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DETERMINATION OF GLUCOSE CONCENTRATION IN AQUEOUS SOLUTION BY USING MODIFIED HILBERT SHAPED MICROWAVE METAMATERIAL SENSOR

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Glucose concentration in the aqueous solution was measured using a microwave metamaterial sensor based on the modified Hilbert curve of the first fractal order. In order to increase the system sensitivity at fixed meta-element sizes, the design of the sensor was optimized by using finite element method. It was observed that S parameters of the metamaterial microstrip line sensor at resonant frequencies strongly depend on the glucose concentration. Consequently, by measuring the microwave responses for the different concentrations one can detect the glucose concentration in the solution. Such structure can be useful in the biological and medical applications.

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***Keywords*:** microwave resonator, biosensor, glucose concentration.

Introduction. Since 1980 the number of people with diabetes has about quadrupled and in 2016, about 422 mln people worldwide have diabetes [1]. People with diabetes mellitus of types 1 and 2 are the highest risky groups, who require intensive glucose therapy including frequent blood glucose level measurements. Presently, the glucose sensors based on the invasive measurement technique are widely used, for example, the finger-prick glucometers, which have low price and provide high accuracy. However, using invasive glucose sensors by patients with diabetes mellitus of types 1 and 2 can cause a discomfort, since patients must prick their finger several times a day, which can be painful and evokes high risk of infections. Moreover, invasive sensors require supplementary components such as lancets and test strips. These inconveniences may lead patients to avoid measuring their blood glucose level as often as required, whereas the blood glucose concentration is significant for life quality [2]. Thus, developing the blood glucose sensors based on non-invasive measurement technique is encouraged for improving and facilitating patients' health care and allowing them to self-monitor the blood glucose level.

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Nowadays there are several types of blood glucose biosensors based on electrochemical [3], ultrasonic [4], temperature measurement [5] and spectroscopic techniques [6]. Particularly the spectroscopic technique involves near-infrared and mid-infrared [7, 8], stimulated Raman [9], terahertz [10] methods. An example of microwave dielectric resonator-based glucose biosensor is presented in [11], which detects the shift of resonant frequency caused by the dielectric permittivity change of the investigated aqueous solution depending on the glucose concentration. In this paper we propose the microwave metamaterial sensor based on the modified Hilbert curve of first order for the glucose concentration measurement in an aqueous solution. The proposed metamaterial sensor is optimized in order to obtain high sensitivity of the dielectric permittivity corresponding the glucose concentration in an aqueous solution. The proposed sensor measures the transmission parameter changes corresponding to various concentrations of the glucose solution.

The modification of the sensor and calculations of S parameters were implemented by using Comsol Multiphysics software. The simulated results for S parameters of the sensor without the material under test were in good agreement with the obtained experimental data. The resonance frequency of the sensor is nearly at 4.25 GHz. As was expected, the quartz vial with aqueous solution onto the sensor changes the transmission/reflection coefficient due to the change of the system impedance. The differences of the dielectric permittivity real and imaginary parts of the aqueous solution corresponding to 0 and 250 mg/dL concentrations (the boundary values) are about 0.9 and -2.5 respectively. Thus, the change of S_{21} parameter is about 6 dB at 6 GHz.

Materials and Methods. The metamaterial sensor is modeled by modified Hilbert-shaped closed curve. We use Al_2O_3 as a substrate the dielectric permittivity of which is about 9.8 and sizes are $20 \times 40 \times 1$ (mm). The geometry of the modified Hilbert-shaped metamaterial sensor is shown in Fig. 1, here h is the width of the stripline, s is the length of the Hilbert-shaped curve, w is the unit of the first order and the width of the curve.

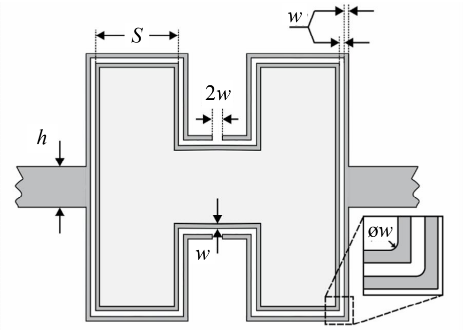

Fig. 1. The geometry of the modified Hilbert-shaped metamaterial sensor.

