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Layer-by-Layer Multifractal Scanning of Optically Anisotropic Architectonics of Blood Plasma Films: Fundamental and Applied Aspects

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Abstract: This study focuses on the topographic structure of optical anisotropy maps (theziograms) of dehydrated blood plasma films (facies) to identify and utilize markers for diagnosing self-similarity (multifractality) in the birefringence parameters of supramolecular protein networks. The research is based on the Jones-matrix analytical framework, which describes the formation of polarization-structural speckle fields in polycrystalline blood plasma facies. In the proposed model, algorithms were developed to relate the real and imaginary parts of the complex elements of the Jones matrix to the theziograms of linear and circular birefringence. To experimentally implement these algorithms, a novel optical technology was introduced for polarization-interference registration and phase scanning of the laser speckle field of blood plasma facies. The laser-based Jones-matrix layer-by-layer theziography relies on polarization filtration and the digital recording of interference patterns from microscopic images of blood plasma facies. This process includes digital 2D Fourier reconstruction and phase-by-phase scanning of the object field of complex amplitudes, enabling the acquisition of phase sections of laser polarization-structural speckle field components scattered with varying multiplicities. Jones-matrix images of supramolecular networks, along with their corresponding theziograms of linear and circular birefringence, were obtained for each phase plane. The experimental data derived from laser layer-by-layer Jones-matrix theziography were quantitatively analyzed using two complementary approaches: statistical analysis (central moments of the 1st to 4th orders) and multifractal analysis (spectra of fractal dimension distributions). As a result, the most sensitive markers—namely asymmetry and kurtosis—were identified, highlighting changes in the statistical and scale self-similar structures of the theziograms of linear and circular birefringence in blood plasma facies. The practical aspect of this work is to evaluate the diagnostic potential of the Jones-matrix theziography method for identifying and differentiating changes in the birefringence of supramolecular networks in blood plasma facies caused by the long-term effects of COVID-19. For this purpose,



Received: 4 November 2024
Revised: 7 January 2025
Accepted: 9 January 2025
Published: 28 February 2025

Citation: Ushenko, A.; Pavlyukovich, N.; Khukhlina, O.; Pavlyukovich, O.; Gorsky, M.; Soltys, I.; Dubolazov, A.; Ushenko, Y.; Salega, O.; Mikirin, I.; et al. Layer-by-Layer Multifractal Scanning of Optically Anisotropic Architectonics of Blood Plasma Films: Fundamental and Applied Aspects. *Photonics* **2025**, *12*, 215. <https://doi.org/10.3390/photonics12030215>

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a control group (healthy donors) and three experimental groups of patients, confirmed to have had COVID-19 one-to-three years prior, were formed. Within the framework of evidence-based medicine, the operational characteristics of the method—sensitivity, specificity, and accuracy—were assessed. The method demonstrated excellent accuracy in the differential diagnosis of the long-term effects of COVID-19. This was achieved by statistically analyzing the spectra of fractal dimensions of Jones-matrix theziograms reconstructed in the phase plane of single scattering within the volume of blood plasma facies.

Keywords: Jones matrix; optical anisotropy; birefringence; polarization interferometry; blood plasma facie; supramolecular networks; fractal dimensions; multifractal spectra; statistical moments

1. Introduction

Recently, numerous studies in biomedical polarimetry [1–5] have widely applied digital methods for data processing, including polarization mapping [6,7], Mueller-matrix imaging [8–14], and optical anisotropy mapping [15]. These advancements have enabled the identification of objective criteria (markers) for detecting changes in the morphological structure of biological tissues and dehydrated films (facies). Such changes are associated with various pathological conditions, including cancer [16], endometriosis [17], and inflammatory processes [18], as well as necrotic states, such as determining the onset, causes, and differentiation of death [19].

Statistical and correlation analysis of polarization maps of biological specimens and the coordinate distributions of Mueller matrix elements serve as the primary algorithmic basis for identifying a set of digital diagnostic markers [20].

Within this framework, diagnostic relationships are established between pathological and necrotic changes in the morphological structure of biological tissues and biological fluid facies, and the statistical moments (1st to 4th orders) and autocorrelation function parameters of microscopic or Mueller-matrix images. These parameters characterize the 2D distributions of polarization properties [21].

The effective implementation of digital algorithms in biomedical polarimetry techniques has driven new research aimed at expanding the statistical and algorithmic foundation. This includes singular analysis (e.g., the distribution of polarization-singular states of the object field [22]), as well as scale-selective wavelet [23,24] and Fourier [25,26] approaches. The identification of objective diagnostic markers has significantly enhanced the sensitivity and accuracy of polarization-based biomedical diagnostic methods, particularly in oncology and gynecology [27].

The widespread use of lasers in biomedical research and the corresponding formation of speckle fields have contributed to the development and enhancement of traditional 2D imaging polarimetry with non-invasive polarization-sensitive optical coherence tomography (PSOCT) methods [28–31]. The application of direct interference recording principles for the structure of object speckle fields has enabled the layer-by-layer measurement of Mueller matrix coordinate distributions (Mueller matrix images, MMI) at various depths within biological objects. This advancement has made it possible to accurately diagnose fibrosis and distinguish tumor regions with low levels of fibrosis [32]. The effectiveness of this approach is demonstrated by numerous biomedical applications, as systematized in the review [33].

An important expansion of PSOCT functionality is the study of various types of objects, such as biological fluids. These materials are easily accessible and do not require invasive biopsy procedures. Biological fluids represent one of the most critical systems

supporting vital bodily functions, as they encompass a range of fluids involved in metabolic processes. Within biological fluids (BF), rapid changes occur in the molecular composition and interactions of various physiological components, particularly under extreme or pathological conditions.

Any physiological or pathological process occurring in a living organism leads to specific changes in the structure of proteins and other organic molecules. These changes are highly informative for studying homeostasis at the molecular level and serve as a foundation for diagnosing various diseases at their earliest stages [34,35].

Modern laboratory and clinical diagnostics primarily focus on numerous quantitative indicators derived from the analysis of biological fluids (BF), which are products of the body's vital activity. While morphological research in biology and medicine traditionally emphasizes cellular elements, the morphological analysis of BF—an essential life-support system—has remained largely inaccessible to clinical practice until recently [36].

A drop of BF placed on a horizontal surface represents a self-organizing system and provides a convenient model for studying physical and chemical processes. The properties of such a system are influenced by the composition of dissolved substances, external dehydration conditions, and the substrate material. As the BF drop undergoes dehydration, a dry film—referred to as a “facia”—is formed. The structure of the facia carries valuable information about the composition and interactions of the substances dissolved in BF. By analyzing such structures at the macroscopic self-organization level, researchers can gain insights into the system's behavior at the molecular level [37–40].

It is important to note that the structure of polycrystalline supramolecular facies of biological fluids is volumetrically heterogeneous and is not always optically thin or singly scattering [39]. This highlights the relevance and potential of employing PSOCT methods for layer-by-layer scanning of facies samples. However, the algorithmic generation of layer-by-layer Mueller matrix images (MMI) of BF facies using PSOCT techniques does not allow for direct measurement of phase shifts caused by the optical anisotropy of biological objects. Such phase information can be extracted from the azimuth and ellipticity distributions of fully polarized speckles in object-coherent fields [41,42] through the application of the Jones-matrix formalism in PSOCT techniques [43–45].

Another critical aspect is the development of methods to isolate components with different light scattering multiplicities in laser speckle fields. These methods aim to extract the singly scattered component, which is uniquely associated with the optical anisotropy parameters of supramolecular networks in BF facies. This component is most accurately described within the framework of the Jones-matrix formalism. This approach enables solving the inverse problem—determining Jones-matrix algorithms for reconstructing and quantitatively assessing the distributions of linear and circular birefringence. However, the PSOCT method's functionality is limited due to the lack of algorithms for obtaining and evaluating (inaccessible to statistical and correlation methods) topological scale-self-similar information about the biological tissues and biological facies polycrystalline architectonics.

One of the possible ways to effectively overcome this biomedical diagnostics problem is to use multifractal analysis [46]. This is evidenced by a few modern publications [22,47], which effectively used blood plasma facies azimuth and ellipticity distribution fractal analysis for the differential diagnosis of healthy and cancerous tissues. For the first time, it was shown that oncological conditions correspond to the transformation of the blood plasma facies polarization maps fractal structure into a multifractal one [47].

Thus, it can be stated that fractal properties are inherent not only in geometric morphological parameters but also in polarization manifestations of optical anisotropy in the biological tissues and biological fluids facies. This fundamental result could become a starting point

in the new direction for biomedical diagnostics formation—biological tissues and biological fluids facies optical anisotropy structure (architectonics) multifractal scanning [48–51].

The instrumental basis for this direction promises to be the polarization-interference layer-by-layer visualization techniques of biological preparations of polycrystalline architectonics [52–54]. Such systems are based on the algorithmically reconstructed complex amplitude field phase scanning principle and differentiation of components with different scattering multiplicities. This makes it possible to obtain the most reliable information on the layer-by-layer statistical structure of biological samples optically anisotropic architectonics, which is inaccessible to traditional 2D polarimetry techniques [1–28]. This is confirmed by the recent results of multifractal analysis of layered maps of polarization ellipticity distributions of structurally polarized laser speckle fields of blood plasma facies in the diagnosis of remote consequences of COVID-19 [55]. However, the data obtained in this work are the first step in detecting pathological changes in the structure of blood plasma facies. The multifractal structure of layered maps of polarization ellipticity does not contain direct information on the parameters of optical anisotropy of polycrystalline supramolecular networks and is their indirect “polarization-phase” portrait. Therefore, further development of this method by obtaining algorithms for direct reconstruction of optical anisotropy maps of the studied samples is relevant. Our article considers the issue of studying the relationship of the large-scale self-similar (multifractal spectra) structure of optical anisotropy maps with the architectonics of dehydrated blood plasma films by using the Jones-matrix formalism and digital holographic reconstruction of complex amplitudes of structurally polarized laser coherent speckle fields to reproduce layer-by-layer distributions of linear and circular birefringence (theziograms) of supramolecular polycrystalline networks. The applied part of the work consisted of developing a method for determining the remote consequences of COVID-19.

2. Materials and Methods

2.1. A Brief Theory

In this section, we will briefly examine the main theoretical relationships that describe the formation processes of phase anisotropy (linear and circular birefringence) in blood plasma facies. Additionally, we will discuss the polarization-interference holographic reconstruction of the polycrystalline structure of theziograms and their subsequent multifractal scanning.

2.1.1. Jones Matrix Theziography

According to traditional concepts [56,57], a polycrystalline film of any biological fluid can be represented as a sequence of partial layers with linear and circular birefringence $LB_{(0.90);(45,135)}$, $CB_{\otimes,\oplus}$. These biological layers include several optically anisotropic components— $LB_{0.90}$, $LB_{45,135}$ —“linear birefringence”; $CB_{\otimes,\oplus}$ —“circular birefringence” for linearly $0^\circ \div 90^\circ$ and $45^\circ \div 135^\circ$ circularly right ($\otimes$) and left ($\oplus$) polarized orts.

The linear birefringence (structural anisotropy $LB_{(0.90);(45,135)}$) mechanisms are inherent in the dendrite polycrystalline networks, which are formed by needle-like crystals. Spherulite crystal’s molecular complexes have optical activity $CB_{\otimes,\oplus}$.

A generalized Jones matrix analytical form of polycrystalline medium with complex anisotropy was found in [57]

$$(J) = \begin{pmatrix} j_{11} & j_{12} \\ j_{21} & j_{22} \end{pmatrix} = \begin{pmatrix} \cos 0.5|V| - i \frac{LB_{0.90}}{|V|} \sin 0.5|V| & \frac{(CB_{\otimes,\oplus} - iLB_{45,135})}{|V|} \sin 0.5|V| \\ -\frac{(CB_{\otimes,\oplus} + iLB_{45,135})}{|V|} \sin 0.5|V| & \cos 0.5|V| + i \frac{LB_{0.90}}{|V|} \sin 0.5|V| \end{pmatrix} \quad (1)$$

where j_{pk} —elements of the Jones matrix; “ i ” is the imaginary unit; V is the complex vector of generalized anisotropy, which includes the parameters of linear $LB_{0;90}$, $LB_{45;135}$ and circular $CB_{\otimes;\oplus}$ birefringence; $| \cdot |$ —modulus of a complex number

$$V = V(LB_{0;90}, LB_{45;135}; -CB_{\otimes;\oplus}) \quad (2)$$

from (2), (3), we obtain a vector modulus V explicit form

$$|V| = \left((LB_{0;90}^2) + (LB_{45;135}^2) + (CB_{\otimes;\oplus}^2) \right)^{0.5} = \left((LB^2 + CB^2) \right)^{0.5} \quad (3)$$

where $LB = \left(LB_{0;90}^2 + LB_{45;135}^2 \right)^{0.5}$; $CB_{\otimes;\oplus}^2 \equiv CB^2$.

