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Method and system of Jones-matrix mapping of blood plasma films with “fuzzy” analysis in differentiation of breast pathology changes

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ABSTRACT

A fibroadenoma diagnosing of breast using statistical analysis (determination and analysis of statistical moments of the 1st-4th order) of the obtained polarization images of Jones matrix imaginary elements of the optically thin (attenuation coefficient $\tau \leq 0,1$) blood plasma films with further intellectual differentiation based on the method of “fuzzy” logic and discriminant analysis were proposed. The accuracy of the intellectual differentiation of blood plasma samples to the "norm" and "fibroadenoma" of breast was 82.7% by the method of linear discriminant analysis, and by the "fuzzy" logic method is 95.3%. The obtained results allow to confirm the potentially high level of reliability of the method of differentiation by "fuzzy" analysis.

Keywords: Jones matrices, blood plasma, fuzzy logic, fibroadenoma, statistical analysis, linear discriminant analysis

1. INTRODUCTION

The problem of breast cancer (BC) in recent years is leading in the structure of morbidity, mortality and is marked by an annual increase among cancerous nosologies in Ukraine. Among the benign tumors, fibroadenoma is ranked first by prevalence. The risk of fibroadenoma is that they can be transformed into malignant neoplasms. Due to the complexity of their timely detection (especially at the early stage of the disease), it is important to develop methods and technologies for early diagnosis of breast pathologies.

A separate area of research in this field are polarimetric methods based on the study of physical processes that occur when electromagnetic radiation interacts with various biological objects, in particular biological fluids: blood, urine, saliva, bile, etc.[1-2] The most widely used among them are the methods and systems for diagnosing biological fluids on the basis of polarization-sensitive optical coherent tomography[3-7] and Stokes, Mueller and Jones polarimetry[8-12]. The application of these methods allows us to evaluate the state of individual organs by determining the appropriate state of blood plasma or biological tissue[11-12]. The practical application of separate methods and systems of laser polarimetry of blood plasma films for diagnostics of mammary glands through polarization mapping and phasometry of blood plasma films were studied in the works[13-16]. However, not all potential possibilities of multiparameter laser polarimetry are involved, in particular, when reproducing and analyzing the orientational-phase parameters of the blood plasma structure.

To increase the authenticity of differentiation of changes in the optical anisotropy of blood plasma conditioned by fibroadenoma of the mammary gland, the development of laser polarimetry systems with an objective complex analysis of the received parameters in conjunction with the technology of decision support is relevant.

The purpose of this work is to investigate the potential possibilities of the Jones-matrix polarimetry method for optically thin ($\tau \leq 0,1$) blood plasma samples in the problems of fibroadenoma diagnosing of breast using statistical analysis (determination and analysis of statistical moments of the 1st-4th order) of the obtained polarization images of Jones matrix imaginary elements of blood plasma with further intellectual differentiation based on the method of “fuzzy” logic and discriminant analysis.

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2. MAIN ANALYTICAL RELATIONS

The analysis of the results presented in the paper is based on the fundamental concepts developed for the description of an optically anisotropic blood plasma[13-15].

- the film of human blood plasma is considered as a two-component amorphous-crystalline structure;
- crystal component is formed by the complex (network) of crystals of albumin and globulin;
- optically liquid crystals of amino acids have the properties of optically uniaxial birefringent crystals, which are characterized by a Jones-matrix operator of the following form[8-9]:

$$\{C\} = \begin{Vmatrix} c_{11} & c_{12} \\ c_{21} & c_{22} \end{Vmatrix} = \begin{vmatrix} \cos^2\rho + \sin^2\rho\exp(-i\delta); & \cos\rho\sin\rho\left[1-\exp(-i\delta)\right]; \\ \cos\rho\sin\rho\left[1-\exp(-i\delta)\right]; & \sin^2\rho + \cos^2\rho\exp(-i\delta); \end{vmatrix}, \quad (1)$$

here $\rho-$ is the direction of the optical axis determined by the direction of birefringent fibril packing; $\delta = 2\pi/\lambda\,\Delta n d$ – the phase shift introduced between the orthogonal components of amplitude of the laser wave with wavelength λ that passes through a fibril with the linear size of geometrical section d and birefringence Δn.

