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DETECTION OF THE BIOLOGICAL CONSTITUENTS IN SOLUTION USING METAMATERIAL SLABS WITH SPECIAL PROPERTIES

BY

DANIELA IONESCU[1,*] and GABRIELA APREOTESEI[2]

“Gheorghe Asachi” Technical University of Iași,
[1]Department of Telecommunications and Informational Technologies
[2]Department of Physics

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Abstract. Particular configurations of metamaterials used for different substances detection in biomedicine have been analyzed. The 3D structure has periodic geometrical constituents with dimensions of tens of micrometers, consisting of nested ring resonators with different configurations, on a RT/Duroid substrate. The exposure microwave field (7 – 28 GHz) propagates distinctly through the structure impregnated with a solution containing biological samples. By estimating the modification of the metamaterial parameters, like refractive index n and effective permittivity ε_r, the detection of the concentration level of biomolecules (components of the blood, protein, lipid and carbohydrate) in the biological liquid was performed. A model of the metamaterial structures has been conceived and analyzed by simulation methods. Concentration levels up to 20% have been detected, determining $\Delta\varepsilon_r$ up to 4% and Δn up to 6% for the metamaterial. By using this nondestructive method, the optimal design for the detection structure can be set.

Keywords: metamaterial; biomolecules; microwave; simulation; permittivity.

[*]Corresponding author; *e-mail*: danaity@yahoo.com

1. Introduction

Using of the metamaterials for detecting has applications in biomedicine for medical diagnosis (Chen *et al*., 2012). The procedure is fast, very sensitive and represents a nondestructive material testing method (Salim and Lim, 2018).

Metamaterial elements exhibit a sensitive response to fluids. Physical parameters of the metamaterial samples suffer modification due to the presence of a particular type of molecules in the solution in contact with the metamaterial. Thus the detection of an analyte and its concentration become possible (Memoli *et al*., 2017). In our case, the physical parameters of interest are the effective electric permittivity and the refractive index of the metamaterial samples.

For medical testing, the constituents of blood and their concentration are of great interest indicating different diseases. The detected substances have been considered like: *a* – protein in blood (albumin/globulin, indicating hyperproteinemia), *b* – lipid in blood (triglycerides, fatty acids and cholesterol, indicating hyperlipidemia), *c* – carbohydrate in blood (sugar, glucose, starches, indicating diabetes disease). Normal concentrations of these substances in blood can be mentioned as: albumin in blood: 33 … 52 g/l; globulin in blood: 26 … 46 g/l; cholesterol in blood < 2 g/l; triglycerides in blood < 1.5 g/l; glucose 0.8 … 1.2 g/l and examples can be continued. Higher levels of these analytes are of interest for diagnosis and have to be indicated by the metamaterial detectors.

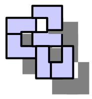
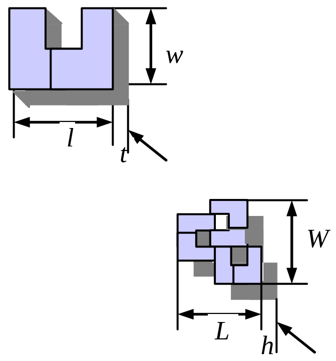
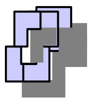
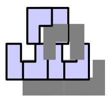
2. Theoretical Considerations

The used metamaterials present negative refractive index and have a nonlinear behavior under the testing conditions. The testing configuration was developed like a 3D metamaterial with periodic geometrical constituents having dimensions of hundreds of nanometers to tens of micrometers, exposed to the electromagnetic field in GHz range (7 – 28 GHz). The material interacts with the wave and modifies its properties in function of the design. Material was placed on a RT/Duroid 5880 substrate (ε_r = 2.2 in GHz range). Low permittivity for the substrate helps to improve the sensitivity to analyte. The internal configuration consists of nested ring resonators (nanocomponents) with different spatial relative positions (see Table 1).

