

Comparative analysis of tissue structure via Mueller matrix characterization of liquid crystals

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ABSTRACT

Polarization properties of light interacting with biological tissues change depending mainly on tissue structure. In this work, a comparative method for the extraction of information about tissue structure is proposed, based on the analysis of polarization properties of liquid crystals. The Mueller matrix of the tissue is decomposed by means of the Lu-Chipman polar decomposition. As long as the scattering is weak, and so depolarization is sufficiently low, the tissue structure can be considered similar to the one of the equivalent liquid crystal. This model is applied to a sample of healthy porcine skin measured in backscattering configuration.

Keywords: tissue characterization, Mueller matrix, liquid crystals, Lu-Chipman decomposition.

1. INTRODUCTION

The importance of optical techniques in the field of biomedicine is clear due to the new tools and procedures that provide to practitioners, as long as the improvements on the existing ones [1]. The use of these techniques can be oriented to mainly two objectives, treatment and characterization of biological tissues. The former comprises examples such as Low Intensity Laser Therapy (LILT) or Photodynamic Therapy (PDT). The latter tries to extract new information from tissues in order to be able to detect diseases in an early stage of development, what could imply in many cases the possibility of treating the disorder successfully.

There are a lot of optical techniques of tissue diagnosis that take advantage of several optical interactions, like Fluorescence Spectroscopy or more recently Optical Coherence Tomography (OCT) [2-3]. Their aim is the acquisition of images of biological tissues that improve the results of conventional imaging techniques such as ultrasounds or X-rays. The inclusion of polarization information, apart from intensity measurements, leads to a contrast increase in the images obtained, and as a consequence a better diagnosis can be made. One example of the inclusion of polarization information is the so-called Polarization Sensitive Optical Coherence Tomography (PS-OCT).

Polarization properties of light interacting with media in general, and biological tissue in particular, strongly depend on tissue structure. A lot of biological tissues show optical anisotropy, owing mainly to the linear birefringence caused by the fibrous structures that abound in the extracellular matrix of connective tissue. This fact, as well as the strong scattering produced in these media, makes it necessary to develop accurate models in order to successfully understand and describe light propagation within tissues. Indeed, biological tissues modelling is an essential step to correctly interpret experimental results. In this work, a comparative method for the extraction of information about tissue structure is proposed, based on the analysis of polarization properties of liquid crystals. The complete polarization characterization of light and media requires the use of Mueller calculus, composed by Mueller matrices and Stokes vectors. As a first particularization of this model, the Mueller matrix of a concrete tissue is decomposed by Lu-Chipman polar decomposition. This decomposition isolates the retardance, absorption and depolarization effects of the biological tissue. The first matrix can be assimilated to the equivalent liquid crystal exhibiting birefringence. A deeper study can show what the liquid crystal structure is like, in terms of particle form and alignment. As long as the scattering is weak, and so depolarization is sufficiently low, the tissue structure can be considered similar to the one of the equivalent liquid crystal. The analysis is applied to healthy porcine skin.

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In order to study these aspects, this work has been structured according to both effects. In section 2, we introduce liquid crystals. After briefly recalling the basic liquid crystal phases, birefringence will be analysed. In section 2.1 form birefringence is shown, while section 2.2 is focused on order-induced birefringence. After that, section 3 briefly summarizes the fundamental Jones matrices for several liquid crystals. In section 4, Mueller calculus as a way of characterizing biological tissues is studied, emphasizing the importance of Lu-Chipman decomposition. Section 5 develops an analysis of a biological tissue sample by means of the analogy with a liquid crystal. Finally, Section 6 constitutes a brief summary of all the previous sections.

2. LIQUID CRYSTALS PROPERTIES

Most substances exist in one of the three basis phases: solid, liquid, and vapor. The main difference between them is determined by the degree of positional order in the material. Liquid crystals are a state of matter whose particles present a state between the liquid phase and the crystalline structure. Liquid crystals molecules always show form anisotropy, usually having an ellipsoid of revolution shape. Therefore, it becomes necessary to take into account the orientational order of the molecules. The main characteristic of liquid crystalline phases is that they show high orientational order, while the positional order may entail some kind of limitation. As a result, three different types, phases or mesophases of liquid crystals can be defined: nematic, if there is a total lack of positional order (i.e. they show a completely random arrangement of particles); smectic, if the molecules exhibit a one-dimensional order (i.e. the centers of the molecules are set in parallel layers); and cholesteric, which is a special type of nematic crystal in which the molecules orientation helicoidally varies along a rotation axis. All these phases are shown in Figure 1.