The generalized Jones matrix (J) (1) elements calculating algorithm includes the polycrystalline film sample irradiation by linearly polarized beams with azimuths 0^0 (Jones vector $\begin{pmatrix} 1 \\ 0 \end{pmatrix}$) and 90^0 (Jones vector $\begin{pmatrix} 0 \\ 1 \end{pmatrix}$)

$$\begin{aligned} U^0 &= \begin{pmatrix} U_x^0 \\ U_y^0 \end{pmatrix} = \begin{pmatrix} |U_x^0| \exp(\varphi_x^0) \\ |U_y^0| \exp(\varphi_y^0) \end{pmatrix} = \begin{pmatrix} j_{11} & j_{12} \\ j_{21} & j_{22} \end{pmatrix} \begin{pmatrix} 1 \\ 0 \end{pmatrix} \Rightarrow \begin{pmatrix} j_{11} \\ j_{21} \end{pmatrix} \\ &\Rightarrow \begin{cases} U_x^0 = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix} \begin{pmatrix} j_{11} \\ j_{12} \end{pmatrix} \Rightarrow j_{11}; \\ U_y^0 = \begin{pmatrix} 0 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} j_{11} \\ j_{12} \end{pmatrix} \Rightarrow j_{21}; \end{cases} \end{aligned} \quad (4)$$

$$\begin{aligned} U^{90} &= \begin{pmatrix} U_x^{90} \\ U_y^{90} \end{pmatrix} = \begin{pmatrix} |U_x^{90}| \exp(\varphi_x^{90}) \\ |U_y^{90}| \exp(\varphi_y^{90}) \end{pmatrix} = \begin{pmatrix} j_{11} & j_{12} \\ j_{21} & j_{22} \end{pmatrix} \begin{pmatrix} 0 \\ 1 \end{pmatrix} \Rightarrow \begin{pmatrix} j_{12} \\ j_{22} \end{pmatrix} \\ &\Rightarrow \begin{cases} U_x^{90} = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix} \begin{pmatrix} j_{12} \\ j_{22} \end{pmatrix} \Rightarrow j_{21}; \\ U_y^{90} = \begin{pmatrix} 0 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} j_{12} \\ j_{22} \end{pmatrix} \Rightarrow j_{22}. \end{cases} \end{aligned} \quad (5)$$

Here, U^0 and U^{90} —Jones vectors of linearly polarized illuminating beams in azimuths 0^0 and 90^0 ; U_x^0 ; U_y^0 and U_x^{90} ; U_y^{90} —orthogonal components of complex amplitudes of vectors U^0 and U^{90} ; their modulus $|U_x^0|$; $|U_y^0|$; $|U_x^{90}|$; $|U_y^{90}|$ and phases φ_x^0 ; φ_y^0 ; φ_x^{90} ; φ_y^{90} .

Based on (1)–(5), theoretical interconnection between the linear and circular birefringence-dichroism parameters and optically anisotropic layer Jones matrix (J) elements were obtained

$$|V| = 2 \arccos[0.5(Re j_{11} + Re j_{22})] \quad (6)$$

$$\begin{cases} LB = \frac{|V|}{2 \sin 0.5|V|} \left((Im j_{22} - Im j_{11})^2 + (Im j_{12} + Im j_{21})^2 \right)^{0.5}; \\ CB_{\otimes;\oplus} = \frac{|V|}{2 \sin 0.5|V|} (Im j_{12} - Im j_{21}). \end{cases} \quad (7)$$

Here, Re and Im —real and complex parts of Jones matrix elements j_{pk} .

As a result, we derive the following equation for the Jones matrix tomography of the polycrystalline structure of the biological fluid film

$$|V| = 2 \arccos \left[0.5 \left(|U_x^{90}| \exp(i\varphi_x^{90}) + |U_y^{90}| \exp(i\varphi_y^{90}) \right) \right] \quad (8)$$

$$\left\{ \begin{array}{l} LB = \frac{|V|}{2\sin 0.5|V|} \times \\ \left(\left(|U_y^{90}| \sin \varphi_y^{90} - |U_x^0| \sin \varphi_x^0 \right)^2 + \left(|U_y^0| \sin \varphi_y^0 - |U_x^{90}| \sin \varphi_x^{90} \right)^2 \right)^{0.5}; \\ CB_{\otimes;\oplus} = \frac{|V|}{2\sin 0.5|V|} \left(|U_y^0| \sin \varphi_y^0 - |U_x^{90}| \sin \varphi_x^{90} \right). \end{array} \right. \quad (9)$$

In what follows, the Jones-matrix reconstructed Equations (8) and (9) coordinate distributions of the linear LB and circular $CB_{\otimes;\oplus}$ birefringence within a set of pixels (m, n) of a digital camera will be called phase anisotropy theziograms $JT(m, n)$

$$JT(m, n) = \begin{pmatrix} LB \\ CB \end{pmatrix} \begin{pmatrix} Rej_{pk} \\ Rej_{pk} \end{pmatrix} (m, n). \quad (10)$$

2.1.2. Multifractal Scanning

As noted previously [46,48–51], fractality is inherent in geometric structures and various processes that exhibit scale-like distributions (fractal measures). In our case, this applies to the theziograms of biological fluid facies $JT(m, n)$.

From the fractal's theory, it is known that such measures $JT(m, n)$ can be fractal JT^{h_r} or multifractal $JT^{F(h_r)}$. Here h_r —fractal dimension; $F(h_r)$ —spectrum of fractal dimensions.

For fractal distributions JT^{h_r} , the one dimension $h_r \equiv h_0$ concepts are introduced. Multifractal distributions $JT^{F(h_r)}$ are characterized by a fractal dimension h_r set or a singularities spectrum $F(h_r)$.

To calculate the fractal dimensions h_r , a specific approach is employed, which involves the introduction of partial functions or a generalized statistical sum

$$Z(r, d) = \sum_{s=1}^{P(d)} JT_s^r(d) \quad (11)$$

where $P(d)$ —multifractal distribution coating elements JT_s^r number; $r \in R$.

As a rule, the dependence described by Equation (11) exhibits a stepwise character

$$Z(r, d) \sim d^{(r-1)h_r} \quad (12)$$

where h_r —generalized fractal dimension, which for the case of the partial function is written as scanning exponents

$$\tau(r) = (r - 1)h_r \quad (13)$$

Here, the exponent $(r - 1)$ is introduced into the exponent to automatically fulfill the equality $Z(1, d) = 1$, which represents the normalization conditions for the distribution $JT_s^r(d)$.

In particular, for monofractals $\tau(r) = \text{const}$.

For more complex scale-like distributions, (13) is transformed into a specific multifractal spectrum $F(h_r)$.

For dependence $F(h_r)$ analytical determination of the wavelet transform modules maxima (WTMM) method [58–61] is used.

WTMM method includes two steps:

The $JT(m, n)$ theziograms wavelet transformation $W(a, b)$ and the skeleton $\sup |W(a^*, x_i(a^*))|$ determination—the maximum modulus local surface extremes values wavelet coefficients $W(a, b)$ lines for scanning soliton-like function $\Psi(b)$ each scale a .

Wavelet coefficient modules $Z(r, d, \sup |W(a^*, x_i(a^*))|)$ local maxima partial functions construction and fractal dimension spectrum $F(h_r)$ determination.

The wavelet analysis of the theziograms $JT(m, n)$ (Equation (9)) is based on an analytical transformation that involves decomposing the distribution over a basis constructed from a soliton-like function (wavelet), using large-scale changes and translations.

The following equation defines the function $JT(x)$ continuous wavelet transforms

$$W(a, b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} JT(x) M\left(\frac{x-b}{a}\right) dx \quad (14)$$

where a is a scale parameter, b is a spatial coordinate, and M is a soliton-like function (wavelet) constructed on the Gaussian function derivative basis.

In our work, the second derivative ($m = 2$) or “Mexican hat” (MHAT) wavelet is used

$$M^{(m)} = (-1)^m \frac{\partial^m}{\partial x^m} \left[\exp\left(\frac{x^2}{2}\right) \right] \Rightarrow M^{(2)} = \frac{\partial^2}{\partial x^2} \left[\exp\left(\frac{x^2}{2}\right) \right] \quad (15)$$

The wavelet Equations (14) and (15) for linear and circular birefringence theziograms (9) can be written as the following equations

$$\begin{cases} W^{LB}(a, b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} LB\left(Im(j_{pk}); (a, x)\right) M\left(\frac{x-b}{a}\right) dx; \\ W^{CB}(a, b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} CB\left(Im(j_{pk}); (a, x)\right) M\left(\frac{x-b}{a}\right) dx. \end{cases} \quad (16)$$

In the expanded form, (16) takes the form

$$W^{LB}(a, b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} \left\{ \frac{|V|}{2\sin 0.5|V|} ((Imj_{22} - Imj_{11})^2 + (Imj_{12} + Imj_{21})^2)^{0.5}(\alpha, x) \right\} M\left(\frac{x-b}{a}\right) dx; \quad (17)$$

$$W^{CB}(a, b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} \left\{ \frac{|V|}{2\sin 0.5|V|} (U_y^0 \sin \varphi_y^0 - U_x^0 \sin \varphi_x^0) \right\} (a, x) M\left(\frac{x-b}{a}\right) dx. \quad (18)$$

Analysis of relations (16)–(18) shows that the wavelet decomposition of the theziograms of optical anisotropy of biological fluid facies is a superposition of fractal or multifractal measures $JT_s^r(d)$ of supramolecular polycrystalline networks with linear and circular birefringence—(11).

In the future, we will focus on finding the possibility of determining the fractal dimensions (13) characterizing $JT_s^r(d)$, based on the use of skeletons $\sup|W(a^*, x_i(a^*))|$.

This analytical procedure is based on the partial function’s construction using the following equation

$$Z(r, d) = \sum_{l \in L(a)} (\sup|W(a^*, x_s(a^*))|)^r \quad (19)$$

According to [62,63], the following dependence $Z(r, d) \sim d^{\tau(r)}$ holds, where the fractal dimension $\tau(r)$ for some r is determined by setting the scanning exponent $\frac{\ln Z(r, d)}{\ln d}$ dependence slope.

Variation of r in construction $\sum_{l \in L(a)} (\sup|W(a^*, x_i(a^*))|)^r$ allows one to obtain:

For fractal distributions, $JT_s^r(d)$ line dependences $\tau(r)$, $-(h_r = \frac{d\tau}{dr} = \text{const})$;

For multifractal distributions, $JT_i^r(d)$ has no line dependences $\tau(r) = rh - D(h)$ with fractal dimensions $h_r = \frac{d\tau}{dr}$ considerable number, which characterized the multifractal spectrum $F(h_r)$.

In our case, we will study the multifractal spectra of JT theziograms based on the partial functions $Z(r, d, \sup|W(a^*, x_i(a^*))|)$ wavelet maximal modules amplitudes skeletons $\sup|W(a^*, x_i(a^*))|$ for two optical anisotropy mechanisms for blood plasma facies—linear ($F^{LB}(h_r)$) and circular ($F^{CB}(h_r)$) birefringence.

2.2. The Experimental Setup and Measurement Methodology

A Mach–Zehnder polarization interferometry scheme [52–55] of the Jones-matrix mapping is shown in Figure 1.

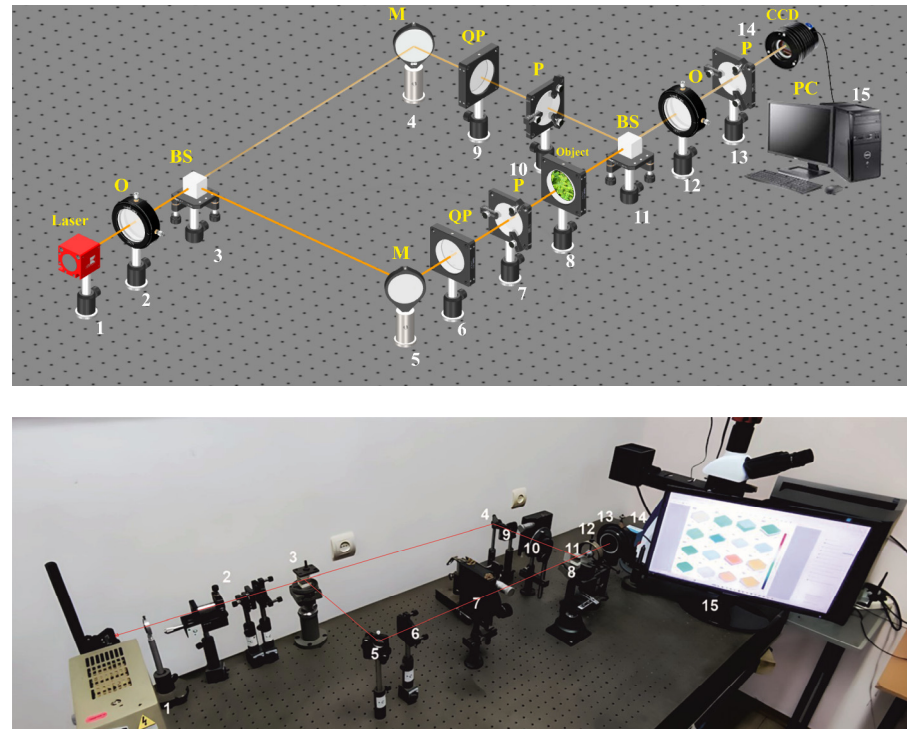


Figure 1. Polarization-interference optical scheme for Jones-matrix mapping. 1—He-Ne laser; 2—collimator—“O”; 3, 11—beam splitters—“BS”; 4, 5—mirrors—“M”; 7, 10, 13—polarizer’s “P”; 6, 9—quarter wave plates—“QP”; 8—object; 12—polarization objective—“O”; 14—digital camera—“CCD”; 15—personal computer—“PC”.

Parallel ($\varnothing = 5 \times 10^3 \mu\text{m}$) beam of He-Ne ($\lambda = 0.6328 \mu\text{m}$) laser 1, formed by spatial-frequency filter 2, with 50% beam splitter 3 is divided into “object” and “reference” ones.

The “object” beam with the help of a rotating mirror 5 is directed through the polarizing filter 6–7 (manufacturer—Achromatic True Zero-Order Waveplate and manufacturer—B + W Kaesemann XS-Pro Polarizer MRC Nano) in the direction of the **BPF** layer 8 sample. The polarization-inhomogeneous image of **BPF** 8 is projected by the strain-free objective 12 (manufacturer—Nikon CFI Achromat P, Nikon Instruments Inc., Melville, NY, USA, focal length—30 mm, numerical aperture—0.1, magnification—4 $\times$) into the digital camera 14 (The Imaging Source DMK 41AU02. AS, monochrome 1/2 “CCD, Sony ICX205AL (progressive scan) resolution—1280 $\times$ 960, size of the photosensitive area—7600 $\times$ 6200 μm ; sensitivity—0.05 lx; dynamic range—8 bit, SNR—9 bit), the photosensitive area of which contains $m \times n = 1280 \times 960$ pixels) plane.

