reasons led us to propose a sensing parameter-based classification for the specific context of microwave planar resonant glucose sensors. The proposed sensor categorization scheme is summarized in **Figure 2**.



Figure 2. Proposed sensing parameter-based classification scheme.

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