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# MODELING BEHAVIOR OF BIOLOGICAL MEMBRANE COMPONENTS

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***Abstract:*** *This paper presents some of our results in modeling biological membrane behavior. Samples of very simple membrane models were built by using fatty acids in liquid crystal state, subjected to different external perturbations, like physical fields and impurities. Typical measurements were performed. Theoretical assumptions and some computer studies by using Table Curve3D capabilities and Matlab libraries allowed us to characterize changes occurred in the structure and ordering of the liquid crystal textures: local mechanical deformations in the systems, director* ***n*** *reorientation, and displacement of the electric charges. These changes determined the nonlinear feature of the the answer of the samples. Theoretical conclusions are experimentally validated and in agreement with other works.*
***Keywords:*** *biological membrane, fatty acids, liquid crystals, mechanical deformation, computer models*

## 1. INTRODUCTION

Computers proved a useful tool for getting information on biological membrane structure and properties.
This study presents the computer help for modeling the changes induced by some external perturbations in some biological membrane simple models, realized by fatty acids (FA). These changes were experimentally evidenced by the nonlinear optical answer of the samples under non-destructive laser light**,** while in the liquid crystal (LC) state, a state involved in many mechanisms of the living matter. Many works proved that, in some conditions, the biological membrane turns in a cooperative manner from a "close-packed", gel-type structure, to a LC phase, responsible for many membrane mechanisms [1]. It is known that all the mesogenic compounds possess a high optical nonlinearity that can be pointed out even at low optical laser power [2]. In our experiments we used a Helium-Neon (He-Ne) laser light, incident on FA typical sandwich cells. Depending on the melting process speed (less than 5°C/min), FA go to a disordered isotropic liquid phase via a LC state. Between some temperature values, our samples are *smectic* liquid crystals.
In electric field, they are nonlinear dielectrics with a weak conduction. In laser field, they generally are nonlinear optical materials, depending on the carbon atom number in the FA molecule, the saturation feature etc. [3]. The connection between the electric and optic behavior is the dielectric constant and refractive index of the material change under the respective external signals. The large change of the refractive index with the light intensity determines a nonlinear transmission of the light through the sample, the possibility of self-focusing of the laser beam (lens-like effect [4]), optical activity change with the intensity of the light, laser pulse width change etc. [5]. By adding small amount of other substances (impurities), they act as an external perturbation as well. Cholesterol (Ch) or some usual drugs (aspirin) proved their role on the membrane behavior, while in the LC state [5].
The experimental data were processed with TableCurve3D computer program that gives the possibility for obtaining the equations that model the answer of the samples and forecast the behavior of different fatty acids.
For simulating the dynamics of the phenomena inside the material, a model based on Runge-Kutta functions in Matlab is used.

## 2. EXPERIMENTAL: MATERIALS AND METHODS

To account for some of biological membrane mechanisms in view of the mosaic-fluid model developed by Singer [6], studies were carried out on saturated fatty acids (SFA) and some mixtures of them and with Ch. As it is known, these acids - butyric (4:0),caproic (6:0), caprilic (8:0), capric (10:0), lauric (12:0), myristic (14:0), palmitic (16:0), stearic (18:0),arachydic (20:0) are very important in animals and plants, too. The unsaturated fatty acids (UFA): linoleic (16:2, 9, 12 cis), elaidic (18:1, 9 trans), arachidonic (20: 5, 8, 11, 14 all cis) were studied as well. FA was sandwiched between two glass plates of transparent $SnO_2$ electrodes, about 2 cm long, with 20μm Mylar spacers at both ends. Each sample had electrical contacts and placed under a polarizing microscope equipped with a camera that allows visualization of microstructural images in polarized light. The temperature (4-150°C) and the electrical voltage applied on the sample (0-50V) were continuously monitored and controlled by a thermo stated setup built in our laboratory.
Hysteresis curves of the current I versus the applied voltage exhibited a nonlinear dielectric feature and a negative resistance of the samples [5]. This behavior is similar to the dielectrics with a spontaneous polarization [7]. I=I(t) plots at a constant temperature T, t being the time, when a step voltage U has been applied and then removed, allow for the determination of the mechanism of the electric conduction of the samples, of the internal resistance, the relaxation time of charge carriers, and of the space charge within the sample. The electric conduction and molecular arrangement of these systems depend on their chemical composition and present memory effects and other modifications under some stimuli from the environment [8, 9], by using a model of the system like in Figure 1:

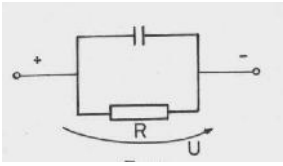


**Figure 1:** The electric system modeling the sample.

The current through the sample has two components [6]:
the residual $I_s$ stationary current:

$$I_s=U/R \quad (1)$$

where R is the internal resistance of the sample.
the absorption current $I_0$:

$$I_0=US\ exp[-t/^2] \quad (2)$$

where S is the conduction, and τ is the relaxation time (after the current decreased of "e" times).
The experimental dependencies I=I(t) for pure acids and mixture samples (see, for example, Figure 2), are quite similar with the theoretical ones, with some differences depending on the type of acid, showing an exponential decreasing of the current, typical for the strong dielectric materials.

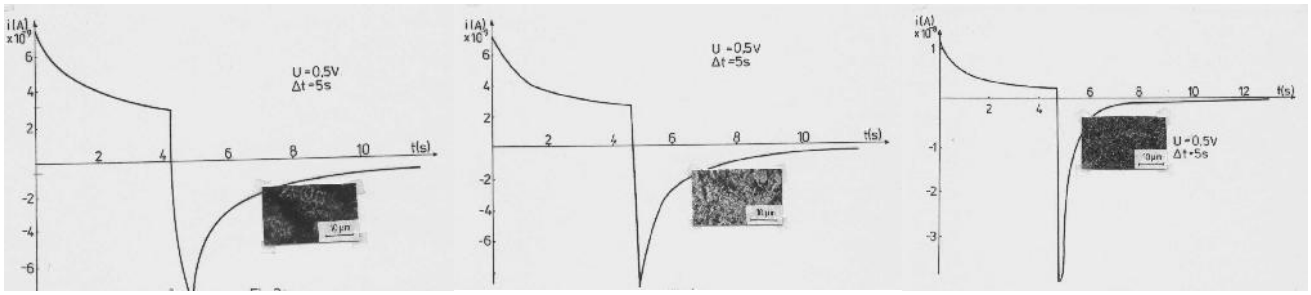


**Figure 2:** Dependency I=I (t) for U=0.5V and Δt=5s for mixture arrachidic-lauric-butyric-cholesterol in molar percentages (0.50÷0.25÷0.25÷0), (0.5÷0.25÷0.15÷0.15), (0.25÷0.25÷0.25÷0.25)

After electric field removal, the curves are similar with the ones for the currents limited by a space charge in dielectrics. The space charge is given by the surface delimited by the curve and the time axis [8]. The sample texture, inserted in Figure2 was obtained at the polarizing microscope, between crossed polarizers.
All the measurements took into consideration the Ch percentage and the discussion of the results has been done with respect with the hypothesis that Ch acts similarly with an external electric field, applied on the sample [8].
Emergent laser power from the samples ($P_{out}$) was registered at increasing and decreasing of the incident laser power ($P_{in}$). The experimental setup contained a He-Ne laser with a linear polarized c.w. beam, a variable

attenuator for varying the input optical power, the sample, and an optical power meter. A feedback mirror (R = 96%) was added to reach the required value for self - focusing, by the return of the beam on the liquid crystal cell. A necessary condition is that the reflected beam touches the cell in the same point with the incident one. At this moment, the on-axis optical power decreases, the optical level being maintained even so the incident power is increased. Typical image is represented in Figure 3.