The nanocomponents dimensions are smaller than the wavelength in order to obtain the effect of negative refractive index at wave propagation. The most important fact is to have a correlation between dimension of the constituents, the wavelength and dimension of the analyte molecules. In this case, resonances occur and the effect of modifying the detector parameters is the strongest.

The metamaterial superlattices consisting of thin films with the thickness *h*, in which the unit cell with dimensions *L* x *W* repeats periodically. A multi-frequency response can be obtained, each of the sublattice resonance being tunable to a resonant frequency of a particular analyte. The same conclusion for metamaterial detectors have been presented in literature (Jakšić, 2010).

Table 1
Superlattices of the Detecting Metamaterials

Metamaterial configuration / slab thickness	Model for the unit cell (600 x 400 x 80 nm)*	
I. first variant	 (60 x 40 x 16 μm)**	
II. second variant	(42 x 52 x 12 μm) 	
III. third variant	 (74 x 42 x 10 μm)	

**l* x *w* x *t*
** *L* x *W* x *h*

The refraction index of the metamaterial can be written as (Datta *et al*., 2020):

$$n = -\sqrt{\varepsilon\mu} \tag{1}$$

$$\varepsilon(\omega) = 1 - \frac{\omega_p^{\ 2}}{\omega(\omega + i\gamma)} \qquad ; \ \mu(\omega) = 1 - \frac{F\omega^2}{\omega^2 - \omega_0^{\ 2} + i\gamma\omega} \tag{2}$$

where ω_p is the plasma frequency, γ is the damping factor for dissipation, ω_0 is the resonant frequency and F is the fractional volume of the metal content. The metamaterial plasma frequency can be estimated with the expression:

$$\omega_p = \left(\frac{e^2 n_{avr}}{\varepsilon_0 m}\right)^{1/2} \tag{3}$$

where n_{avr} is the free electron density averaged over a volume on the order of $(\lambda/2)^3$; e, m are the electron charge, respectively electron mass, and ε_0 is the vacuum permittivity.

The permittivity $\varepsilon(\omega)$ is negative for $\omega < \omega_p$. The negative permeability can be obtained with help of an array of conducting loops (the ring resonators in our case) at microwave frequencies. The dimensions of the unit cell representing the metamaterial periodic array structure must be much smaller than the operating wavelength to act as an effective medium. The propagating modes exist for $\omega < \omega_0$ and for $\omega > \omega_0 / \sqrt{1-F}$.

The electromagnetic wave propagates distinctly through the structure impregnated with a solution containing the biological sample with different constituents (an analyte). The plasmon propagation is modified (Steigmann *et al.*, 2016). By estimating the variation of the metamaterial sample parameters, like refractive index and effective permittivity, the detection of the concentration level of a biological product (biomolecules) in the aqueous solution (biological sample) can be performed. Variation of the effective permittivity for the metamaterial consisting of split ring resonators in the volume containing the biological sample will strongly influence the resonance condition, making the detector metamaterial sensitive to the presence of analyte. This is confirmed by the detailed numerical analysis of the propagation properties through the medium with split ring resonators (Berkowitz, 2009).

Particle diameter of the inclusions inside the liquid sample, which cause modifications of the field propagation, can be of nanometers order. The detected substances were included in three classes: *a* – protein in blood (albumin, globulin, indicating hyperproteinemia), *b* – lipid in blood (triglycerides, fatty acids and cholesterol, indicating hyperlipidemia), *c* – carbohydrate in blood (sugar, glucose, starches, indicating diabetes disease). The molecular size of the analytes was considered as follows: *a* – protein: albumin 7 nm, globulin 11 … 15 nm; *b* – lipid: cholesterol $C_{27}H_{46}O$ up to 22 … 27 nm), *c* – carbohydrate: glucose $C_6H_{12}O_6$ 0.9 nm.