As part of Jones Matrix mapping, for the experimental measurement of phase shifts, it becomes necessary to determine the real and imaginary part of the Jones matrix elements. Therefore, we write the Jones matrix (1) in a different generalized form[8-9]:

$$\{\aleph\} = \begin{Vmatrix} R_{11}\exp\Theta_{11} & R_{11}\exp\Theta_{12} \\ R_{11}\exp\Theta_{21} & R_{11}\exp\Theta_{22} \end{Vmatrix}, \quad (2)$$

where R_{ik} - real component of Jones-matrix elements; Θ_{ik} - phase angles.

The real "orientation" $R_{11;22}(m\times n)$ and "phase" $R_{12;21}(m\times n)$ components of the Jones-matrix elements characterize the corresponding manifestations of the orientational ρ and phase δ structure of blood plasma crystals[8-9].

When measuring the imaginary components of the Jones matrix, their totality is taken as[8-9]:

$$\chi_{12;21} \approx \cos(\Theta_{11;12} - \Theta_{12;22}), \quad (3)$$

$$\chi_{11;22} \equiv \sin(\Theta_{11;21} - \Theta_{12;22}). \quad (4)$$

The relations (3), (4), which are determined by the combination of phase angles, are called the imaginary parts of the "orientation" $\chi_{11;22}$ and "phase" $\chi_{12;21}$ elements, which also characterize manifestations of the orientational ρ and phase δ structure of the blood plasma crystal ensemble structure[8-9].

The further study of human blood plasma films by the Jones matrix method is to sequentially measure the "orientation" and "phase" distributions of the corresponding elements of Jones matrix for each sample. Then the statistical

processing of the received polarization maps is carried out. The final stage is the choice of the most informative parameters and conducting on their basis of intellectual differentiation on the basis of the method of "fuzzy" logic and discriminant analysis.

3. JONES-MATRIX MAPPING OF THE OPTICAL-ANISOTROPIC BLOOD PLASMA FILMS AND ITS IMPLEMENTATION IN THE SYSTEM OF 2D LASER POLARIMETRY

Jones-matrix mapping is considered to be a set of experimental steps for the measuring coordinate distributions of Jones-matrix (real and imaginary components) element totality with the subsequent analytical (statistical) algorithmic analysis of obtained data arrays in order to determine the diagnostics criteria (interconnections) and differentiate the parameters of anisotropy of blood plasma films. Jones-matrix mapping algorithm is implemented on the existing architecture of the universal automated system of two-dimensional polarimetry shown in Fig. 1[17-18].