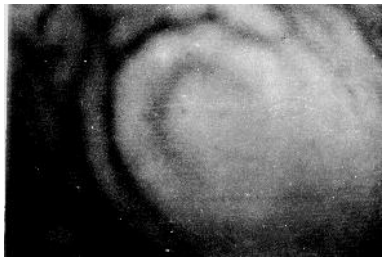

**Figure 3:** Mixture (0.25÷0.25÷0.25÷0.25), laser mode $TEM_{00}$

At the incident optical power decreasing, the molecules relax gradually to the initial positions and the output power takes more raised values, by the competition between the self -focusing effect - who is maintained until a certain power level - and the increased on-axis power. In almost all cases, the dependencies of $P_{out}$ versus $P_{in}$ were nonlinear and presented an optical hysteresis, similar with some of our previous results [9, 10].

## 3. COMPUTER STUDY OF THE EXPERIMENTAL RESULTS

The proposed computer models are in agreement with basic mathematical assumptions [11], and with the optical textures of the samples [12], as they were experimentally observed. The optical output power versus the input one and carbon atom number in FA was processed and analyzed by means of the TableCurve3D software, which gives also numerical information, including method/criteria of choosing equation, standard deviation and confidence limits for the fitted parameters, function extreme, an analysis of variance, and data table statistics. Precision Summary display was used to determine how much precision is preserved in the current equation. A residuals graph is also displaying the residuals for the current surface-fit. The data table can be weighted, if necessary. Thus, the program gives the possibility to choose other experimental conditions in terms of the future experiment requirements and purposes.
Figure 4 shows the dependencies of laser power ($P_{max}$=45mW), in terms of carbon C atoms number in SFA and Figure 5 – in UFA. One can observe the changes occurred in laser field, beginning with a small C number for SFA, but especially at a big C number for UFA; the nonlinear feature of the curves is different, increasing for UFA and decreasing for SFA. Working with a certain number of samples, graphs could forecast the behavior of other FA, with a different C number, by indicating the used equation.