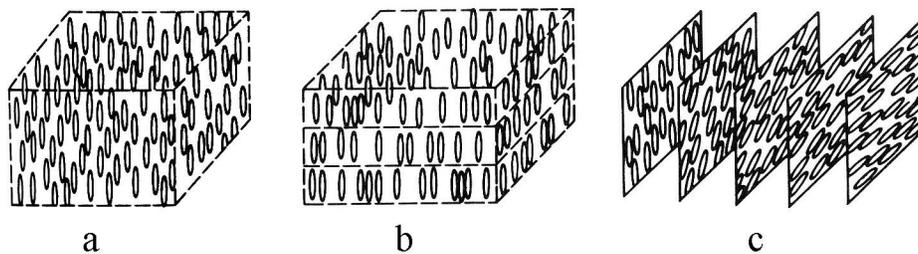


Fig. 1. Basic liquid crystal phases: a) Nematic, b) Smectic, and c) Cholesteric [4].

In this section, the fundamental optical birefringence properties of liquid crystals will be analysed. We assume a uniaxial liquid crystal texture composed of some kind of organic materials, such as polymers, which present an anisotropic behaviour due to their internal structure. The relationship between microscopic characteristics and macroscopic optical properties will be emphasized.

2.1 Form birefringence

Form birefringence occurs in media with two or more phases with different refractive indexes, and in which their constituent parts are small in comparison to the wavelength.

We will consider an isotropic medium with refractive index n_1 , with ellipsoidal particles of refractive index n_2 immersed in it. The material of the ellipsoid presents a susceptibility χ , and it is under a field that induces a dielectric polarization. The internal field varies with the permittivity of the particles and with their shape, which is included in depolarization factor Q . Relating polarization to the electric field by means of the electric permittivity and susceptibility, the following expression for the main refractive indexes of the media is obtained [5]:

$$\frac{n_a^2}{n_1^2} - 1 = \frac{f \left(\frac{n_2^2}{n_1^2} - 1 \right)}{1 + (1 - f) Q_\alpha \left(\frac{n_2^2}{n_1^2} - 1 \right)}, \tag{1}$$

where f is the filling factor, defined as the volume fraction occupied by the particles, and Q is the depolarization factor of the microscopic structure. Factor Q is a function of the particles shape. In a general situation, Q is different for

each one of the principal axes. However, in the case of revolution ellipsoids, there exists an uniaxial anisotropy that provokes a reduction of the possible different values of Q, thereby existing only two different values of Q instead of three, due to the symmetry properties of the material. The following table shows the value of Q for different types of particles.

Table 1. Depolarization factors for particles with different shapes.

Form	Depolarization factors
Cylinders, $m \gg 1$	$Q_o = 1/2$ $Q_e = 0$
Ellipsoids, $m > 1$	$Q_o = 1/2(1-Q_e)$ $Q_e = \frac{1}{m^2 - 1} \left(\frac{m}{\sqrt{m^2 - 1}} \operatorname{Ln} \left(m + \sqrt{m^2 - 1} \right) - 1 \right)$
Spheres, $m = 1$	$Q_o = 1/3$ $Q_e = 1/3$
Ellipsoids, $m < 1$	$Q_o = 1/2(1-Q_e)$ $Q_e = \frac{1}{1 - m^2} \left(1 - \frac{m}{\sqrt{1 - m^2}} \arccos(m) \right)$
Plates, $m \ll 1$	$Q_o = 0$ $Q_e = 1$

If the shape of the particles is known, it is possible to obtain the value of Q from the previous table. Introducing the filling factors and the refractive indexes in the equation, the ordinary and extraordinary refractive indexes of the uniaxial medium results.