Analysis was performed by simulation methods, using the 3D HFSS structural simulator. The test configuration was sample inside the waveguide. A rectangular waveguide was used, having dimensions *a* x *b* of 3.556 mm x 7.112 mm, working in microwave range (7 – 28 GHz). The propagation mode was TE_{10} and the DC pre-polarization field $H_{=}$ was of 0 ÷ 20 kOe depending on the sample (Fig. 1).

Geometrical parameters of the detecting metamaterial have been set in order to obtain the resonances of the structural sample when the analyte is present. The eigenmode solver of the High Frequency Structure Simulator has given the resonant frequencies by solving the matrix equation:

$$\boldsymbol{S} \cdot \boldsymbol{x} + k_0^2 \boldsymbol{T} \cdot \boldsymbol{x} = \boldsymbol{b} \qquad (4)$$

where the solver sets the source field vector ***b*** to zero. The ***S*** and ***T*** matrices depend on the geometry and the mesh defined by the finite element method (FEM); ***x*** is the electric field vector solution; k_0 is the free-space wave number corresponding to that ***x*** mode and ***b*** is the value of the source (field vector) defined for the problem. Equation is solved for different sets of (k_0, ***x***), one for every ***x***.

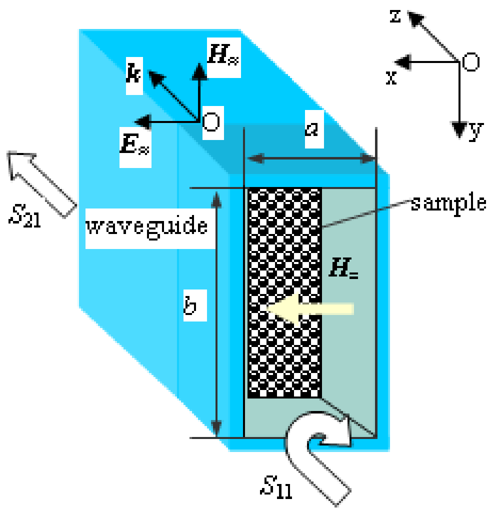


Fig. 1 − Waveguide with metamaterial sample.

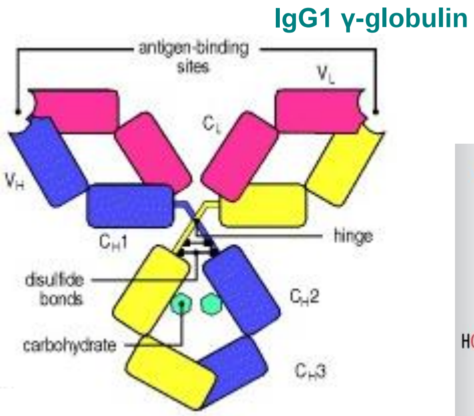
3. Results for the Analyte Concentration

A theoretical model for the samples of metamaterial structures + analyte isolated in aqueous solution has been conceived. Analysis was performed by simulation methods at structure level and the *S* parameters have been determined for the propagation cases through the metamaterial with biological sample inside. As a result, the electromagnetic properties were determined at different frequencies in the domain 7 – 28 GHz.

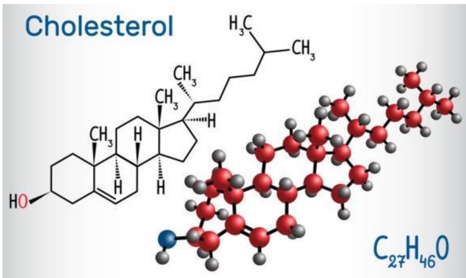
The parameter of interest for the biological samples is the concentration level, its calculation been based on the modification of the refracted wave intensity. In the presence of analyte a refractive index variation occurs, modifying plasmons propagation at the metamaterial sample level. In the same time, the effective permittivity variation, modifying the electric induction of the sample has been computed. We have taken as reference water ($n \approx 1.33$; $\varepsilon_r \approx 80$ in GHz range).