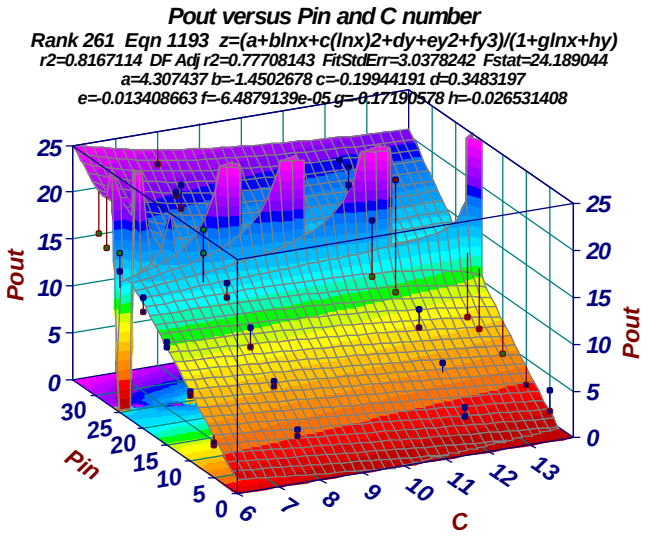


**Figure 4:** Output laser power versus input laser power and number of carbon atoms in molecule (SFA)

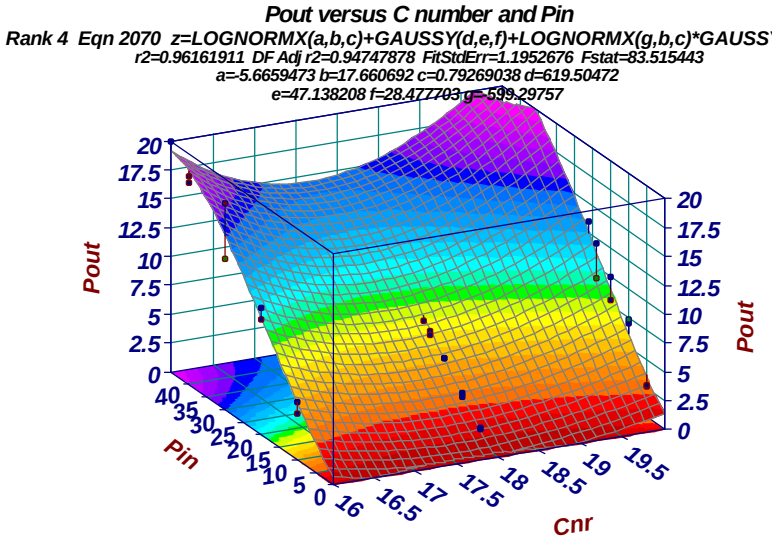


**Figure 5:** Output laser power versus input laser power and number of carbon atoms in molecule (UFA)

These equations showed the nonlinear answer of the samples. Taking into account these results and previous results for other saturated and unsaturated FA and mixtures [13, 14], we believe that external interventions - physical fields or impurities - led to changes of the molecular arrangement and of the electric state of the samples. The length of the molecule is important in SFA and the carbon atom number in UFA; the distance between the double bound and the carboxyl group is also important [13]. These modifications can lead to some local mechanical deformations in the system, namely the director n orientation direction can be forced to modify by external perturbations. This reorientation of the director determines the observed changes of the refractive index, connected with the dielectric constant of the material. Relatively low laser power [15] can be useful for emphasizing the changes of the structure and properties in these membrane models, by their nonlinear interaction with these substances, in LC state- which represents a noninvasive method for analyzing real biological samples.

The mathematical model of the dynamics of phenomena inside the material, by using similar considerations as in [12], is based on Runge –Kutta functions in Matlab, by means of considering differential equations, adequate for the imprecise behavior which is inherent to many real processes [11]. To deal with periodic phenomena, by considering some derivatives with a switching point, providing sufficient conditions that the solutions match adequately and illustrate the real process.

The free term u (t) of the differential equation corresponds to the magnitude of the external perturbation; the working period is chosen about 0.2ms. The function f:

$$f^{(2)} = [(6\tau^4 - 2)/(\tau^2 - 1)^4]\, f + u(t) \quad (3)$$

generated by the material under the influence of the external perturbation, can be integrated on this working time. For the external observer, the behavior of the material presents a slowly varying evolution in time, a single oscillation on the whole working interval, similar to the behavior noticed during the experiment.

For simulating the dielectric answer (z) of the material under the influence of an external electrical perturbation, we consider a differential equation able to generate an adequate truncated "test-function" φ similar to a Dirac pulse, in filtering and sampling procedures:

$$\ddot{\varphi} = exp\,[1/(\tau^2 - 1)] \quad (4)$$

where $\tau = t - t_m$, $t_m$ being the middle of the working period. This function has nonzero values only for $\tau \in [-1, 1]$. The derivative $\varphi^{(2)}$ of this function related to τ is:

$$\ddot{\varphi}^{(2)} = [(6\tau^4 - 2)/(\tau^2 - 1)^4]\, \ddot{\varphi} + u(\tau) \quad (5)$$

This corresponds to the magnitude of the external signal, where $u(\tau) = 1$ on the working interval (-0.99; 0.99).

As it is known, such an equation of evolution, beginning to act at an initial moment of time, involves the derivative $f^{(n)}$ of certain order n jumps at the initial moment from the a null value to another one, in contradiction with the property of the test-functions to have continuous derivatives of any order on the whole real axis ( time axis). Our truncated function φ has nonzero values on the interval $\tau \in [-1, 1]$ and a certain number of continuous derivatives on the whole time axis, and plays the role of the function f at a certain time moment, very close to the initial moment $\tau = -1$. Taking into account the expression of φ, the simplest differential equation satisfying these requirements, has the form:

$$f^{(1)} = [-2\tau/(\tau^2 - 1)]\, f \quad (6)$$

and has the function φ as a possible solution. We use the initial moment of time is $\tau_0 = -1 + 0.01$ and the initial condition for f is $\varphi(\tau_0)$ for numerical simulation using equations Runge-Kutta of 4-5 order in Matlab.
The influence of the function φ is a sum of all effects, which can be mathematically represented as an integral of function φ multiplied by the progressive wave inside the material. Then one can write:

$$z^{(1)}(²) = ¨(²) \sin(®² - c) \quad (7)$$

where Φ represents an initial phase of the progressive wave. The function z (t) is represented in Figure 6, for u (τ) = 1 and $\Phi = \pi/12$, that models the experimental dielectric behavior presented in Figure 2.