The “reference” beam is directed by the mirror 4 through the polarization filter 9–10 (manufacturer—Achromatic True Zero-Order Waveplate and manufacturer—B + W Kaesemann XS-Pro Polarizer MRC Nano) into the polarization image plane of **BPF** 8.

As 50 measurements result for each object, the optical anisotropy errors were determined $\Delta T = 5 \times 10^{-5}$ rad.

The Jones matrix measurement is based on algorithms (4) and (5), which involve four polarization measurements. The main feature and functional advantage, compared to the known interference technique [63], is the ability to obtain a series of layer-by-layer Jones matrix images of volumetrically inhomogeneous polycrystalline BPFs using 3D digital holographic scanning [55–58].

The linear polarizations of two states are sequentially formed in the “irradiating” (*Ir*) and “reference” (*Ref*) parallel laser beams— $Ir(0^0) - Ref(0^0)$ и $Ir(90^0) - Ref(90^0)$.

For polarization states (0^0 and 90^0), two partial interference patterns are recorded through the polarizer-analyzer 14 with the transmission plane orientation at angles $\Omega = 0^0$; and $\Omega = 90^0$.

For each partial interference distribution $I_{\Omega=0^0;90^0}(m, n)$, we perform a two-dimensional discrete Fourier transform $\Phi(v, v)$, where v, v —spatial frequencies for the m and n directions of the photosensitive area of the digital camera pixels [25,26]:

$$\begin{cases} j_{11} \equiv \Phi_x^0 = \frac{1}{M \times N} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} U_x^0(m, n) (U_x^0)^* \times (m, n) \exp \left[-i2\pi \left(\frac{m \times v}{M} + \frac{n \times v}{N} \right) \right]; \\ j_{12} \equiv \Phi_y^0 = \frac{1}{M \times N} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} U_y^0(m, n) (U_y^0)^* \times (m, n) \exp \left[-i2\pi \left(\frac{m \times v}{M} + \frac{n \times v}{N} \right) \right]; \\ j_{21} \equiv \Phi_x^{90} = \frac{1}{M \times N} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} U_x^{90}(m, n) (U_x^{90})^* \times (m, n) \exp \left[-i2\pi \left(\frac{m \times v}{M} + \frac{n \times v}{N} \right) \right]; \\ j_{22} \equiv \Phi_y^{90} = \frac{1}{M \times N} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} U_y^{90}(m, n) (U_y^{90})^* \times (m, n) \exp \left[-i2\pi \left(\frac{m \times v}{M} + \frac{n \times v}{N} \right) \right] \end{cases} \quad (20)$$

The digital Fourier transforms (20) of Jones matrix theziograms $JT(m, n) = \begin{pmatrix} LB(Rej_{pk}) \\ CB(Rej_{pk}) \end{pmatrix}$ taking into account algorithms (9), can be rewritten in the following form

$$Im \begin{cases} j_{11} \equiv \Phi_x^0 = \frac{1}{M \times N} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} U_x^0(m, n) (U_x^0)^* \times (m, n) \sin \left(\frac{m \times v}{M} + \frac{n \times v}{N} \right); \\ j_{12} \equiv \Phi_y^0 = \frac{1}{M \times N} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} U_y^0(m, n) (U_y^0)^* \times (m, n) \sin \left(\frac{m \times v}{M} + \frac{n \times v}{N} \right); \\ j_{21} \equiv \Phi_x^{90} = \frac{1}{M \times N} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} U_x^{90}(m, n) (U_x^{90})^* \times (m, n) \sin \left(\frac{m \times v}{M} + \frac{n \times v}{N} \right); \\ j_{22} \equiv \Phi_y^{90} = \frac{1}{M \times N} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} U_y^{90}(m, n) (U_y^{90})^* \times (m, n) \sin \left(\frac{m \times v}{M} + \frac{n \times v}{N} \right), \end{cases} \quad (21)$$

where $\Phi_x^0; \Phi_y^0$ and $\Phi_x^{90}; \Phi_y^{90}$ —digital Fourier transforms of complex amplitude orthogonal components $U_{x,y}^{0,90}$ for different orientation $\Omega = 0^0$; $\Omega = 90^0$; “*”—denotes the complex conjugation operation; (v, v) are the spatial frequencies and $(M = 1120; N = 960)$ are the CCD camera pixel quantities

The results of the digital Fourier transforms (21) are used to obtain complex amplitude distributions according to the following algorithms.

$$\begin{cases} U_{0^0} \rightarrow |U_x^0(\Omega = 0^0)|; \\ U_{90^0} \rightarrow |U_x^{90}(\Omega = 90^0)| \exp(i(\varphi_x^{90} - \varphi_x^0)); \end{cases} \quad (22)$$

$$\begin{cases} U_{0^0} \rightarrow |U_y^0(\Omega = 0^0)|; \\ U_{90^0} \rightarrow |U_y^{90}(\Omega = 90^0)| \exp(i(\varphi_y^{90} - \varphi_y^0)). \end{cases} \quad (23)$$

By reconstructed field complex amplitudes (22) and (23) stepwise ($\Delta\varphi$) phase (φ_k) scanning means using algorithms (9), we obtain Jones matrix theziograms

$$JT = \begin{pmatrix} LB \\ CB \end{pmatrix} \left(Rej_{pk} \right) (\varphi_k, m, n).$$

For all theziograms $JT = \begin{pmatrix} LB \\ CB \end{pmatrix} \left(Rej_{pk} \right) (\varphi_k, m, n)$ we apply the wavelet schedule $W^{LB}(a, b)$ i $W^{CB}(a, b)$ (17) and (18).

We determine the wavelet amplitudes maxima modules skeletons $\sup |W(a^*, x_j(a^*))|$ for blood plasma facies optical anisotropy theziograms, which serve as the basis for linear ($F^{LB}(h_r)$) and circular ($F^{CB}(h_r)$) birefringence calculating multifractal spectra by the **WTMM** method, $-Z(r, d, \sup |W(a^*, x_j(a^*))|) \iff \frac{\ln Z(r, d)}{\ln d}$.

The Jones matrix theziograms $JT(m, n)$ and multifractal spectra $(F(h_r))_j$ resulting set were analyzed with a statistical approach using the following algorithms to calculate the mean (Z_1), dispersion (Z_2), skewness (Z_3), and kurtosis (Z_4) [16–27]

$$\begin{pmatrix} Z_1 = \frac{1}{K} \sum_{j=1}^K (JT_j); \\ Z_2 = \sqrt{\frac{1}{K} \sum_{j=1}^K (JT_j^2)}; \\ Z_3 = \frac{1}{Z_2^3} \frac{1}{K} \sum_{j=1}^K (JT_j^3); \\ Z_4 = \frac{1}{Z_2^4} \frac{1}{K} \sum_{j=1}^K (JT_j^4), \end{pmatrix} \quad (24a)$$

$$\begin{pmatrix} Z_1 = \frac{1}{K} \sum_{j=1}^K (F(h_r))_j; \\ Z_2 = \sqrt{\frac{1}{K} \sum_{j=1}^K (F(h_r))_j^2}; \\ Z_3 = \frac{1}{Z_2^3} \frac{1}{K} \sum_{j=1}^K (F(h_r))_j^3; \\ Z_4 = \frac{1}{Z_2^4} \frac{1}{K} \sum_{j=1}^K (F(h_r))_j^4, \end{pmatrix}. \quad (24b)$$

where $K = M \times N$ —CCD pixel quantity.

2.3. Objects of Investigations

In our work, we will consider two types of blood plasma facies:

Blood plasma films (**BPF1**) without COVID-19 history (50 samples)—healthy donors (24 men and 26 women aged 18 to 63 years)—control group 1.

Blood plasma films (**BPF2**) from people who had COVID-19 one year ago (50 samples) (27 men and 23 women aged 19 to 65 years)—study group 2.

The choice of such objects is motivated by both fundamental and applied aspects.

Fundamental—during the blood plasma facies dehydration process and molecular self-assembly, polycrystalline networks with various architectonics and optical anisotropy are formed. The data obtained on the scale-self-similar optical properties of such networks can be used to establish physical and quantitative relationships between the topology of optical anisotropy maps and the spatial-angular structure specifics of biological crystals [22,31,32].

Applied—quantitative parameters (1st–4th orders statistical moments), which characterize the Jones matrix theziograms $\begin{pmatrix} LB \\ CB \end{pmatrix} \left(Rej_{pk} \right) (m, n)$ multifractal spectra $F(h_r)$, can be used as markers for COVID-19 remote consequences differential diagnosis.

Blood plasma is a heterogeneous liquid with a complex structure, consisting of a heterogeneous colloidal polymer solution. Traditionally, the molecular components of blood plasma (albumin monomers (~60%), globulin monomers (~40%), fibrinogen, and hemoglobin) are effectively studied using biochemical methods. However, there is currently

a lack of effective research methods to study the supramolecular optically anisotropic protein structures (dimers, trimers, monomers) in blood plasma, which range in size from 100 nm to 2000 nm [39].

Three zones of different thicknesses L are distinguished in the blood plasma surface structure:

Edge (polycrystalline albumin layer with linear birefringence and dichroism, $L \sim 50 \mu\text{m}$ – $60 \mu\text{m}$).

Transitional (outer and inner layers of optically isotropic cubic crystals of Na-Cl salt, intermediate globulin layer with circular birefringence and dichroism, $L \sim 25 \mu\text{m}$ – $30 \mu\text{m}$).

The central (outer layer of cubic crystals of salt Na-Cl, $L \sim 5 \mu\text{m}$ – $15 \mu\text{m}$).

Such an image of plasma binding primarily exhibits a volumetrically inhomogeneous dendritic supramolecular polycrystalline network with structural anisotropy (LB) and minimal optical activity (CB).

Blood plasma samples were obtained through wedge dehydration. Blood was collected into a dry, clean test tube with a volume of 5 mL to obtain serum. The blood was then centrifuged for 30 min at 1000 revolutions per minute. A 10 μL sample of the obtained serum was applied to a specially prepared defatted slide, positioned horizontally. Drying occurred at a constant temperature of 24 °C and a relative humidity of 65%. During the drying process, the slide remained motionless in a strictly horizontal position, with no air movement in the surrounding environment. Jones-matrix assessment of the structure-forming elements was performed after 24 h.

The **BPF** optical-geometric parameters are presented in Table 1.

Table 1. BPF optical-geometric parameters.

BPF1	
Parameters	
Attenuation (extinction) coefficient τ, cm^{-1}	0.28 ± 0.016
Depolarization degree $\Lambda, \%$	16 ± 0.13
Facies diameter D, mm	5.5 ± 0.27
BPF2	
Parameters	
Attenuation (extinction) coefficient τ, cm^{-1}	0.39 ± 0.022
Depolarization degree $\Lambda, \%$	24 ± 0.15
Facies diameter D, mm	5.5 ± 0.27

The blood plasma facies samples extinction coefficient (τ, cm^{-1}) was measured according to the standard photometry illuminating beam intensity attenuation method [61] using an integral light-scattering sphere [62].

The commensurability of the diameters of the blood plasma facies samples D (Table 1) and the illuminating (coordinately homogeneous) single-mode laser beam $\varnothing$ (Figure 1) ensures the “stability” of the array of measurements of the distributions of the Jones matrix elements and the reconstruction of the optical anisotropy theziograms.

The integral depolarization degree ($\Lambda, \%$) of the blood plasma facies samples was measured using a convenient laser polarimeter setup with a classic photodetector. The results showed a certain level of depolarized background, ranging from $\Lambda \sim 16\%$ to 24% , in the object fields of the samples BPF1 and BPF2. As previously noted, for coherent scattered fields, it is not the “destruction” of polarization that occurs, but rather the presence of a polarization structure—specifically, the distributions of azimuths and ellipticities of a set of fully 100% polarized speckles [41,42]. Therefore, the measured depolarized background

level is the result of statistical (integral) averaging of various polarization states across the photodetector's area. Two important consequences follow from this:

The possibility of using the Jones-matrix formalism is based on analyzing the transformation of completely polarized coherent radiation (in our case, individual speckles) by BPF samples. This approach is relevant for phase scanning of the reconstructed field of complex amplitudes (relations (20)–(23)) and for selecting Jones matrix images that correspond to the single scattering component of the polycrystalline architecture of BPF supramolecular networks.

Representative sample number sampling to determine the statistical significance by the cross-validation method [63]. The standard deviation σ^2 for all the statistical moments $Z_{i=1;2;3;4}(n)$ was determined. The specified sample number (50 for each group) provided the level $\sigma^2 \leq 0.025$. This standard deviation corresponds to a confidence interval of $p < 0.05$, which demonstrates the Jones-matrix mapping and **WTMM** method's statistical reliability.

3. Results and Discussion

This section presents the results of the BPF1 and BPF2 theziograms, as well as comparative statistical and multifractal analysis.