The geometry of the sensor was optimized by using COMSOL Multiphysics software in order to obtain high sensitivity. The optimized parameters are, mm: $h = 1,\ w = 0.1,\ s = 2$. To achieve more accurate results and avoid overabundance of the mesh in simulations, the metal cover was implemented by using "Transition Boundary Condition" with the thickness of 50 μm. The complex dielectric permittivity of the metal was defined by the equation $\varepsilon = \varepsilon_r - j\sigma/\omega\varepsilon_0$, where the relative permittivity $\varepsilon_r = 1$, conductivity $\sigma = 6.16 \cdot 10^7\ S/m$, the dielectric permittivity of vacuum $\varepsilon_0 = 8.85 \cdot 10^{-12} F/m$, the angular frequency $\omega = \pi f$. Downside of the substrate was set to be as a Perfect Electric Conductor.

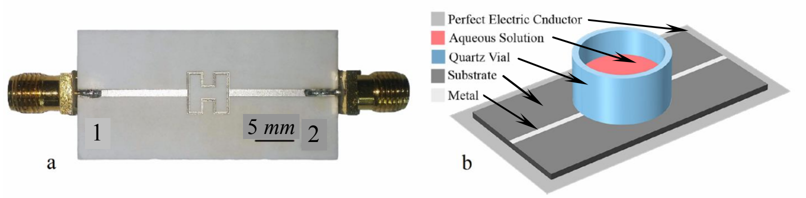

Fig. 2. a) Real image of the prepared metamaterial sensor; b) Geometry of the simulated model.

Fig. 2, a shows the real image of prepared sensor. The substrate of the sensor was covered from both upside and downside by thin layer of silver paste about 50 μm and after that the metamaterial structure was patterned by using a laser patterning technique on one side. The inner edges of metamaterial sensor in simulated model have a diameter of curvature of 0.1 *mm*, which corresponds to the diameter of the patterning laser beam. The reflection/transmission coefficients of the sensor were measured by an Agilent 8753ES Network analyzer. The numerical analysis was carried out for 6 types of aqueous solutions with glucose concentrations ranged from 0 (ultrapure water) up to 250 mg/dL by a step of 50 mg/dL. To bring the simulated model closer to the real case, the aqueous solution was modeled in cylindrical vial.

Fig. 2, b shows the geometry of the simulated model. The dielectric constant of the modeled vial was 4.2 (quartz), height was 8 *mm*, thickness was 1 *mm* and inner radius was 6.5 *mm*. Note that the influence of the vial on the sensor's *S* parameters is negligible, whereas the aqueous solution affects significantly due to its high dielectric constant. The volume of aqueous solution was kept 500 *mL* during all simulations.

Results and Discussion. The dielectric permittivity of solution has complex form of $\varepsilon(f) = \varepsilon'(f) - j\varepsilon'' f$, where ε' and ε'' are real and imaginary parts, and f is the frequency. The real part of the permittivity corresponds to energy storage in the material under test (MUT), while the imaginary part of the permittivity is related to conductivity and corresponds to energy losses in MUT with loss tangent of $\tan\delta = \varepsilon''/\varepsilon'$. By increasing the glucose concentration in the solution the real part of permittivity of the solution increases and the imaginary part-decreases, whereas by increasing the operation frequency the real part of permittivity shows decreasing behavior and the imaginary part shows increasing behavior. In other words, the loss tangent of MUT increases by increasing the frequency and decreases by increasing the glucose concentration.

One can see that the both results of *S* parameters obtained by simulation and experiment are close enough and correspond to each other (Fig. 3). The sensor resonant frequency is nearly at the 4.25 *GHz*.