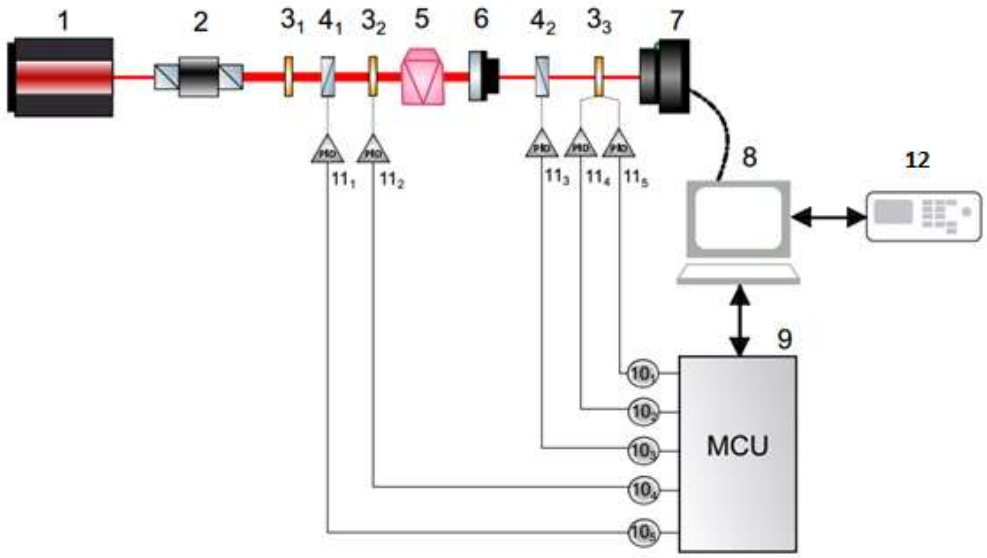

Fig.1 Multifunctional automated system of 2D laser polarimetry.

The system consists of a semiconductor laser 1 with λ=0,638 wavelength, collimator 2, quarter-wave plates 3_1, 3_2, 3_3, a linear polarizer 4_1 and an analyzer 4_2; blood plasma sample 5, projection block 6, a CCD-based (charge-coupled device) camera 7, connected to the computer 8; special microcontroller control block 9, engine drivers 10_1-10_5, positioning control of engines 11_1-11_5, decision support block 12. More details about the operation of this system are described in past works[17-19].

Algorithm of the Jones matrix mapping of blood plasma films consist in experimental determining the real R_{ik} and imaginary χ_{ik} component of the Jones matrix. By successively changing the values of the light streams of laser radiation 1 in a system formed by orientation combinations of the polarization components of the system, a series of ten polarization images of the human blood plasma sample are obtained[19].

In fact, the whole process of measurement is reduced to determining the value of the intensity I_n of the laser beam falling into the corresponding pixel of the camera 7 CCD matrix. Further, on the basis of the obtained values of intensities, with the help of the specialized software complex in 8 the corresponding values of the real and imaginary component of the Jones matrix are calculated and, respectively, the resulting Jones matrix is formed[19].

4. STATISTICS PARAMETERS OF JONES-MATRIX BLOOD PLASMA IMAGES

To estimate the distributions $\chi_{ik}(X,Y)$ quantitatively their quantitative estimation is introduced on the basis of the definition of a set of their statistical moments of the 1st-4th order[17-19]:

$$M_1 = \frac{1}{N}\sum_{j=1}^{N}\left(|\chi_{ik}|\right)_j ; M_2 = \sqrt{\frac{1}{N}\sum_{j=1}^{N}\left(\chi_{ik}{}^2\right)_j} ;$$
$$M_3 = \frac{1}{M_2^3}\frac{1}{N}\sum_{j=1}^{N}\left(\chi_{ik}{}^3\right)_j ; M_4 = \frac{1}{M_2^4}\frac{1}{N}\sum_{j=1}^{N}\left(\chi_{ik}{}^4\right)_j . \quad (5)$$

5. RESULTS AND DISCUSSION

Forty (40) samples of blood plasma taken from a patients with healthy breast and adenoma were selected for the study.

Blood plasma specimens were prepared under the following conditions: a drop of blood plasma from the pipette was applied to a plate of optically homogeneous glass so that the plasma spread evenly over the glass surface. The resulting film was dried at room temperature for 24 hours[13-15].

The results of the study are presented in the form of coordinate distributions of two groups of elements: the "orientation" $\chi_{11;22}(m\times n)$ and "phase" $\chi_{12;21}(m\times n)$ imaginary elements of the Jones matrix, which characterize the optical activity of the polycrystalline networks of albumin and globulin proteins of blood plasma films of patients with healthy breast and, consequently, of fibroadenoma. In fig. 2-3 shows examples of polarization images of the Jones matrix (imaginary component) elements distributions of the "orientation" and "phase" elements.