At the first stage, we performed the traditional statistical analysis of **BPF1** (Figure 2, Table 2) and **BPF2** (Figure 3, Table 3) algorithmically reconstructed theziograms

$$JT = \begin{pmatrix} LB \\ CB \end{pmatrix} \left(Rej_{pk} \right) (\varphi_k, m, n).$$

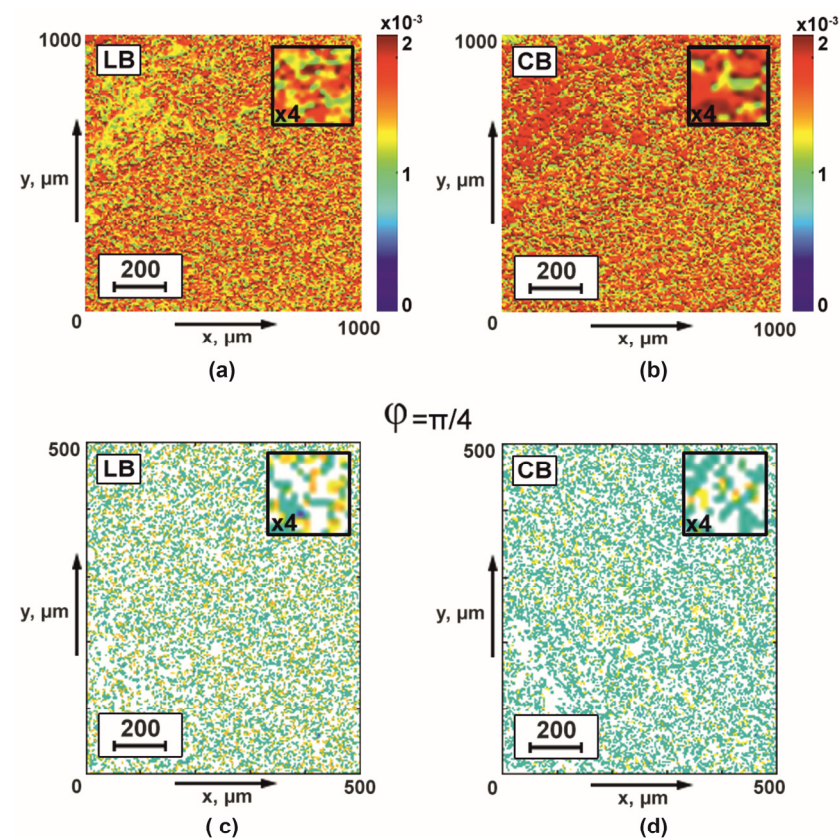


Figure 2. Cont.

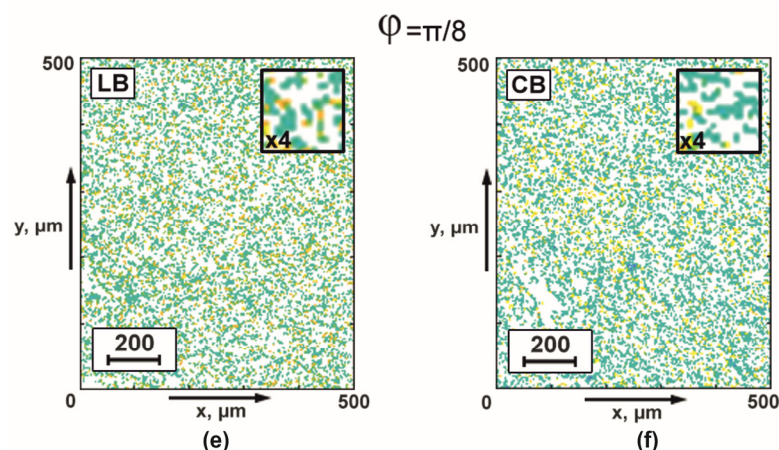


Figure 2. Jones-matrix reconstructed integral (a,b), layer-by-layer (c–f) theziograms of phase anisotropy $JT = \begin{pmatrix} LB \\ CB \end{pmatrix} \begin{pmatrix} Rej_{pk} \\ Rej_{pk} \end{pmatrix}$ coordinate distributions of linear birefringence (LB) (a,c,e) and circular birefringence (CB) (b,d,f) of the supramolecular networks of the **BPF1** sample.

Table 2. The 1st–4th orders central statistical moments that characterize the **BPF1** phase anisotropy maps JT .

JT	LB	CB
$Z_1 \times 10^{-3}$	1.21 ± 0.077	1.03 ± 0.059
$Z_2 \times 10^{-3}$	0.22 ± 0.014	0.18 ± 0.011
Z_3	0.34 ± 0.019	0.42 ± 0.023
Z_4	0.48 ± 0.028	0.51 ± 0.028
$\varphi_k = \frac{\pi}{4}$		
$Z_1 \times 10^{-3}$	1.09 ± 0.058	0.94 ± 0.052
$Z_2 \times 10^{-3}$	0.17 ± 0.009	0.15 ± 0.008
Z_3	0.42 ± 0.025	0.51 ± 0.027
Z_4	0.54 ± 0.029	0.63 ± 0.024
$\varphi_k = \frac{\pi}{8}$		
$Z_1 \times 10^{-3}$	0.95 ± 0.052	0.89 ± 0.049
$Z_2 \times 10^{-3}$	0.14 ± 0.008	0.12 ± 0.007
Z_3	0.53 ± 0.029	0.62 ± 0.037
Z_4	0.64 ± 0.035	0.73 ± 0.039

From JT (Figure 2, Table 2 and Figure 3, Table 3) statistical analysis, we found that all linear and circular birefringence distributions are different from Gaussian—all central statistical moments are different from zero.

In all phase planes (Tables 2 and 3), insignificant differences were found between the central statistical moment's values that characterize theziograms $JT = \begin{pmatrix} LB \\ CB \end{pmatrix} \begin{pmatrix} Rej_{pk} \\ Rej_{pk} \end{pmatrix} (\varphi_k, m, n)$.

The maximum differences do not exceed 35% to 40%.

Thus, it can be stated that the **BPF1** and **BPF2** phase anisotropy distribution statistical analysis sensitivity was not high enough.

At the second stage, to analyze the phase (LB,CB) anisotropy parameter topographic distributions, we applied the fractal dimension (h_r) method, which was well-tested in previous studies [21–24,27,33,34]. This method is based on determining the slope angles (θ) of approximating curves ($H(\theta)$) linear sections in power spectra (PD) logarithmic dependencies $\ln(PD(JT(m, n))) - \ln L^{-1}$ for theziogram $JT(m, n)$.

The fractal analysis of **BPF1** theziogram results are shown in Figure 4— JT^{LB} (fragment (1)) and JT^{CB} (fragment (4)).

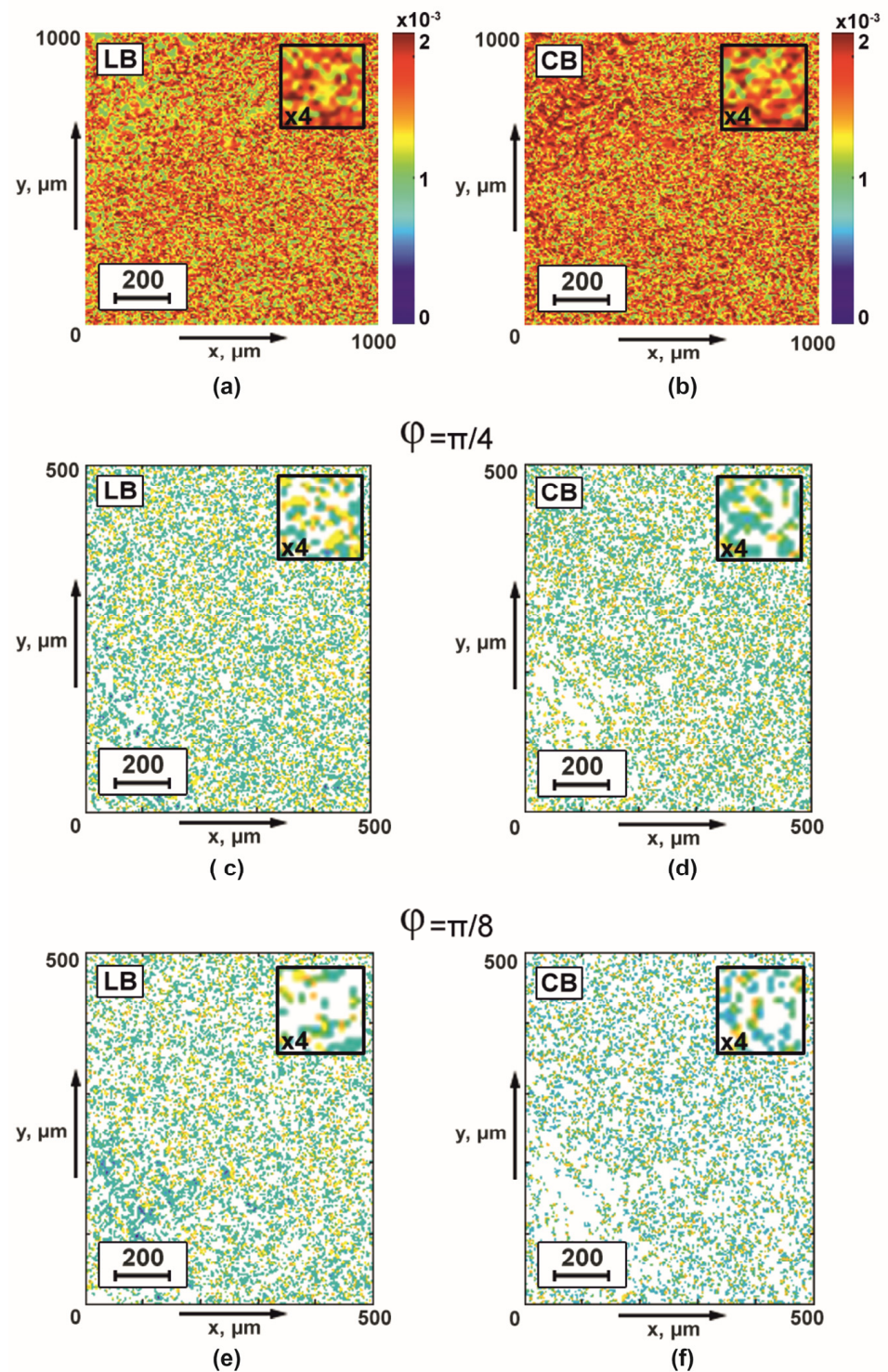
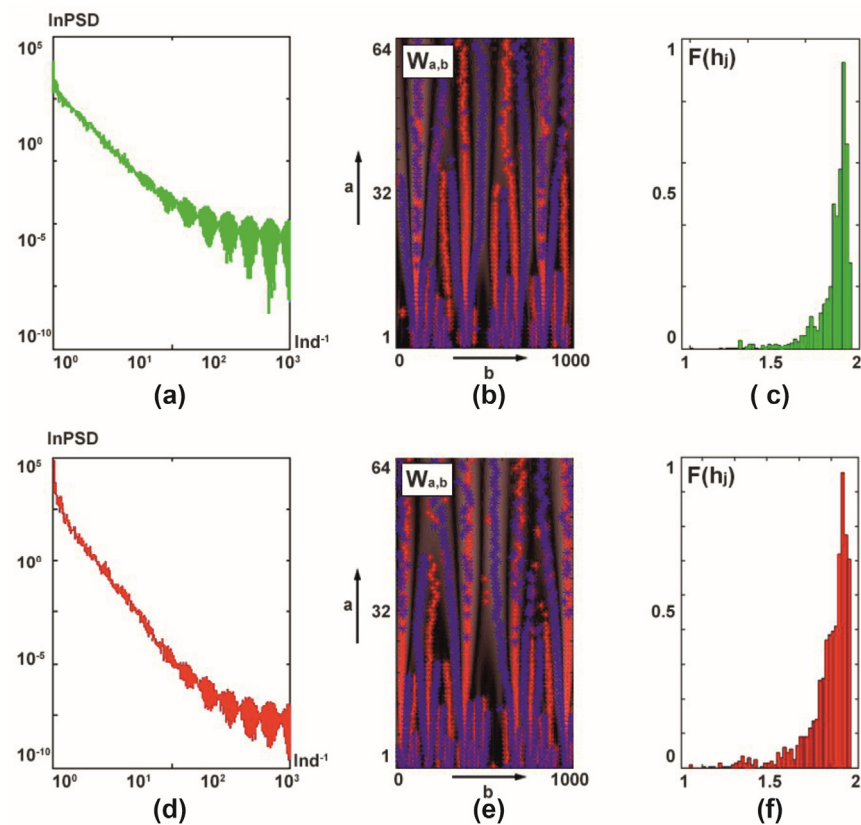


Figure 3. Jones-matrix reconstructed integral (a,b), layer-by-layer (c–f) theziograms of phase anisotropy $T = \begin{pmatrix} LB \\ CB \end{pmatrix} \begin{pmatrix} Rej_{pk} \\ Rej_{pk} \end{pmatrix}$ coordinate distributions of linear birefringence (LB) (a,c,e) and circular birefringence (CB) (b,d,f) of the supramolecular networks of the **BPF2** sample.

Table 3. The 1st–4th orders central statistical moments that characterize the **BPF2** phase anisotropy maps JT .

JT	LB	CB
$Z_1 \times 10^{-3}$	1.12 ± 0.068	1.23 ± 0.071
$Z_2 \times 10^{-3}$	0.19 ± 0.011	0.24 ± 0.014
Z_3	0.39 ± 0.022	0.34 ± 0.019
Z_4	0.54 ± 0.029	0.45 ± 0.025
$\varphi_k = \frac{\pi}{4}$		
$Z_1 \times 10^{-3}$	0.99 ± 0.054	1.14 ± 0.069
$Z_2 \times 10^{-3}$	0.15 ± 0.008	0.21 ± 0.012
Z_3	0.48 ± 0.027	0.44 ± 0.027
Z_4	0.63 ± 0.035	0.53 ± 0.029
$\varphi_k = \frac{\pi}{8}$		
$Z_1 \times 10^{-3}$	0.91 ± 0.048	0.98 ± 0.058
$Z_2 \times 10^{-3}$	0.11 ± 0.006	0.12 ± 0.007
Z_3	0.65 ± 0.036	0.56 ± 0.031
Z_4	0.76 ± 0.041	0.67 ± 0.036

**Figure 4.** Power spectra logarithmic dependences (fragments (a,d)); wavelet transform module maxima skeletons (fragments (b,e)) and multifractal spectra of **BPF1** phase anisotropy theziograms (fragments (c,f)).