2.2 Order-induced birefringence

The principal source of birefringence in liquid crystals and polymers is the ordered structure of the system. The orientational order measures the tendency of the molecules to align along the director vector of the system. Therefore, an order parameter S is defined, that quantifies the amount of orientational order within the system:

$$S = \frac{1}{2} \langle 3 \cos^2(\theta) - 1 \rangle, \quad (2)$$

being θ the angle between the particle and the optical axis. It is assumed that the local field is isotropic, and that $\epsilon = n^2$ as long as we are dealing with optical frequencies. If we consider an uniaxial symmetry, the average refractive index is defined as

$$\langle n^2 \rangle = \frac{1}{3} (n_e^2 + 2n_o^2). \quad (3)$$

This expression takes into account the local field correction. From this statement, the following equation results [5]:

$$\frac{n_e^2 - n_o^2}{\langle n^2 \rangle + 2} = \frac{\rho N_A}{3\epsilon_0 M} (\alpha_p - \alpha_s) S. \quad (4)$$

where α_p is the parallel molecular polarizability, α_s is the perpendicular molecular polarizability, N_A is the Avogadro number and ρ/M is the reciprocal molar volume. As it can be observed, the left term of the equation has a close relationship with the medium birefringence, and the term on the right is directly proportional to the orientational order parameter S. It can be concluded that it has been demonstrated that the birefringence of a liquid crystal depends on the orientational order, as well as the molecular polarizability anisotropy and the reciprocal modal volume.

3. JONES MATRIX CHARACTERIZATION OF LIQUID CRYSTALS

Jones calculus is a very useful technique for successfully analysing a wide range of situations, being an appropriate way to characterize liquid crystals, as long as normal incidence is maintained. For oblique incidence, the method can be used to some extent. However, it is not always valid, due to the fact that this method does not take into account some interference effects that entail a great importance for high angles, owing to Fresnel reflection in the interfaces. The method can be extended to oblique incidence by means of the extended Jones matrix. For more complex situations, it becomes necessary to make use of other calculus, like the Berreman method [5].

Jones calculus is the conventional technique for calculating the optical properties of birefringent multilayer media for normal incidence [6]. The global Jones matrix of a system composed of a series of concatenated devices can be obtained by the ordered matrixial product of the individual Jones matrices. In the following table, the Jones matrices for thin liquid crystal layers are shown for each of the four basic liquid crystal structures: homeotropic, planar, hybrid and twisted. These structures make it possible to characterize most of the liquid crystal combinations that can be found in any particular situation.

Table 2. Jones matrices for various liquid crystal textures.

Homeotropic	$J = \begin{bmatrix} e^{-\frac{2\pi i}{\lambda} n_o d} & 0 \\ 0 & e^{-\frac{2\pi i}{\lambda} n_o d} \end{bmatrix}$
Planar	$J = \begin{bmatrix} e^{-\frac{2\pi i}{\lambda} n_e d} & 0 \\ 0 & e^{-\frac{2\pi i}{\lambda} n_o d} \end{bmatrix}$
Hybrid	$J = \begin{bmatrix} e^{-\frac{2\pi i}{\lambda} n_{eff} d} & 0 \\ 0 & e^{-\frac{2\pi i}{\lambda} n_o d} \end{bmatrix}$ $n_{eff} = n_o \left(\frac{2}{\pi} \int_0^{\frac{\pi}{2}} \frac{1}{\sqrt{1 - R \sin^2(z)}} dz \right) \text{ and } R = \frac{n_e^2 - n_o^2}{n_e^2}$
Twisted (macroscopic twist angle Φ and input direction \mathbf{x})	$J = e^{i\frac{\pi d}{\lambda}(n_e + n_o)} \begin{bmatrix} a & b \\ -b^* & a^* \end{bmatrix}$ $a = \frac{\Phi}{\gamma} \sin \Phi \sin \gamma + \cos \Phi \cos \gamma - i \frac{\beta}{\gamma} \cos \Phi \sin \gamma$ $b = \frac{\Phi}{\gamma} \cos \Phi \sin \gamma - \sin \Phi \cos \gamma - i \frac{\beta}{\gamma} \sin \Phi \sin \gamma$ $\gamma = \sqrt{\beta^2 + \Phi^2} \text{ and } \beta = \frac{\pi d (n_e - n_o)}{\lambda}$

4. MUELLER MATRIX CHARACTERIZATION OF BIOLOGICAL TISSUES

Biological tissues present in general a very high degree of heterogeneity and then they depolarize the optical radiation when irradiated [1,10]. Due to this behaviour the Mueller matrices are the most useful tool in order to study polarization dependent interaction between light and tissues. The Mueller matrix has 16 elements, and they include all the polarization dependent properties of the tissue [7-9].