Table 1 presents the calculated values of statistical moments of the 1st-4th orders M_n of coordinate distributions of the Jones-matrix (imaginary component) elements of polycrystalline networks laser images of albumin and globulin proteins of blood plasma films in patients of both groups.

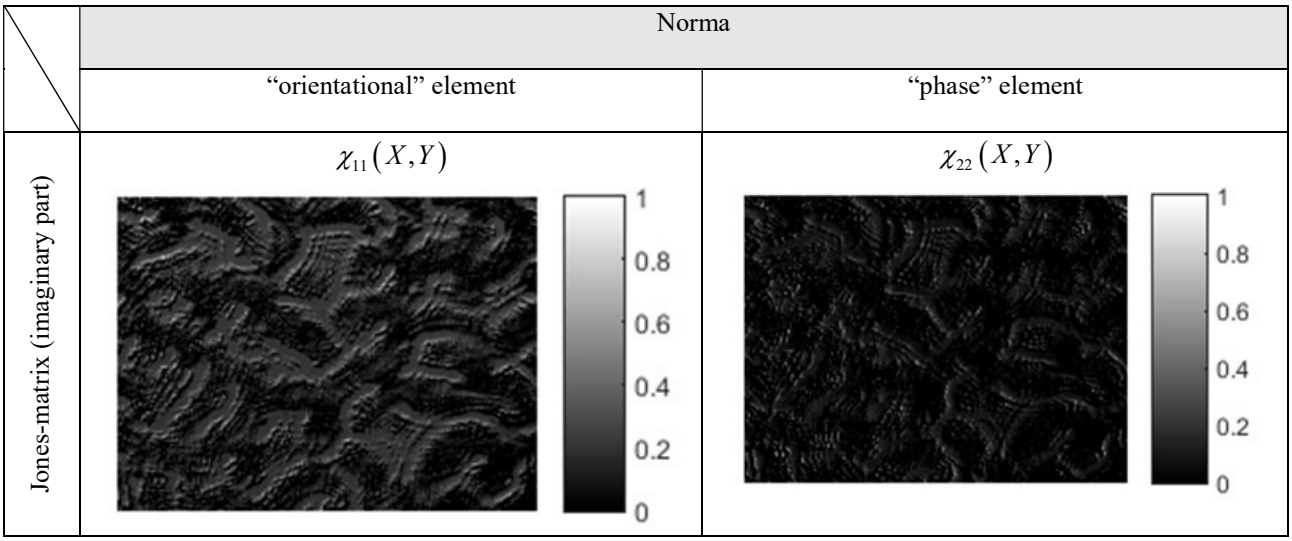

Fig.2 Images of polarizationally reproduced "orientational" and “phase” elements (imaginary component of Jones-matrix) of a healthy blood plasma.