Analysis of the obtained data (Figure 4) revealed a monotonous decrease in the $\ln(PD(JT^{LB,CB}) - \ln L^{-1})$ dependencies over the entire size L_i range changes in **BPF1** structural elements $JT^{LB,CB}$.

Linear plots with different inclination ($\vartheta_i \approx const$) angles to $\ln(PD(JT^{LB,CB}) - \ln L^{-1})$ were found, which indicates a complex, generally speaking, multifractal structure of $JT^{LB,CB}$ theziograms.

From a physical point of view, this $\ln(PD(JT^{LB,CB}) - \ln L^{-1})$ structure can be related to the fact that each fractal measure in the distributions $JT^{LB,CB}(m, n)$ corresponds to a

certain (partial) scale-self-like (with dimension h_r within $L_{min} \leq L_i \ll L_{max}$) set of the **BPF1** biological crystals. Such partial polycrystalline networks are gradually formed during the blood plasma drop dehydration.

Conventionally, there are several main (structural) stages in this process:

The first is rudimentary or “prefractal”. The small-scale ($2 \mu\text{m} \leq L_{i(min)} \leq 10 \mu\text{m}$) molecular domains crystallization process occurs. Such measure’s topographic structure is $JT^{LB}(L_{i(min)})$ (albumin molecules crystallites) and circular $JT^{CB}(L_{i(min)})$ (globulin molecules crystallites). This fact is indicated by the absence of a stable inclination angle of approximating curve $H(\vartheta)$ to the distributions $\ln(PD(JT^{LB,CB}) - \ln L^{-1}$ —Figure 4.

The second is intermediate or “quasi-fractal” **BPF1** crystallite molecular birefringence domains are sequentially combined into larger ($20 \mu\text{m} \leq L_{i(middle)} \leq 200 \mu\text{m} \div 400 \mu\text{m}$) spatially structured needle crystals networks. Thus, a birefringence theziograms $JT^{LB,CB}(h_r, L_{i(middle)})$ scale-self-like (h_r) measure set is formed. These processes in **BPF1** polycrystalline self-assembly illustrate linear slope plots approximating $H(\vartheta)$ dependences $\ln(PD(JT^{LB,CB}) - \ln L^{-1}$ —Figure 4.

The third is final or “multifractal”. The local fractal measure set that form biological crystals theziograms $JT^{LB,CB}(L_{i(middle)})$ is combined into a single macroscale ($200 \mu\text{m} \div 400 \mu\text{m} \leq L_{i(max)} \leq 1000 \mu\text{m}$) supramolecular **BPF1** network. The structural element size corresponding range in coordinate distributions $JT^{LB,CB}(L_{i(max)})$ has the fractal structure—dependence $\ln(PD(JT^{LB,CB}) - \ln L^{-1}$ is characterized by a single slope angle (ϑ_i) $\left\{ \begin{array}{l} h_1(LB, L_{i(max)}) \iff \vartheta_1(LB, L_{i(max)}) = const; \\ h_2(CB, L_{i(middle)}) \iff \vartheta_2(CB, L_{i(max)}) = const. \end{array} \right.$

The dependence $\ln(PD(JT^{LB,CB}) - \ln L^{-1}$ oscillation presence may be because, in the blood plasma drop dehydration process, molecular complexes with statistically distributed birefringence parameters are formed.

Therefore, it can be stated that the **BPF1** polycrystalline network self-assembly process leads to the predominant multifractal supramolecular optically anisotropic network structure formation. This **BPF1** structure consists of optical anisotropy $JT^{LB,CB}(L_i, h_r = const)$ partial scale-self-like (fractal) distributions, which are characterized by the fractal dimension spectra $F(h_r)$ of linear and circular birefringence. Moreover, the $max F(h_r)$ extreme values will fall on the supramolecular polycrystalline formation’s large scales ($L_{i(max)}$), while the minimum values will correspond to the small-scale molecular optical anisotropy formations.

We used the **WTMM** method (14–19) to analyze **BPF1**’s optically anisotropic multifractal structure in more detail and objectively.

Figure 4 shows the maximum magnitudes (wavelet coefficient amplitudes) of the skeletons—“red dots” represent the maxima, and “blue dots” represent the minima—of the wavelet coefficient lines of the maps $W^{LB,CB}(a, b)$ and **BPF1** theziograms JT^{LB} (fragments (b),(c)) and JT^{CB} (fragments (e),(f)) multifractal spectra $F(h_i)$.

A comparative analysis of **WTMM** method results revealed that:

Supramolecular **BPF1** network optically anisotropic properties $JT^{LB,CB}$ is characterized by a complex scale-like structure, which is characterized by individual multifractal spectra $F^{LB}(h_r)$ and $F^{CB}(h_r)$ for linear and circular birefringence—Figure 4, (fragments (c),(f)).

The **BPF1** theziograms $JT^{LB,CB}$ multifractal spectra $F^{LB,CB}(h_r)$ have an asymmetric structure with a distinct extremum and fractal dimension changes of $1.35 \lesssim h_r \lesssim 1.75$ range.

For **BPF1** linear birefringence theziograms JT^{LB} the multifractal spectra $F^{LB}(h_r)$ are “narrower” and more asymmetric (Figure 4, fragment (c)) than similar multifractal spectral dependences $F^{CB}(h_r)$, which are calculated for circular birefringence (Figure 4, fragment (f)) theziograms JT^{CB} .

The phase anisotropy theziogram multifractal spectra $F^{LB}(h_r)$ and $F^{CB}(h_r)$ main extremes are localized in the different parts of the fractal dimension scale— $\begin{cases} \max(F^{LB}) \Leftrightarrow h_r = 1.56; \\ \max(F^{CB}) \Leftrightarrow h_r = 1.68 \end{cases}$.

The fractal dimensions range Δh_r is more significant for the spectrum $F^{CB}(h_r)$ than for $F^{LB}(h_r)$ — $\Delta h_r(CB) > \Delta h_r(LB)$.

From a physical point of view, the results obtained can be linked to the following considerations:

First of all, each local optically anisotropic degree formed during dehydration in the **BPF1** theziograms corresponds to its fractal dimension h_i value, the probability and the magnitude of which ($F(h_r)$) is determined by the specific self-assembled supramolecular crystallite complexes.

Secondly, the fractal dimension's highest probability is inherent in the **BPF1** birefringence distributions $LB; CB$ ($200 \mu\text{m} \div 400 \mu\text{m} \leq L_{i(max)} \leq 1000 \mu\text{m}$).

Thirdly, from the fractal geometry theory point of view, in the extreme case, the supramolecular needle crystal dendritic network spatial organization architectonics can lead to a straight line. For such a boundary situation, the multifractal spectrum degenerates into a delta function with the base value of the fractal dimension $h_{LB} \Rightarrow 1.0$. A different situation is realized for spherulite supramolecular networks that form fractal measures in circular birefringence theziograms. Here, the boundary geometric situation is polycrystalline architectonics in the plane form, which corresponds to another fractal dimension value $h_{LB} \Rightarrow 2.0$.

For a real physical situation, such trends are found in different localization multifractal spectra main extremes ($\max(F^{CB}(h_r))$ and $\max(F^{LB}(h_r))$). In this case, the fractal dimensions variation range Δh_i is larger for the spectrum $F^{CB}(h_r)$ than for $F^{LB}(h_r)$ — $\Delta h_r(CB) > \Delta h_r(LB)$. A quantitative statistical estimate (ratio (24)) of the multifractal spectrum $F^{LB}(h_r)$ and $F^{CB}(h_r)$ is illustrated in Table 4.

Table 4. The multifractal spectra $F^{LB}(h_r)$ and $F^{CB}(h_r)$ statistical characteristics—**BPF 1**.

$Z_{i=1;2;3;4}$	$F^{LB}(h_r)$	$F^{CB}(h_r)$
Z_1	1.31 ± 0.065	1.65 ± 0.076
Z_2	0.11 ± 0.008	0.21 ± 0.012
Z_3	1.47 ± 0.074	0.91 ± 0.047
Z_4	2.03 ± 0.092	1.46 ± 0.076

Multifractal structure physical and statistical analysis $JT^{LB;CB}$ theziograms comparison results revealed a correlation between them. Namely, $Z_{i=1;2}(F^{LB}(h_r)) < Z_{i=1;2}(F^{CB}(h_r))$, which is due to the extrema $F^{LB}(h_r)$ and $F^{CB}(h_r)$ different localization ($h_r(CB) > h_r(LB)$), as well as differences between the fractal dimensions ranges— $\Delta h_r(CB) > \Delta h_r(LB)$. The reverse trend $Z_{i=3;4}(F^{LB}(h_r)) > Z_{i=3;4}(F^{CB}(h_r))$ is realized for the 3rd and 4th orders statistical moments, which characterize the linear and circular birefringence multifractal spectra distributions skewness and kurtosis. Mathematically, this regularity (relation (24)) is associated with the inversely proportional dependencies $Z_3 \sim \frac{1}{Z_2^3}$ and $Z_4 \sim \frac{1}{Z_2^4}$.

The **BPF2** polycrystalline structure fractal analysis found that the main difference between the dependencies from the previously obtained for **BPF1** ones (Figure 4, fragments (a),(d)) is the larger number of quasi-linear sections (h_r) with a smaller geometric length (d_i) presence. In parallel with this, distribution oscillations in optical anisotropy parameter power spectra and logarithmic dependences are observed (Figure 5, fragments (a),(d)). These facts indicate that different **BPF2** theziograms JT^{LB} and JT^{CB} exist, as well as multifractal (with more fractal measures) constructions.

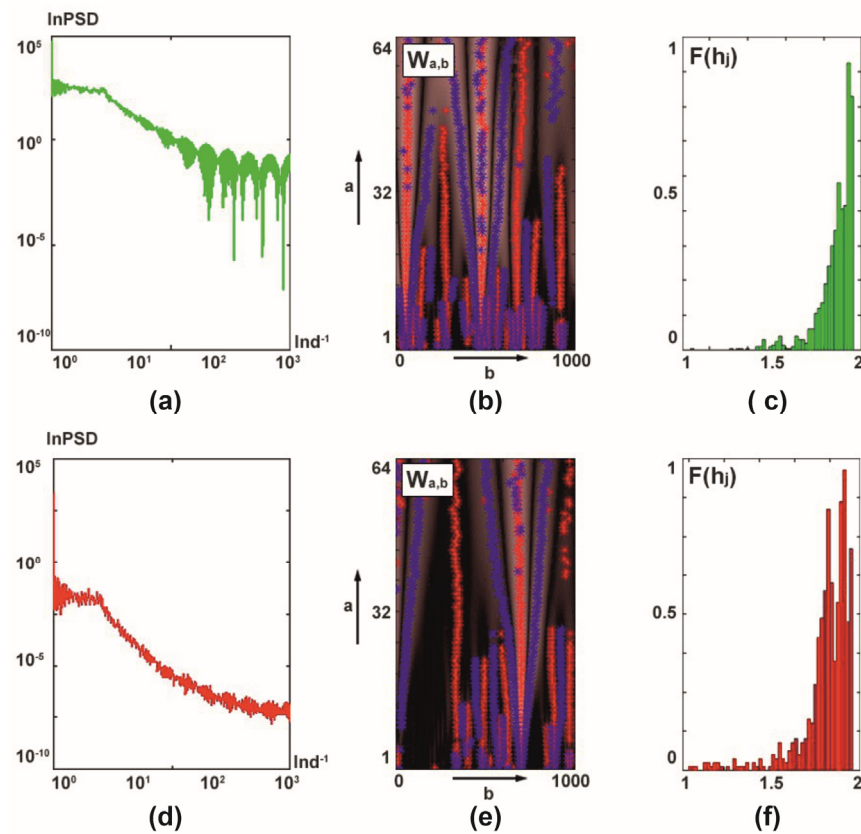


Figure 5. Power spectra logarithmic dependences (fragments (a,d)); wavelet transform modules maxima skeletons (fragments (b,e)) and multifractal spectra of **BPF2** phase anisotropy theziograms (fragments (c,f)).

The **BPF2** theziograms $JT^{LB;CB}$ fractal analysis results are shown in Figure 5, fragments (b),(c),(e) (f).

The **BPF2** theziograms $F^{LB;CB}(F_B, h_r)$ WTMM analysis results confirmed the presence of multifractal spectra, the parameters of which differ from those previously obtained for the supramolecular facies network dependencies $F^{LB}(h_r)$ and $F^{CB}(h_r)$ (Figure 4).

In particular, the **BPF2** theziograms $JT^{LB;CB}$ multifractal spectra $F^{LB;CB}(h_r)$ are less asymmetric and have greater width of fractal dimensions $1.3 \lesssim h_r \lesssim 1.89$. At the same time, these multifractal spectra $F^{LB}(h_r)$ and $F^{CB}(h_r)$ characterized the differences between main extremes localization—

$$\begin{cases} \max(F^{LB}) \Leftrightarrow h_r = 1.45; \\ \max(F^{CB}) \Leftrightarrow h_r = 1.83. \end{cases}$$

From a physical point of view, the **BPF2** self-assembled supramolecular network multifractal structure $JT^{LB;CB}$ reveal that specificity can be associated with a large number of linearly (albumin needle crystals) and circularly (globulin microspherulites) birefringent crystallites.

By this, the **BPF2** theziograms fractal dimension number that characterizes local scale-like measures increases. As a result, the **BPF2** supramolecular crystallite complex “self-assembled” multifractal spectra $F^{LB;CB}(h_r)$ half-width increases.

A **BPF2** phase anisotropy theziograms multifractal spectra $F^{LB}(h_r)$ and $F^{CB}(h_r)$ quantitative statistical assessment is illustrated in Table 5.