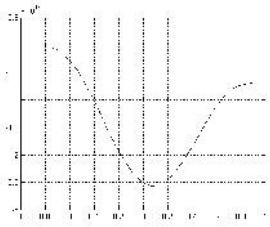

**Figure 6:** z versus t (u = 1, $\Phi = \pi/12$)

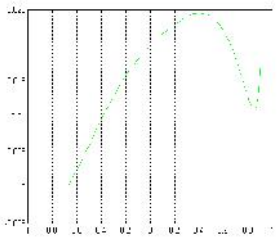

**Figure 7:**f versus t for u=sin($10^{11}\pi$t)

Figure 7 models the action of Ch, similar with the one of the electric field, but dependent on the Ch percentage added. The increase of this over 75% leads to some clusters formation inside the sample, and the fluidity of this decreased drastically.
Changes inside the material appeared due to the external optical pulse of the laser can be similarly taken into account. Let's consider null initial conditions for the system and add a free term in the differential equation – corresponding to the magnitude of the electrical field of the external optical signal, at a frequency of about $10^{15}$Hz. The working period was chosen approximately equal to the period when the optical signal is received by the detector - about 0.2ms. The differential equation can be written as:

$$f^{(2)} = [(0.6\tau^4 – 0.36\tau^2 –0.2)/(\tau^2 – 1)^4] f + u(t) \quad (8)$$

where *u* is represented by an alternating function with a frequency $10^{11}$ times greater than the working period of 0.2 ms. By similar numerical simulations, we have obtained for f the results presented in Figure 8 for $u = cos(10^{11}\pi\tau)$.

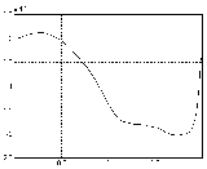

**Figure 8:** *f* versus *t* for $u = cos(10^{11}\pi\tau)$.

Similar considerations could be applied for other kind of perturbations, as for example some drugs (aspirin). We summarized in [13] some of these results.

## 4. CONCLUSIONS

In this paper, we present experimental and computer studies of behavior of substances involved in the structure and functions of the biological membrane, namely systems based on fatty acids, with a mesomorphic behavior.

Typical sandwich cells containing thin films of saturated and unsaturated fatty acids, components or forerunners of the biological membrane, were built in our laboratory and generally showed smectic liquid crystal textures during their evolution between some temperature values, characteristic for every of them. The electric conduction and molecular arrangement of these systems depend on their chemical composition and present modifications under some stimuli from the environment, as a result of the local mechanical deformations in the systems, director **n** reorientation, and displacement of the electric charges.

Relatively low electric fields and undistructive laser powers are useful for emphasizing the changes of the structure and properties of the samples, by their nonlinear interaction with these substances, easy to obtain in the liquid crystal state.

The experimental data can be processed by using TableCurve 3D computer program, and the adequate equation describing the sample behavior, precision intervals, confidence limit etc. are directly evidenced.

The experimental graphs and the theoretical ones are in agreement each other and with other results from the literature [16, 17]. Samples present a nonlinear dielectric feature, which evidenced the changes occurred in connection with the carbon number, the length of the molecule and the distance between the double bound and the carboxyl group is also important. Data processing and simulations were performed with computer help, modeled by Runge-Kutta functions in Matlab, with truncated test-functions generated by differential equations. The perturbation - let's be it electric, laser, or "impurities" with importance for biology and medicine (cholesterol, drugs, other acids etc.) – can be treated as a free term of the used equation, and adequate initial conditions and working intervals should be taken into account.

The obtained results and conclusions are important for the living processes and show once more our responsibility to proceed in a way that sustains life healthy.

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