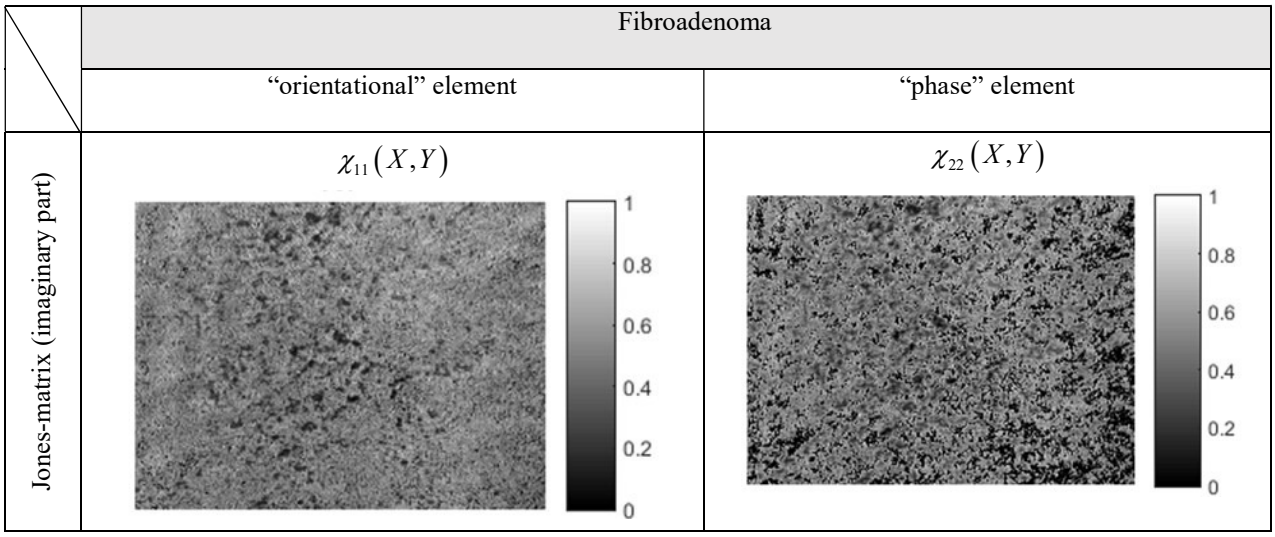

Fig.3 Images of polarizationally reproduced "orientational" and "phase" elements (imaginary component of Jones-matrix) of a blood plasma with fibroadenoma.

Table 1. Average M_1, variance M_2, asymmetry M_3 and excess M_4 of distributions of "orientation" $\chi_{11;22}(m\times n)$ and «phase» $\chi_{12;21}(m\times n)$ elements of the Jones-matrix (imaginary component) of blood plasma films polarization images.

M_n	$\chi_{11;22}(m\times n)$ norma	$\chi_{12;21}(m\times n)$ norma	$\chi_{11;22}(m\times n)$ fibroadenoma	$\chi_{12;21}(m\times n)$ fibroadenoma
$M^{(1)}$	0,12±0,04	0,07±0,01	0,47±0,09	0,49±0,05
$M^{(2)}$	0,01±0,001	0,02±0,001	0,01±0,0009	0,02±0,001
$M^{(3)}$	0,36±0,04	0,28±0,01	-0,52±0,05	-0,6±0,03
$M^{(4)}$	3,37±0,4	2,97±0,5	3,39±0,4	3,55±0,5

Calculated statistical moments of the 1st to 4th orders of polarization maps of the real component of the Jones-matrix elements of the blood plasma of both states («norm» and «fibroadenoma») will be as input informative parameters for future discriminant analysis and "fuzzy" analysis.

For the quantitative assessment of the difference degree of the corresponding set of statistical moments of the 1st to 4th order for the groups "norm" and "fibroadenoma", the Euclidean distance[20] between the vectors of "norm" and "pathology" was calculated for each statistical moment. It is known that the greater the value of the Euclidean distance between the groups, the more they differ between each other. Thus, on the basis of the determining of the Euclidean distance, it is possible to separate the most informative parameters that will be as accurate as possible to characterize the separation of groups "norm" and "fibroadenoma", as a result - further intellectual analysis will have greater accuracy.

Euclidean distance is calculated by the formula[20]:

$$D = \sqrt{\sum_{i=1}^{v}\left(p_{ni} - p_{pi}\right)^2}, \tag{6}$$

where: υ – number of plasma samples of one group, p_{ni} - vector of values of statistical moment *Mn* – th order for the «norm», p_{pi} - for «fibroadenoma» respectively.

For $M^{(1)}$ the Euclidean distance is 1,705; for $M^{(2)}$ - 0,18; for $M^{(3)}$ - 3,9149; for $M^{(4)}$ - 0,191. Thus, $M^{(1)}$ and $M^{(3)}$ are the most suitable for intellectual differentiation.

On the basis of the determined informative differentiation parameters a discriminant analysis is conducted. Measured values of statistical moments from Table 1 will serve as a "training" sample (database). The basic idea of discriminant analysis is to determine the differences between the values vectors of the average of any variable (or a linear combination of variables) with the subsequent use of this variable in order to predict belonging of the new terms to one or another group. The classic method is the Linear Discriminant Analysis (LDA) method[21].