It is possible to extract precise information about the depolarization, retardance and diattenuation of a Mueller matrix by means of the so-called polar decomposition proposed by Lu and Chipman [11]. This method decomposes this

matrix in a product of three components, $M = M_{\Delta} \cdot M_R \cdot M_D$. The decomposition can be also carried out in a reverse form as suggested by R. Ossikovski, A. De Martino and S. Guyot [12], $M = M_D \cdot M_R \cdot M_{\Delta}$.

The calculation process of these decomposition components will be briefly described now. First of all, the diattenuation component is calculated. From the first row of the Mueller matrix, the diattenuation vector \vec{D} is obtained, and from its unitary vector and module, the submatrix m_D is constructed. The diattenuation matrix appears then as:

$$M_D = m_{00} \begin{bmatrix} 1 & \vec{D}' \\ \vec{D} & m_D \end{bmatrix}. \quad (5)$$

The calculus of the depolarization component M_{Δ} requires that of the submatrix m_{Δ} , that is carried out by the following expression:

$$m_{\Delta} = \varepsilon \left[m'(m')^t + (\sqrt{\lambda_1 \lambda_2} + \sqrt{\lambda_2 \lambda_3} + \sqrt{\lambda_1 \lambda_3}) I \right]^{-1} \cdot \left[(\sqrt{\lambda_1} + \sqrt{\lambda_2} + \sqrt{\lambda_3}) m'(m')^t + \sqrt{\lambda_1 \lambda_2 \lambda_3} I \right]. \quad (6)$$

With this equation, the final expression results:

$$M_{\Delta} = \begin{bmatrix} 1 & \vec{0}' \\ \vec{P}_{\Delta} & m_{\Delta} \end{bmatrix}. \quad (7)$$

The retardance matrix M_R can be calculated from the previous ones, and from this matrix several parameters like the total retardance R , the linear retardance δ , the optical rotation ψ and the fast axis orientation respect to the horizontal axis θ can be obtained [11].

An ideal and pure depolarizer, with null retardance and diattenuation, can be expressed by the following Mueller matrix:

$$\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & a & 0 & 0 \\ 0 & 0 & b & 0 \\ 0 & 0 & 0 & c \end{bmatrix}, \quad |a|, |b|, |c| \leq 1. \quad (8)$$

A natural consequence is that the component M_{Δ} from the Lu-Chipman decomposition will resemble to this matrix, but it will not be completely identical, due to the fact that in spite of the heterogeneous structure of biological tissues, in general samples measured do not behave like totally depolarizing media.

Due to this similarity, it is convenient to introduce a parameter, called depolarization power, which comes directly from a, b and c parameters. Like the entropy, it measures the depolarization introduced by the component M_{Δ} in a simpler way:

$$\Delta = 1 - \frac{|a| + |b| + |c|}{3}, \quad 0 \leq \Delta \leq 1. \quad (9)$$

5. BIOLOGICAL TISSUES MODELLING

All the aspects mentioned in the previous sections will now converge in a practical application: modelling a biological tissue by the analogy with a liquid crystal plate. The analysis will be applied to a porcine skin sample. Before performing the optical characterization of this sample, it is advisable to briefly review the basic structure and composition of skin [13]. Skin is a turbid medium that consists of two main layers: epidermis and dermis. Epidermis is the outermost layer of the skin. It is composed of stratified squamous epithelium, and it has an average thickness comprised between 0.07 and 0.12 mm. It has five layers: stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum and stratum germinativum or basal. Keratin has a key role in this layer. Stratum spinosum contains

developing keratin fibers, stratum spinosum has shrunken fibers of keratin, and stratum corneum is composed of many layers of keratinized dead epithelial cells. Dermis, in turn, is composed connective tissue. It has a thickness in the range of 0.5 mm to 3 mm, as there exists thin and thick skin. The average values are between 1 and 2 mm. It has two layers: the papillary layer, next to the epidermis and formed by loose connective tissue; and the reticular layer, made of dense connective tissue. Both of them have elastin and collagen fibers. The underlying hypodermis, formed by connective and adipose tissue, connects the skin with the deeper structures. Figure 2 comparatively shows all these layers for both thick and thin skin, except for the stratum lucidum, as it is a small clear layer, which is only visible in thick skin.