Table 5. Statistical characteristics of **BPF2** multifractal spectra $F^{LB}(h_r)$ and $F^{CB}(h_r)$.

$Z_{i=1;2;3;4}$	$F^{LB}(h_i)$	$F^{CB}(h_i)$
Z_1	1.49 ± 0.075	1.76 ± 0.086
Z_2	0.15 ± 0.008	0.18 ± 0.009
Z_3	1.07 ± 0.005	0.69 ± 0.041
Z_4	1.32 ± 0.07	0.99 ± 0.048

The data analysis presented in Table 5 confirmed the physical interpretations of **BPF2** theziograms JT^{LB} and JT^{CB} multifractal structure. In particular, minor differences were found between the 1st–2nd orders statistical moments values— $Z_{i=1,2}(F^{LB}(h_r)) \gtrsim Z_{i=1,2}(F^{CB}(h_r))$. This fact indicates the “statistical weight” of the fractal measures in the BPF2 linearly and circularly birefringent crystallite supramolecular network similarity. Therefore, such a network can be considered “dendritic-spherulitic”, in contrast to the “dendritic” type of the **BPF1** polycrystalline structure.

At the same time, the specificity of dendritic and spherulite fractal measures is manifested in significant differences between the 3rd–4th orders statistical moments values, which characterize the multifractal spectra $F^{CB}(h_r)$ and $F^{LB}(h_r)$ skewness and kurtosis— $Z_{i=3,4}(F^{LB}(h_r)) > Z_{i=3,4}(F^{CB}(h_r))$.

Thus, we demonstrate that the self-assembly of supramolecular network processes during blood plasma dehydration led to the formation of facies with complex optically anisotropic architecture. The facies polarization properties are characterized by individual multifractality spectra $F^{CB}(h_r)$ and $F^{LB}(h_r)$ for various blood facies types (**BPF1** and **BPF2**). In more detail, the **BPF1** and **BPF2** supramolecular polycrystalline network theziograms multifractal properties can be obtained by Jones matrix images polarization-interference phase scanning (ratios (20)–(23)).

Figures 6 and 7 series fragments (1)–(6), as well as Tables 6 and 7, present the **BPF1** linear ($JT^{LB}(\varphi_k)$) and circular ($JT^{LB}(\varphi_k)$) birefringence multifractal and statistical analysis results in the phase planes $\varphi_k = \pi/4$ and $\varphi_k = \pi/8$, respectively.

Within the fractal analysis framework (Figures 6 and 7, fragments (a),(d)) in various phase sections ($\varphi_k = \frac{\pi}{4}$ and $\varphi_k = \frac{\pi}{8}$), it was found that with a decrease in the phase scanning parameter $\varphi_k \downarrow$ value, the number (h_j) decreases and the linear sections geometric extent (L_i) in dependencies $\ln(PD(JT^{LB,CB}) - \ln L^{-1})$ increases. At the same time, the oscillation amplitude decreases, indicating an increase in the crystallite measures of the large-scale self-similar organization within the supramolecular **BPF1** network.

Multifractal structure $F^{LB,CB}(h_i, \varphi_k)$ statistical analysis revealed the following $JT^{LB,CB}(h_r, \varphi_k = \frac{\pi}{4}; \frac{\pi}{8})$ regularities:

Individual multifractal spectra for linearly and circularly birefringent fractal measures, which are objectively characterized by sets 1st–4th orders central statistical moments (24)— $Z_{i=1;2;3;4}(F^{LB}(h_r, \varphi_k)) \neq Z_{i=1;2;3;4}(F^{CB}(h_r, \varphi_k))$ —Tables 6 and 7;

In all phase scanning φ_k planes, the following statistical relations take place $\left(\begin{array}{l} Z_{i=1;2}(F^{CB}(h_r, \varphi_k)) > Z_{i=1;2}(F^{LB}(h_r, \varphi_k)) \\ Z_{i=3;4}F^{CB}(h_r, \varphi_k) < Z_{i=3;4}(F^{LB}(h_r, \varphi_k)) \end{array} \right)$ —Tables 6 and 7;

With phase parameter $\varphi_k \downarrow$ values, a decrease ($\downarrow$) progressively declined in the spectra $F^{LB,CB}(h_r, \varphi_k)$ half-width—Figures 6 and 7, fragments (b),(c),(e),(f);

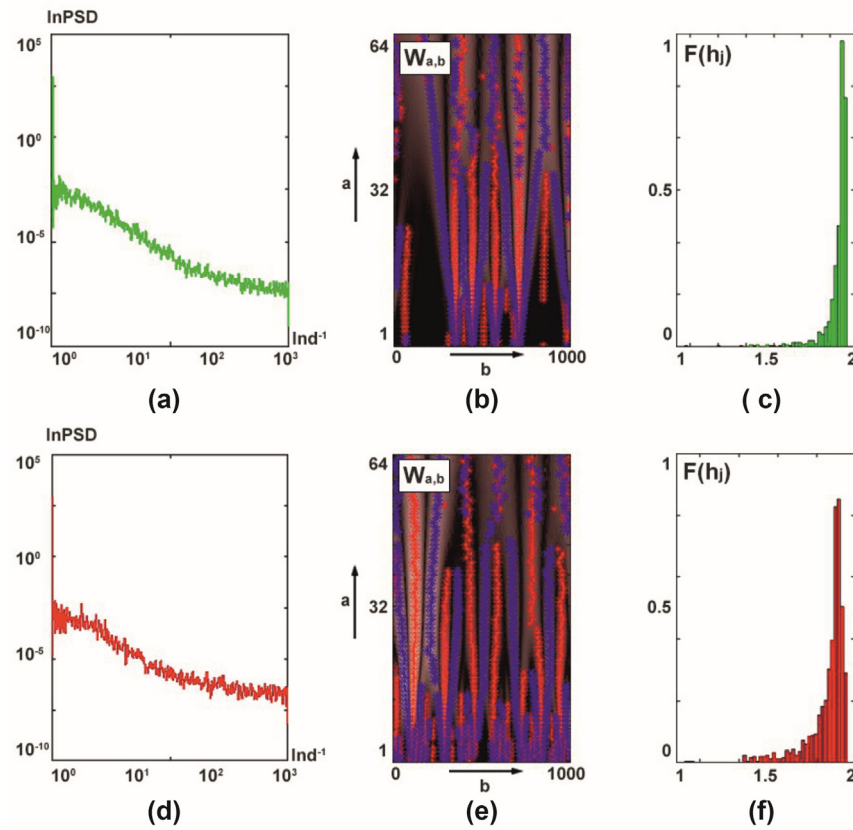


Figure 6. Power spectra logarithmic dependences (fragments (a,d)); wavelet transform module maxima skeletons (fragments (b,e)) and multifractal spectra of BPF1 phase anisotropy theziograms $JT^{LB;CB}(\varphi_k = \frac{\pi}{4})$ (fragments (c,f)).

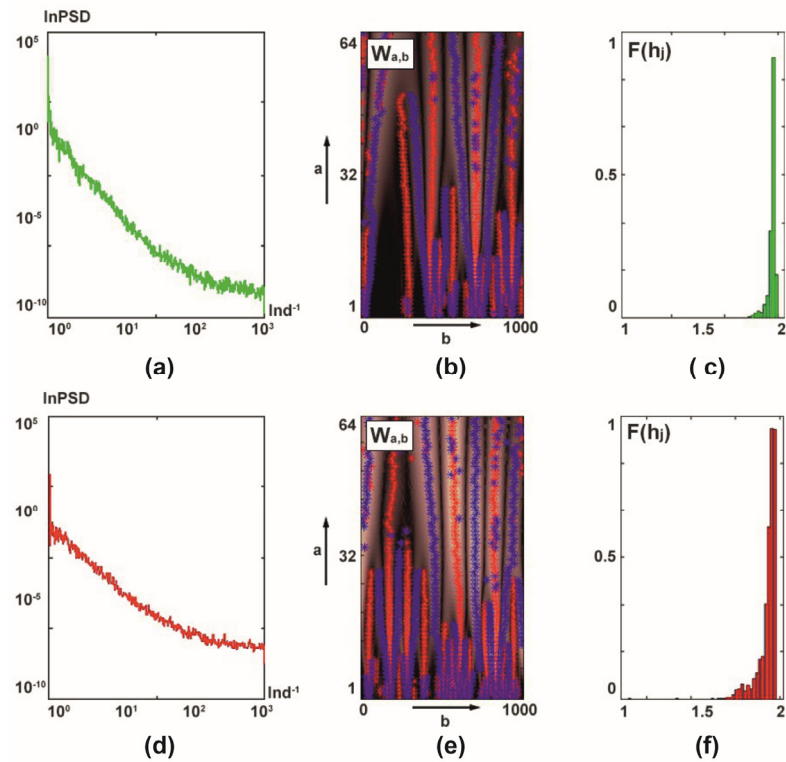


Figure 7. Power spectra logarithmic dependences (fragments (a,d)); wavelet transform module maxima skeletons (fragments (b,e)) and multifractal spectra of BPF1 phase anisotropy theziograms $JT^{LB;CB}(\varphi_k = \frac{\pi}{8})$ (fragments (c,f)).

Table 6. Statistical characteristics of $JT^{LB;CB}$.

JT	LB	CB
Z_1	1.31 ± 0.065	1.65 ± 0.076
Z_2	0.09 ± 0.005	0.18 ± 0.009
Z_3	2.64 ± 0.14	1.63 ± 0.093
Z_4	3.35 ± 0.19	2.24 ± 0.13

Table 7. Statistical characteristics of $JT^{LB;CB}$ multifractal spectra $F^{LB;CB}(h_r, \varphi_k = \frac{\pi}{4})$ —**BPF1**.

JT	LB	CB
Z_1	1.23 ± 0.065	1.34 ± 0.076
Z_2	0.07 ± 0.004	0.16 ± 0.008
Z_3	3.24 ± 0.19	1.98 ± 0.11
Z_4	4.41 ± 0.28	2.91 ± 0.16

The following magnitude $Z_{i=1;2;3;4}(F^{LB;CB}(h_r, \varphi_k \downarrow)) \Rightarrow \begin{pmatrix} Z_{i=1;2}(F^{LB;CB}(h_r, \varphi_k)) \downarrow \\ Z_{i=3;4}(F^{LB;CB}(h_r, \varphi_k)) \uparrow \end{pmatrix}$.
phase transformations $\varphi_k \downarrow$ —Tables 6 and 7.

The 3rd–4th orders statistical moments, which characterize the distributions $Z_{3;4}(F^{LB;CB}(h_r, \varphi_k \downarrow))$, were the most sensitive and, accordingly, diagnostically promising to changes in the matrix-reproduced theziograms $JT^{LB;CB}$ multifractal structure:

The change $\Delta Z_{3;4}^{LB}(\varphi_k \downarrow)$ range is from 2 to 2.5 times;

The change $\Delta Z_{3;4}^{CB}(\varphi_k \downarrow)$ range is from 1.6 to 2.1 times.

From a physical perspective, the results obtained can be attributed to the fact that during phase scanning ($\varphi_k \downarrow$), the **BPF1** geometric depths decrease. As a result, the Jones matrix increasingly reproduces large-scale, self-similar (monofractal) optically anisotropic measures of the polycrystalline supramolecular network. Due to this birefringence parameter, $JT^{LB;CB}(h_r, \varphi_k)$ distribution approaches a fractal to form a fairly narrow multifractal spectrum $F^{LB;CB}(h_r, \varphi_k)$.

For multifractal measures $JT^{CB}(h_r, \varphi_k)$ optically active crystals implemented a similar but less pronounced trend over the larger set fractal dimensions expense in spectrum $F^{CB}(h_r, \varphi_k)$ —Figures 4, 6 and 7, fragments (b),(c),(e),(f)).

The Figures 8 and 9 series fragments (a)–(f), as well as Tables 8 and 9, present the multifractal and statistical analysis results of **BPF2** linear ($JT^{LB}(\varphi_k)$) and circular ($JT^{LB}(\varphi_k)$) birefringence in the phase planes $\varphi_k = \pi/4$ and $\varphi_k = \pi/8$, respectively.

Within the **BPF2** theziograms (Figures 8 and 9, fragments (a),(d)) in various phase section ($\varphi_k = \frac{\pi}{4}$ and $\varphi_k = \frac{\pi}{8}$) fractal analysis framework, it was found (similar as for **BPF1**) that with a decrease in the phase scanning parameter $\varphi_k \downarrow$ value, number (L_i) decreases and the linear sections in dependencies $\ln(PD(JT^{LB;CB}) - \ln L^{-1})$ geometric extent (d_i) increases. At the same time, the oscillation amplitude decreases. This fact indicates an increase in the supramolecular **BPF2** network large-scale self-similar organization crystallite measure level.

The analysis of the **BPF2 WTMM** method results revealed generally similar trends for these facies across all phase scanning planes, though they were less distinct φ_k .

A similar difference exists between the values of the statistical moments that characterize the multifractal spectra across the phase planes— $\begin{pmatrix} Z_{i=1;2}(F^{CB}(h_r, \varphi_k)) < Z_{i=1;2}(F^{LB}(h_r, \varphi_k)) \\ Z_{i=3;4}F^{CB}(h_r, \varphi_k) > Z_{i=3;4}(F^{LB}(h_r, \varphi_k)) \end{pmatrix}$ —Tables 8 and 9.