The obtained 3D graphs are available for the biological constituent concentration level versus metamaterial constituent dimensions, for different material models, with the variation of the effective permittivity, respectively the variation of the refractive index like parameter (Fig. 3). The graphs were denoted: $c(l, \Delta\varepsilon_r)$, $c(L, \Delta\varepsilon_r)$, $c(h, \Delta\varepsilon_r)$, respectively $c(l, \Delta n)$, $c(L, \Delta n)$ and $c(h, \Delta n)$, with *l*, *L* and *h* being geometrical parameters characteristic for the metamaterial unit cell, indicated in Table 1.

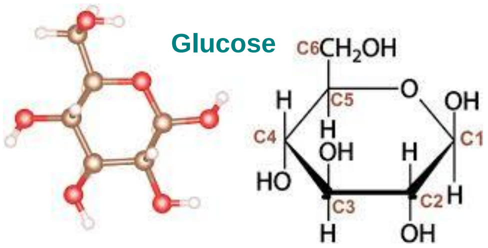
Considering that the maxim response was obtained at resonance, the dimensions of the metamaterial unit cells given in Table 1 (1^{st}, 2^{nd}, respectively 3^{rd} variant) were set in agreement with the following detected analytes (Fig. 2): *a* – protein: a γ-globulin IgG1 (molecular dimensions ~14 nm, 13.7 nm width, 8.4 nm height; Tan *et al*., 2008), *b* – lipid: *cholesterol* $C_{27}H_{46}O$, 22 nm (average molecular size), *c* – carbohydrate: *glucose* $C_6H_{12}O_6$, 0.9 nm, in aqueous solution.



a) *Source:* agrisera.com



b) *Source:* docsopinion.com



c) *Source:* researchgate.net

Fig. 2 − Examples of detected analytes: *a* – γ-globulin IgG1;
b – cholesterol; *c* – glucose.

One observes that the modification induced to the physical parameters depends on the analyte nature. The absence of the analyte in the aqueous solution in contact with the metamaterial detector corresponds to the reference value of the $\Delta\varepsilon_r$, respectively Δn. The presence of the analyte decreases the variation of the physical parameter in respect with the metamaterial sample without solution.