For clarity, in Fig.4 we will demonstrate the result of plotting a discriminant function with two variables ("orientation" and "phase" parameters) for the "training" values sample of the 1st statistical moment $M^{(1)}$.

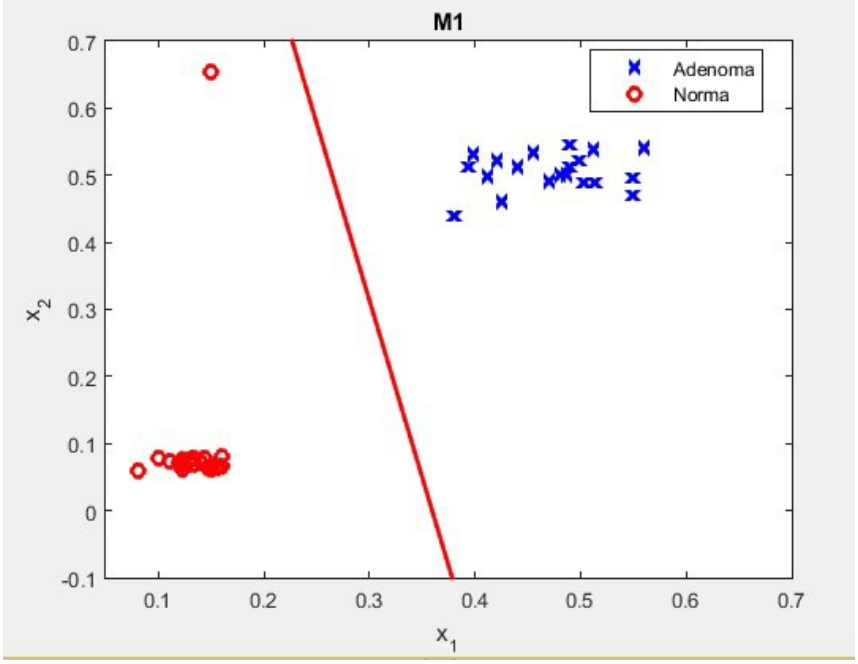

Fig.4 Discriminant function for the "training" sample of the 1st statistical moment $M^{(1)}$ of "orientation" and "phase" parameters

Similarly, for the "training" sample, a function of 4 variables (the values of the 1st $M^{(1)}$ and 3rd $M^{(3)}$ statistical moments of the "orientation" and "phase" parameters) were plotted. Then on the basis of the plotted function, a discrimination for 40 samples from the "test" sample without specifying diagnoses (reference samples whose diagnosis is reliably known: 20 with "norm" and 20 with "fibroadenoma") was carried out. As a result of testing, 16 samples of "norms" were correctly classified, for "fibroadenoma" - 17 samples. To assess the validity of differentiation in terms of evidence-based medicine, sensitivity, specificity and accuracy were calculated: $Se = 81\%$, $Sp = 84,2\%$, $Ac = 82,7\%$. In terms of evidence-based medicine, the results are of "good" quality, but they are not effective enough.

Often the problem of staging a diagnosis is not limited to clear criterias. To solve such problems, methods of "fuzzy" analysis are used. The essence of "fuzzy" analysis is reduced to obtaining unambiguous numerical expressions for criterias that have such features as: L - low, BA - below average, A - average, AA - above average, H - high. Each of these terms

is a fuzzy set defined with the help of special belonging functions, which can be represented by an appropriate interval from 0 to 1. Absolute non-belonging to the set indicates 0, and to absolute belonging – 1[22].

For "fuzzy" analysis, the selected parameters which are same to discriminant analysis. Table 2 shows the formed values of nosologies "norm" and "fibroadenoma" informative parameters (statistical moments $M^{(1)}$, $M^{(3)}$ of "orientation" $\chi_{11;22}(m \times n)$ and «phase» $\chi_{12;21}(m \times n)$ elements of the Jones-matrix imaginary component).