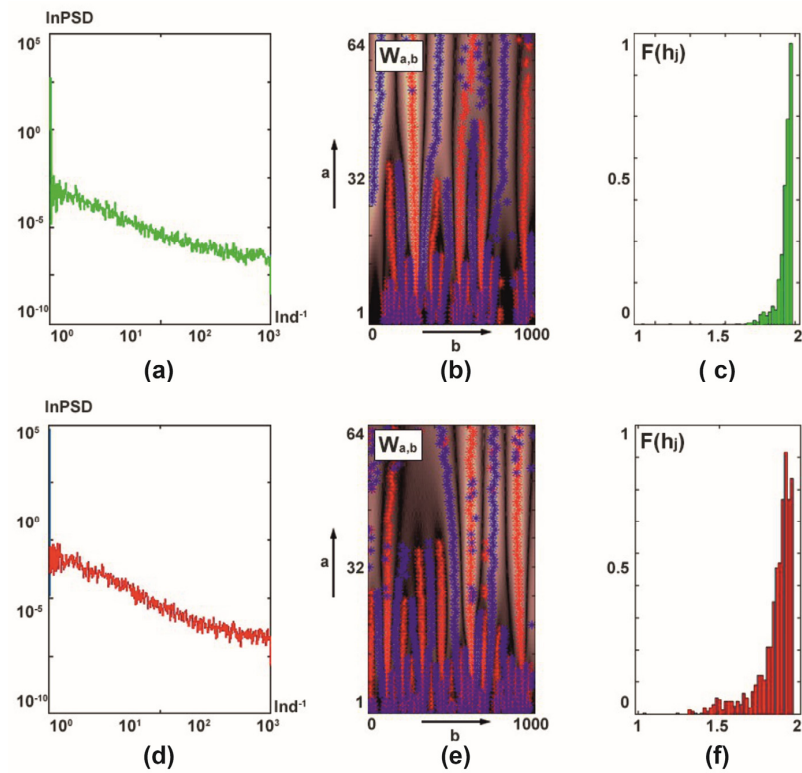


Figure 8. Power spectra logarithmic dependences (fragments (a,d)); wavelet transform module maxima skeletons (fragments (b,e)) and multifractal spectra of BPF2 phase anisotropy theziograms $J^{LB;CB}(\varphi_k = \frac{\pi}{4})$ (fragments (c,f)).

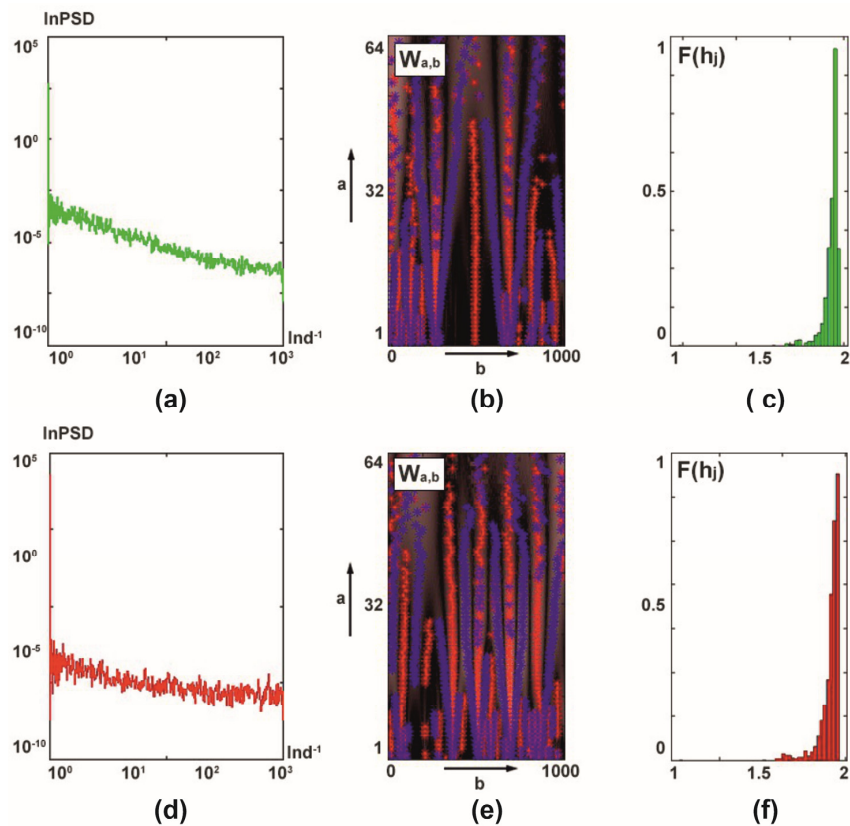


Figure 9. Power spectra logarithmic dependences (fragments (a,d)); wavelet transform module maxima skeletons (fragments (b,e)) and multifractal spectra of BPF2 phase anisotropy theziograms $J^{LB;CB}(\varphi_k = \frac{\pi}{8})$ (fragments (c,f)).

Table 8. Statistical characteristics of BPF2 theziograms $F^{LB;CB}(h_r, \varphi_k = \frac{\pi}{4})$.

<i>JT</i>	<i>LB</i>	<i>CB</i>
Z_1	1.41 ± 0.075	1.67 ± 0.086
Z_2	0.13 ± 0.008	0.16 ± 0.009
Z_3	1.49 ± 0.074	1.18 ± 0.053
Z_4	1.81 ± 0.082	1.41 ± 0.076

Table 9. Statistical characteristics of BPF2 theziograms $F^{LB;CB}(h_r, \varphi_k = \frac{\pi}{8})$.

<i>JT</i>	<i>LB</i>	<i>CB</i>
Z_1	1.34 ± 0.079	1.51 ± 0.098
Z_2	0.07 ± 0.004	0.11 ± 0.011
Z_3	1.83 ± 0.079	1.48 ± 0.065
Z_4	2.44 ± 0.099	2.02 ± 0.086

When a phase parameter φ_k decrease is implemented, the previously discovered statistical scenario occurs— $Z_{i=1,2,3,4}(F^{LB;CB}(h_r, \varphi_k \downarrow)) \Rightarrow \left(\begin{matrix} Z_{i=1,2}(F^{LB;CB}(h_r, \varphi_k)) \downarrow \\ Z_{i=3,4}(F^{LB;CB}(h_r, \varphi_k)) \uparrow \end{matrix} \right)$ —Tables 8 and 9.

The 3rd–4th-order statistical moments, which characterize the distributions $F^{LB;CB}(h_r, \varphi_k \downarrow)$, were also the most sensitive:

The change $\Delta Z_{3,4}^{LB}(\varphi_k \downarrow)$ range is from 1.3 to 1.7 times.

The change $\Delta Z_{3,4}^{CB}(\varphi_k \downarrow)$ range is from 1.4 to 1.8 times.

Therefore, in the **BPF2** phase scanning ($\varphi_k \downarrow$) case demonstrated the process of “approximation” $JT^{LB;CB}(h_r, \varphi_k)$ large-scale self-similar measures monofractal to which they correspond fairly narrow multifractal spectra $F^{LB;CB}(h_r, \varphi_k)$.

However, the polycrystalline **BPF2** scale-self-similar architectonic network specificity in comparison with **BPF1** fractal measures is found in a different construction of $F^{LB;CB}(h_r, \varphi_k)$ —Tables 8 and 9.

4. Biomedical Applications Examples

Our information analysis method involves the use of operational characteristics from evidence-based medicine [64]:

Sensitivity (*Se*)—is the diagnostic method true positive result (*A*) proportion among all samples in the experimental group 2 (*N*)

$$Se = \frac{A}{N} 100\% \quad (25)$$

Specificity (*Sp*)—is the diagnostic method true negative result (*B*) proportion among all samples in the control group 1 (*H*)

$$Sp = \frac{B}{H} 100\% \quad (26)$$

Accuracy (*Ac*)—is the test correct result (*A* + *B*) proportion among all samples (*N* + *H*)

$$Ac = \frac{A + B}{N + H} 100\% \quad (27)$$

If (*N* + *H*) = (*A* + *B*)—*Ac* is referred to as balanced accuracy.

In our work, we use the following scale to evaluate diagnostic accuracy—Table 10.

Table 10. Balanced accuracy of COVID-19 remote consequence differential diagnosis.

Diagnostic Accuracy Assessment	Accuracy, Ac, %
Satisfactory	81–85
Good	86–90
Very good	91–95
Excellent	>95

We studied the following blood facies groups:

Control group 1–50 samples (24 men and 26 women aged 18 to 63 years).

Experimental group 2 (COVID-19 duration—one year)—50 samples (27 men and 23 women aged 19 to 65 years).

Experimental group 3 (COVID-19 duration—two years)—50 samples (22 men and 28 women aged 16 to 69 years).

Experimental group 4 (COVID-19 duration—three years)—50 samples (26 men and 24 women aged 22 to 65 years).

Tables 11–14 present the values of operational characteristics (25)–(27) for diagnosis (“1-(2;3;4)”) and intergroup (“2–4”, “2–3”, “3–4”) COVID-19 long-term consequences differentiation within the statistical and multifractal analysis of blood facies theziograms $JT^{LB;CB}(h_r, \varphi_k)$; p^{LB} and p^{CB} —statistical significance of parameters $Z_{3;4}^{LB;CB}$.

Table 11. Operational characteristics (Se, Sp, Ac) of COVID-19 remote consequence differential diagnosis—groups “1”–“2;3;4” (150 samples).

Parameters	JT^{LB}	JT^{CB}	Parameters	$F^{LB}(h_r)$	$F^{CB}(h_r)$
$Z_3, p^{LB} > 0.05;$ $p^{CB} < 0.05$	$Se = 81.3\%; Sp = 72\%; Ac = 79\%$	$Se = 82\%; Sp = 78\%; Ac = 81\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 90\%; Sp = 86\%; Ac = 89\%$	$Se = 92.7\%; Sp = 90\%; Ac = 92\%$
$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 82\%; Sp = 78\%; Ac = 81\%$	$Se = 84\%; Sp = 80\%; Ac = 83\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 92\%; Sp = 88\%; Ac = 91\%$	$Se = 93.3\%; Sp = 90\%; Ac = 93\%$
Parameters	$JT^{LB}(\varphi_k = \frac{\pi}{4})$	$JT^{CB}(\varphi_k = \frac{\pi}{4})$	Parameters	$F^{LB}(h_r, \varphi_k = \frac{\pi}{4})$	$F^{CB}(h_r, \varphi_k = \frac{\pi}{4})$
$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 83.3\%; Sp = 78\%; Ac = 82\%$	$Se = 84\%; Sp = 80\%; Ac = 83\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 92.7\%; Sp = 90\%; Ac = 92\%$	$Se = 94.7\%; Sp = 90\%; Ac = 95\%$
$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 84\%; Sp = 80\%; Ac = 83\%$	$Se = 84.7\%; Sp = 82\%; Ac = 84\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 92.7\%; Sp = 90\%; Ac = 92\%$	$Se = 94.7\%; Sp = 90\%; Ac = 95\%$
Parameters	$JT^{LB}(\varphi_k = \frac{\pi}{8})$	$JT^{CB}(\varphi_k = \frac{\pi}{8})$	Parameters	$F^{LB}(h_r, \varphi_k = \frac{\pi}{8})$	$F^{CB}(h_r, \varphi_k = \frac{\pi}{8})$
$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 84.7\%; Sp = 82\%; Ac = 84\%$	$Se = 84.7\%; Sp = 82\%; Ac = 84\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 93.3\%; Sp = 90\%; Ac = 93\%$	$Se = 96\%; Sp = 92\%; Ac = 96\%$
$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 84.7\%; Sp = 82\%; Ac = 84\%$	$Se = 84.7\%; Sp = 82\%; Ac = 84\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 94\%; Sp = 90\%; Ac = 94\%$	$Se = 97.3\%; Sp = 92\%; Ac = 97\%$

It was established that the maximum accuracy of diagnosing the remote consequences of COVID-19 by the method of statistical analysis of the theziograms of linear and circular birefringence $JT^{LB;CB}$ of blood plasma facies reaches a satisfactory level of $Ac(Z_{3;4}(LB, CB)) = 84\%$ in the phase plane $\varphi_k = \frac{\pi}{8}$.

The satisfactory level of accuracy in diagnosing the long-term consequences of COVID-19, achieved through direct statistical analysis of the coordinate distributions (theziograms) of the linear and circular birefringence of blood facets, corresponds to low values of sensitivity and specificity of the method— $Se = 84.7\%; Sp = 82\%$.

The maximum accuracy of diagnosing the remote consequences of COVID-19 by the method of statistical analysis of multifractal spectra $F^{LB;CB}$ of the theziograms $JT^{LB;CB}$ of blood plasma facies reaches a very good level of $Ac(Z_{3;4}(LB)) = 93\text{--}94\%$ and an excellent level of $Ac(Z_{3;4}(CB)) = 96\text{--}97\%$ in the phase plane $\varphi_k = \frac{\pi}{8}$.

Table 12. Operational characteristics (Se, Sp, Ac) of COVID-19 remote consequence differential diagnosis—groups “2”–“4”.