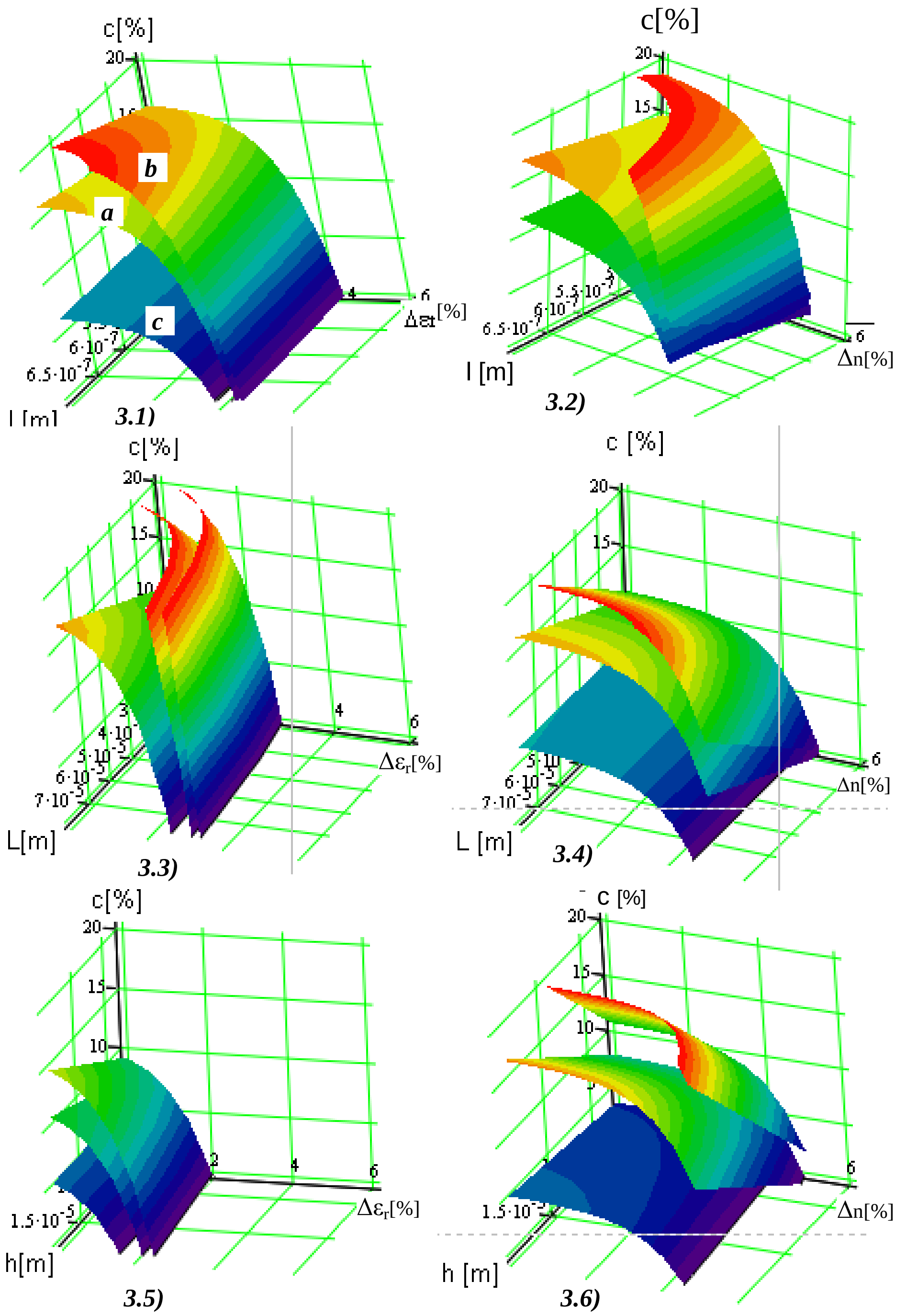


Fig. 3 − Analytes concentration in function of geometrical parameters of the metamaterial detector and the corresponding variation of sample physical parameters.

The dependence of analyte concentration in solution on metamaterial constituents dimensions is almost linear. The most significant dependence is on the *L* parameter, notation for the length of the unit cell. The refractive index is influenced more on the geometrical parameters variation than the effective permittivity, the influence being double, via electric permittivity and magnetic permeability of the metamaterial plus the analyte solution.

Higher values of analyte concentration can be detected for molecules with bigger dimensions – one observes the position of the surfaces in the surface plots in order *b* (above), *a*, *c* (below), the order in which molecular dimensions are decreasing. This effect is strongly correlated with the dimensions of the channel of the ring resonator in the unit cell and occurs only for a narrow interval of values of these dimensions. If this interval is determined by simulation, the proper dimensions for the detector unit cell can be designed in practice.

Thickness of the unit cell, *h*, meaning in the same time separation of the planes with ring resonators in the metamaterial influences the global level of curves $c(\Delta n)$, respectively $c(\Delta\varepsilon_r)$ corresponding to the three categories of analytes (*a*, *b*, *c*), the starting point (for h = 8 μm) of the curves being always different. Tuning of this parameter represents the main factor for obtaining the resonance.

A synthesis of the results is presented in Table 2. By tuning the geometrical parameters of the metamaterial detector, firstly the resonance was achieved and then the determinations of the physical parameters was performed in order to observe the effect of the analyte concentration on the modifications of these parameters. The higher is the difference in dielectric constants of the detector and the analyte, the wider is the shift in resonant frequency was achieved. The ring resonators inside the metamaterial confer to it the property of negative permeability in a specific frequency domain and due to the fact that their dimensions have to be tuned for obtaining the resonance, they also influence the refraction index at wave propagation through the sample.