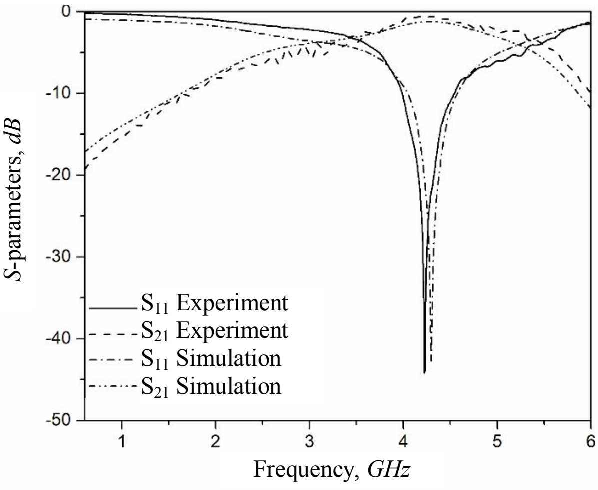

Fig. 3. The experimental and simulated reflection/transmission coefficients of the sensor.

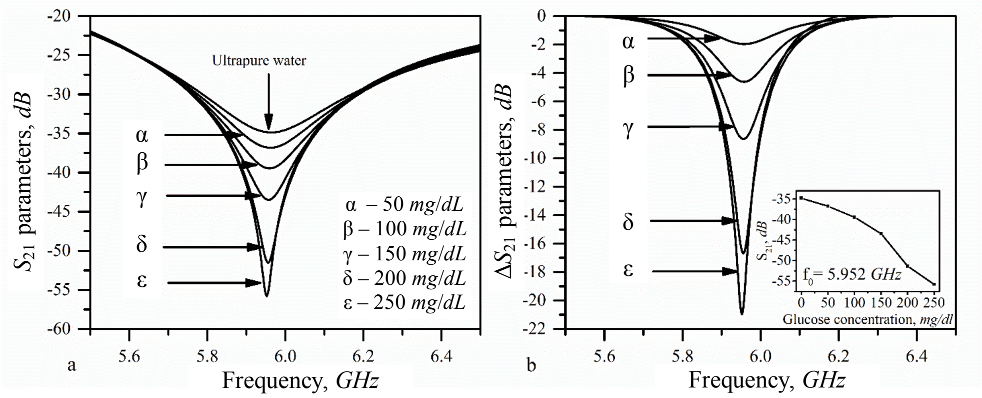

Fig. 4. S_{21} (a) and ΔS_{21} (b) spectrum in the frequency range of 5.5–6.5 *GHz*, for different solutions. Inset plot shows dependence of S_{21} parameter on the glucose concentration of the solution at 5.952 *GHz*.

Putting the quartz vial with aqueous solution on the sensor causes the change of scattering parameters due of change of the impedance of the system. As was expected, S parameters are depended on the variations of the glucose concentration in the aqueous solution. Fig. 4 shows the $S_{21}(a)$ and ΔS_{21} (b) spectrum in the frequency range of $5.5-6.5$ *GHz* for different solutions with concentrations: $\alpha-50$; $\beta-$ 100; $\gamma-150$; $\delta-200$; $\varepsilon-250$, mg/dL. Here, as a background value for the ΔS_{21} is taken the data of the ultrapure solution. All curves have minimum value of S_{21} parameter at the frequency around 5.95 *GHz*. As was expected, the maximum difference from S_{21} parameter of sensor loaded by ultrapure water has aqueous solution with 250 mg/dL glucose concentration, which is about 21 *dB* at 5.952 *GHz*. In other cases, the difference monotonously decreases by decreasing the glucose concentration, as can be seen from inset plot of Fig. 4, a.

Conclusion. The metamaterial sensor based on modified Hilbert-shaped closed curve was designed and prepared as a non-invasive glucometer. The resonance frequency of the metamaterial sensor is about 4.25 GHz. The analysis of influence of the glucose concentration on S parameters spectrum was carried out by numerical simulations. The simulation results show changing of S_{21} parameter in frequency range of $5.5-6.5$ GHz. As a background for calculate the differences the S parameter spectrum the ultrapure water was chosen. The maximum values of ΔS_{21} parameter had aqueous solution with glucose concentration of 250 mg/dL, about 21 dB at 5.952 GHz for ΔS_{21}.

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