Parameters	JT^{LB}	JT^{CB}	Parameters	$F^{LB}(h_r)$	$F^{CB}(h_r)$
$Z_3, p^{LB} > 0.05;$ $p^{CB} > 0.05$	$Se = 80\%; Sp = 74\%; Ac = 77\%$	$Se = 81\%; Sp = 77\%; Ac = 79\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 89\%; Sp = 85\%; Ac = 87\%$	$Se = 92\%; Sp = 86\%; Ac = 89\%$
$Z_4, p^{LB} > 0.05;$ $p^{CB} > 0.05$	$Se = 81\%; Sp = 77\%; Ac = 79\%$	$Se = 84\%; Sp = 78\%; Ac = 81\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 91\%; Sp = 87\%; Ac = 89\%$	$Se = 93\%; Sp = 87\%; Ac = 90\%$
Parameters	$JT^{LB}(\varphi_k = \frac{\pi}{4})$	$JT^{CB}(\varphi_k = \frac{\pi}{4})$	Parameters	$F^{LB}(h_r, \varphi_k = \frac{\pi}{4})$	$F^{CB}(h_r, \varphi_k = \frac{\pi}{4})$
$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 83\%; Sp = 77\%; Ac = 80\%$	$Se = 85\%; Sp = 79\%; Ac = 82\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 93\%; Sp = 87\%; Ac = 90\%$	$Se = 95\%; Sp = 91\%; Ac = 93\%$
$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 84\%; Sp = 78\%; Ac = 81\%$	$Se = 85\%; Sp = 81\%; Ac = 83\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 93\%; Sp = 89\%; Ac = 91\%$	$Se = 94\%; Sp = 92\%; Ac = 93\%$
Parameters	$JT^{LB}(\varphi_k = \frac{\pi}{8})$	$JT^{CB}(\varphi_k = \frac{\pi}{8})$	Parameters	$F^{LB}(h_r, \varphi_k = \frac{\pi}{8})$	$F^{CB}(h_r, \varphi_k = \frac{\pi}{8})$
$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 85\%; Sp = 81\%; Ac = 83\%$	$Se = 87\%; Sp = 81\%; Ac = 84\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 93\%; Sp = 89\%; Ac = 91\%$	$Se = 96\%; Sp = 92\%; Ac = 94\%$
$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 86\%; Sp = 82\%; Ac = 84\%$	$Se = 88\%; Sp = 82\%; Ac = 85\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 94\%; Sp = 90\%; Ac = 92\%$	$Se = 96\%; Sp = 94\%; Ac = 95\%$

Table 13. Operational characteristics (Se, Sp, Ac) of COVID-19 remote consequence differential diagnosis—groups “2”–“3”.

Parameters	JT^{LB}	JT^{CB}	Parameters	$F^{LB}(h_r)$	$F^{CB}(h_r)$
$Z_3, p^{LB} > 0.05;$ $p^{CB} > 0.05$	$Se = 80\%; Sp = 72\%; Ac = 76\%$	$Se = 81\%; Sp = 77\%; Ac = 79\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 89\%; Sp = 85\%; Ac = 87\%$	$Se = 93\%; Sp = 87\%; Ac = 90\%$
$Z_4, p^{LB} > 0.05;$ $p^{CB} > 0.05$	$Se = 81\%; Sp = 75\%; Ac = 78\%$	$Se = 83\%; Sp = 77\%; Ac = 80\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 91\%; Sp = 87\%; Ac = 89\%$	$Se = 93\%; Sp = 89\%; Ac = 91\%$
Parameters	$JT^{LB}(\varphi_k = \frac{\pi}{4})$	$JT^{CB}(\varphi_k = \frac{\pi}{4})$	Parameters	$F^{LB}(h_r, \varphi_k = \frac{\pi}{4})$	$F^{CB}(h_r, \varphi_k = \frac{\pi}{4})$
$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 80\%; Sp = 72\%; Ac = 76\%$	$Se = 85\%; Sp = 79\%; Ac = 82\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 93\%; Sp = 87\%; Ac = 90\%$	$Se = 94\%; Sp = 92\%; Ac = 93\%$
$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 81\%; Sp = 75\%; Ac = 78\%$	$Se = 87\%; Sp = 81\%; Ac = 84\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 93\%; Sp = 89\%; Ac = 91\%$	$Se = 96\%; Sp = 92\%; Ac = 94\%$
Parameters	$JT^{LB}(\varphi_k = \frac{\pi}{8})$	$JT^{CB}(\varphi_k = \frac{\pi}{8})$	Parameters	$F^{LB}(h_r, \varphi_k = \frac{\pi}{8})$	$F^{CB}(h_r, \varphi_k = \frac{\pi}{8})$
$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 85\%; Sp = 81\%; Ac = 83\%$	$Se = 85\%; Sp = 81\%; Ac = 83\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 94\%; Sp = 90\%; Ac = 92\%$	$Se = 96\%; Sp = 94\%; Ac = 95\%$
$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 85\%; Sp = 81\%; Ac = 83\%$	$Se = 88\%; Sp = 82\%; Ac = 85\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 94\%; Sp = 92\%; Ac = 93\%$	$Se = 96\%; Sp = 94\%; Ac = 95\%$

In the context of multifractal analysis of theziograms $JT^{LB;CB}$, the level of sensitivity and specificity of the diagnostic power of the method is also very high (>90%). For linear birefringence— $Se(Z_{3;4}(LB)) = 96\text{--}97.3\%$ and $Sp(Z_{3;4}(LB)) = 90\%$. For circular birefringence— $Se(Z_{3;4}(CB)) = 93.3\text{--}94\%$ and $Sp(Z_{3;4}(CB)) = 92\%$.

It was established that the maximum accuracy of differentiation of the age (1–3 years) of the remote consequences of COVID-19 by the method of statistical analysis of the theziograms of linear and circular birefringence $JT^{LB;CB}$ of blood plasma facies reaches a satisfactory level $Ac(Z_{3;4}) = 83\text{--}85\%$ in the phase plane $\varphi_k = \frac{\pi}{8}$. The sensitivity and specificity of differential diagnosis are also low and do not exceed 90%— $Se = 82\text{--}88\%; Sp = 81\text{--}82\%$.

The maximum accuracy of differentiation of the age (1–3 years) of the remote consequences of COVID-19 by the method of statistical analysis of the multifractal spectra $F^{LB;CB}$ of the theziograms $JT^{LB;CB}$ of blood plasma facies reaches a very good $Ac(Z_{3;4}(LB, CB)) = 91\text{--}95\%$ level in the phase plane $\varphi_k = \frac{\pi}{8}$. Statistical analysis of multifractal spectra of linear and circular refraction distributions provided high (>90%) values of sensitivity and specificity of differential diagnostics— $Se = 93\text{--}96\%; Sp = 89\text{--}94\%$.

Table 14. Operational characteristics (Se, Sp, Ac) of COVID-19 remote consequence differential diagnosis—groups “3”–“4”.

Parameters	JT^{LB}	JT^{CB}	Parameters	$F^{LB}(h_r)$	$F^{CB}(h_r)$
$Z_3, p^{LB} > 0.05;$ $p^{CB} > 0.05$	$Se = 78\%; Sp =$ $= 76\%; Ac = 74\%$	$Se = 81\%; Sp =$ $= 75\%; Ac = 78\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 89\%; Sp =$ $= 85\%; Ac = 87\%$	$Se = 93\%; Sp =$ $= 87\%; Ac = 90\%$
$Z_4, p^{LB} > 0.05;$ $p^{CB} > 0.05$	$Se = 80\%; Sp =$ $= 72\%; Ac = 76\%$	$Se = 83\%; Sp =$ $= 77\%; Ac = 80\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 91\%; Sp =$ $= 87\%; Ac = 89\%$	$Se = 93\%; Sp =$ $= 89\%; Ac = 91\%$
Parameters	$JT^{LB}(\varphi_k = \frac{\pi}{4})$	$JT^{CB}(\varphi_k = \frac{\pi}{4})$	Parameters	$F^{LB}(h_r, \varphi_k = \frac{\pi}{4})$	$F^{CB}(h_r, \varphi_k = \frac{\pi}{4})$
$Z_3, p^{LB} > 0.05;$ $p^{CB} > 0.05$	$Se = 81\%; Sp =$ $= 75\%; Ac = 78\%$	$Se = 85\%; Sp =$ $= 79\%; Ac = 82\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 91\%; Sp =$ $= 87\%; Ac = 89\%$	$Se = 94\%; Sp =$ $= 90\%; Ac = 92\%$
$Z_4, p^{LB} > 0.05;$ $p^{CB} < 0.05$	$Se = 83\%; Sp =$ $= 77\%; Ac = 80\%$	$Se = 85\%; Sp =$ $= 79\%; Ac = 82\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 93\%; Sp =$ $= 87\%; Ac = 90\%$	$Se = 94\%; Sp =$ $= 92\%; Ac = 93\%$
Parameters	$JT^{LB}(\varphi_k = \frac{\pi}{8})$	$JT^{CB}(\varphi_k = \frac{\pi}{8})$	Parameters	$F^{LB}(h_r, \varphi_k = \frac{\pi}{8})$	$F^{CB}(h_r, \varphi_k = \frac{\pi}{8})$
$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 81\%; Sp =$ $= 77\%; Ac = 79\%$	$Se = 84.7\%; Sp =$ $= 82\%; Ac = 84\%$	$Z_3, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 93\%; Sp =$ $= 89\%; Ac = 91\%$	$Se = 96\%; Sp =$ $= 94\%; Ac = 95\%$
$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.05$	$Se = 83\%; Sp =$ $= 77\%; Ac = 80\%$	$Se = 88\%; Sp =$ $= 82\%; Ac = 85\%$	$Z_4, p^{LB} < 0.05;$ $p^{CB} < 0.001$	$Se = 94\%; Sp =$ $= 90\%; Ac = 92\%$	$Se = 98\%; Sp =$ $94\%; Ac = 96\%$

The maximum accuracy of differentiation of the age (1–2 years) of the remote consequences of COVID-19 by the method of statistical analysis of the theziograms of linear and circular birefringence $JT^{LB;CB}$ of blood plasma facies reaches a satisfactory level of $Ac(Z_{3,4}) = 83$ – 85% in the phase plane $\varphi_k = \frac{\pi}{8}$. The parameters of sensitivity and specificity of differential diagnostics also do not exceed 90% — $Se = 85$ – 88% ; $Sp = 81$ – 82% .

The maximum accuracy of differentiation of the age (1–3 years) of the remote consequences of COVID-19 by the method of statistical analysis of the multifractal spectra $F^{LB;CB}$ of the theziograms $JT^{LB;CB}$ of blood plasma facies reaches a very good $Ac(Z_{3,4}) = 92$ – 95% level in the phase plane $\varphi_k = \frac{\pi}{8}$. Within the framework of the multifractal approach, the sensitivity and specificity of differential diagnostics of blood facies samples increase by 6–8% and reach the following high levels— $Se = 94$ – 96% ; $Sp = 90$ – 94% .

The maximum accuracy of differentiation of the age (2–3 years) of the remote consequences of COVID-19 by the method of statistical analysis of the theziograms of linear and circular birefringence $JT^{LB;CB}$ of blood plasma facies reaches a satisfactory level $Ac(Z_{3,4}(LB)) = 84$ – 85% in the phase plane $\varphi_k = \frac{\pi}{8}$. The parameters of sensitivity and specificity of differential diagnostics of the method of direct statistical analysis of theziograms $JT^{LB;CB}$ are also insignificant and do not exceed 90% — $Se = 81$ – 88% ; $Sp = 77$ – 82% .

The maximum accuracy of differentiation of the age (2–3 years) of the remote consequences of COVID-19 by the method of statistical analysis of the multifractal spectra $F^{LB;CB}$ of the theziograms $JT^{LB;CB}$ of blood plasma facies reaches a very good $Ac(Z_{3,4}(LB)) = 92$ – 95% and excellent $Ac(Z_4(LB)) = 96\%$ level in the phase plane $\varphi_k = \frac{\pi}{8}$. The sensitivity and specificity of differential diagnostics within the framework of statistical analysis of multifractal spectra also reach a high level— $Se = 93$ – 98% ; $Sp = 89$ – 94% .

5. Conclusions

A method for Jones-matrix layer-by-layer theziography was developed and experimentally tested to analyze the optically anisotropic architecture of supramolecular networks in blood plasma facies.

Theziograms showing linear and circular birefringence in different phase sections of the complex amplitude field of blood plasma facies were measured and analyzed.

The COVID-19 late consequences differential diagnosis accuracy based on the statistical markers $Z_{3,4}(JT^{LB;CB}(h_r, \varphi_k))$ does not exceed satisfactory ($Ac(Z_{3,4}, \varphi_k = \frac{\pi}{8}) = 83$ – 85%) levels.

Blood plasma facies theziograms $JT^{LB;CB}$ power spectra logarithmic dependences $\ln(PD(JT^{LB;CB})) - \ln L^{-1}$ analysis revealed the supramolecular polycrystalline network's multifractal structure signs—approximating curve $H(\theta)$ linear sections (monofractal measures) for various geometric dimension d_i presence.

For the first time, the method of wavelet transform applied to the maxima of moduli in linear and circular birefringence distributions was used to assess the multifractal structure of blood plasma facies, specifically the optically anisotropic supramolecular networks, through layer-by-layer theziograms.

The fractal dimension spectra distributions of the layered optical anisotropy theziograms were algorithmically obtained and analyzed using statistical methods.

Multifractal analysis revealed statistically significant markers that provided differential diagnostic levels for the architectonics of supramolecular networks in blood plasma during COVID-19 transformation. These multifractal statistical markers enable very good ($Ac(Z_{3;4}) = 92\%$) and excellent ($Ac(Z_{3;4}, \varphi_k = \frac{\pi}{8}) = 97\%$) accuracy in diagnosing the long-term consequences of COVID-19 over time intervals ranging from one to three years.

Author Contributions: Conceptualization, A.U. and Z.C.; Methodology, A.U. and I.S.; Software, M.G., A.D. and I.M.; Validation, O.P. and L.B.; Formal analysis, Y.U.; Investigation, N.P., I.S., Y.U., O.S. and I.M.; Resources, N.P.; Data curation, O.K.; Writing—original draft, A.U.; Writing—review & editing, O.K. and A.D.; Visualization, O.P. and A.D.; Supervision, J.Z. and L.B.; Project administration, A.U. and Z.C.; Funding acquisition, J.Z. All authors have read and agreed to the published version of the manuscript.

Funding: Authors acknowledge the support from the National Research Foundation of Ukraine, Project 2023.01/0174.

Informed Consent Statement: This study was conducted by the principles of the Declaration of Helsinki, and in compliance with the International Conference on Harmonization Good Clinical Practice and local regulatory requirements. Ethical approval was obtained from the Ethics Committee at Bukovinian State Medical University (Chernivtsi, Ukraine).

Data Availability Statement: Data are contained within the article.

Conflicts of Interest: The authors declare no conflicts of interest.

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