Table 2

Parameters Detection Results

Metamaterial configuration	concentration level [%]			refractive index variation, Δn [%]			effective permittivity variation, $\Delta\varepsilon_r$ [%]		
	*a**	*b**	*c**	*a*	*b*	*c*	*a*	*b*	*c*
I. first variant	7…17	–	–	3.2…5.4	–	–	1.9…4.2	–	–
II. second variant	–	9…25	–	–	4.1…5.4	–	–	2.0…4.2	–
III. third variant	–	–	3…9	–	-	3.8…4.1	–	–	1.6…3.9

*a = blood protein; *b* = blood lipid; *c* = blood carbohydrate

Concentration level variation of 2-3 …25-27% have been demonstrated for the considered categories of analyte (protein, lipid and carbohydrate of blood) separated in aqueous solution. These sets of values correspond to refractive index variation of the detector with analyte up to 6%, while the effective permittivity variation was up to 4%.

One remarks on graphs almost linear dependences of analyte concentration on metamaterial constituent dimensions, which are to be set in order to obtain the resonance.

4. Conclusions

An electromagnetic nondestructive evaluation of the detection process using metamaterials was performed, in order to design the optimal geometric structure, the most proper for detection of different analytes. The simulation method is solving the task of synthesis for the unit cell in function of the parameter which has to be detected in our material analysis. Results: 1^{st}, 2^{nd} and 3^{rd} variant of metamaterial detectors in the material table for the marked analytes (a = blood protein, b = blood lipid, respectively c = blood carbohydrate).

The resonant phenomena which maximize the physical effects when the geometrical parameters are correlated are essential for the detection process. Shift in resonant frequency occurs, depending on analyte molecular dimensions and structure of the metamaterial unit cell. Conclusion is that the detection process can be controlled by dimensional tuning of the metamaterial constituents.

A strong interdependence was demonstrated between physical and chemical parameters: electrical permittivity, refraction index of detector / spatial structure, molecular size of analyte / wavelength of the propagating field. Variation of a parameter generates variation of the others, in agreement with the physics laws.

Future directions of research can be oriented to the design methods of the structures proper for detection of more than one analyte simultaneously, by nondestructive control. The idea is that each analyte in the same solution generate a modification of a physical parameter and than different responses can be compared by their secondary effect on a common quantity. In the same time, the solvents need also to be diversified, their response being considered as reference.

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DETECŢIA COMPUŞILOR BIOLOGICI ÎN SOLUŢIE FOLOSIND STRATURI DE METAMATERIALE CU PROPRIETĂŢI SPECIALE

(Rezumat)

În această lucrare au fost analizate câteva configuraţii particulare de metamateriale utilizate pentru detecţia diferitelor substanţe în biomedicină. Structurile metamateriale 3D prezintă constituienţi geometrici periodici având dimensiunile de zeci de micrometri, şi constau din rezonatori inelari imbricaţi, cu diferite configuraţii spaţiale, implementaţi pe substrat de RT/Duroid. Probele sunt expuse unui câmp de microunde (7 – 28 GHz) care se propagă în mod diferit prin structura impregnată cu soluţie apoasă conţinând proba biologică. Detecţia concentraţiei biomoleculelor (componenţi ai sângelui: proteine, lipide şi carbohidraţi) din lichidul biologic a fost realizată prin estimarea modificării unor parametri de material, cum ar fi permitivitatea electrică efectivă ε_r şi indicele de refracţie n. A fost conceput un model al structurilor de metamaterial potrivit pentru detecţie şi analizat prin metode de simulare. Au fost detectate nivele de concentraţie ai analitului de până la 20%, prin determinarea de variaţii ale parametrilor $\Delta\varepsilon_r$ până la 4% şi Δn de până la 6% pentru probele de metamaterial. Prin folosirea acestei metode nedistructive se poate realiza proiectarea optimă a structurii de detecţie.