Table 2. Nosology values of statistical moments $M^{(1)}$, $M^{(3)}$ of "orientation" $\chi_{11;22}(m \times n)$ and «phase» $\chi_{12;21}(m \times n)$ elements of the Jones-matrix imaginary component for «norm» та «fibroadenoma»

State	$M_o^{(1)}(\chi_{11;22})$	$M_p^{(1)}(\chi_{12;21})$	$M_o^{(3)}(\chi_{11;22})$	$M_p^{(3)}(\chi_{12;21})$
Norm	L	L	AA H	AA A
Fibroadenoma	AA H	AA H	L	L

Graphical and analytic view of membership functions for statistical moments $M^{(1)}$, $M^{(3)}$ of "orientation" $\chi_{11;22}(m \times n)$ and «phase» $\chi_{12;21}(m \times n)$ elements of the Jones-matrix imaginary component shown on Fig. 5:

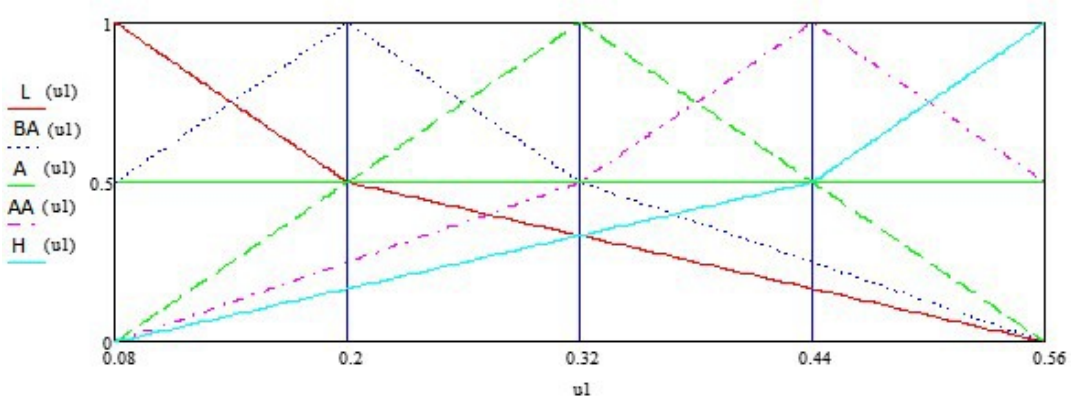

Fig.5 View of membership functions for statistical moments $M^{(1)}$, $M^{(3)}$ of "orientation" $\chi_{11;22}(m \times n)$ and «phase» $\chi_{12;21}(m \times n)$ elements of the Jones-matrix imaginary component

Next, the meaning of nosologies for "norm" and "fibroadenoma" was calculated for each of the 40 "test" samples. As a result, out of 20 samples of the "norm" 18 samples were correctly differentiated; for "fibroadenoma" - 19 samples; no diagnosis ("unidentified" value) was given for 1 sample, which was a true "fibroadenoma". To assess the validity of differentiation in terms of evidence-based medicine, sensitivity, specificity and accuracy were calculated: $Se = 90,5\%$, $Sp = 100\%$, $Ac = 95,3\%$. In terms of evidence-based medicine, the results have a "high" quality.

6. CONCLUSIONS

Further development of intellectual decision support systems has been found based on "fuzzy" logic and discriminant analysis to assess the physiological state of the breast. As a result of the conducted experimental researches, it was established that the accuracy of the blood plasma samples differentiation to the "norm" and "fibroadenoma" of the breast was 82.7% by the method of linear discriminant analysis, and by the "fuzzy" logic method is 95.3%. The obtained results allow us to confirm the potentially high level of reliability of the method of differentiation by "fuzzy" analysis.

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