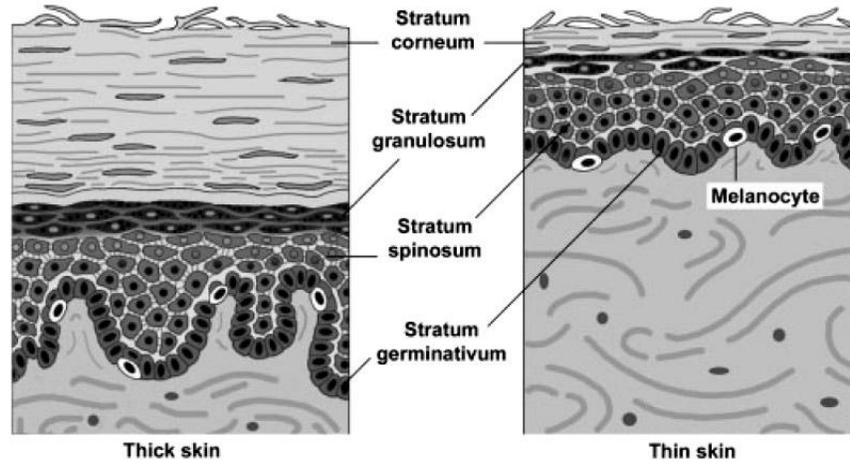


Fig. 2. Thick and thin skin structure [14].

The sample considered in this work corresponds to a healthy cutaneous region, without any pathologic alteration. We use a Mueller matrix measured in backscattering configuration for a wavelength of 550 nm with such a detection angle that the specular reflection is avoided [15]. This Mueller matrix completely characterizes the polarization behaviour of this undamaged skin region.

$$M = \begin{pmatrix} 1 & 0.045 & -0.036 & -0.004 \\ 0.045 & 0.268 & -0.033 & 0.008 \\ -0.021 & 0.034 & -0.289 & 0.0047 \\ 0.007 & -0.006 & -0.026 & -0.205 \end{pmatrix}. \quad (10)$$

This matrix contains all the information regarding the polarization behaviour of the sample, i.e., its effects on any incident optical radiation interacting with the tissue. Our main objective is to work on this matrix, performing the algorithms and processes needed to isolate its main effects and achieve a better understanding of its intrinsic behaviour. In order to achieve this purpose, the forward Lu-Chipman polar decomposition described in the previous section has been applied, giving the following matrices as a result:

$$M_D = \begin{pmatrix} 1 & 0.045 & -0.036 & -0.004 \\ 0.045 & 1 & -0.0013 & -0.0001 \\ -0.036 & -0.0013 & 0.9994 & 0.0001 \\ -0.004 & -0.0001 & 0.0001 & 0.9983 \end{pmatrix}, \quad (11)$$

$$M_\Delta = \begin{pmatrix} 1 & 0.045 & -0.036 & -0.004 \\ 0.045 & 1 & -0.0013 & -0.0001 \\ -0.036 & -0.0013 & 0.9994 & 0.0001 \\ -0.004 & -0.0001 & 0.0001 & 0.9983 \end{pmatrix}, \quad (12)$$

$$M_R = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0.0056 & -0.0007 \\ 0 & 0.0057 & -0.9981 & 0.0612 \\ 0 & -0.0003 & -0.0612 & -0.9981 \end{pmatrix}. \quad (13)$$

These are the diattenuation, depolarization and retardance components, respectively. Assuming that the scattering is weak, and so depolarization is sufficiently low, the retardance behaviour of the tissue structure can be considered similar to the one of an equivalent liquid crystal. Therefore, as a first approximation, the retardance component matrix can be assimilated to be equivalent to that of a liquid crystal exhibiting the same birefringence. This operation potentially enables to perform a deep analysis of the tissue microstructure by means of the analogy with liquid crystals.

Consequently, the retardance component Mueller matrix has been taken, checking that it verifies the physical realizability conditions, which implies that neither experimental errors nor processing errors have been produced. Once this verification has been made, we obtain the equivalent Jones matrix. This is possible as long as this matrix does not show depolarization effects, as a consequence of Lu-Chipman decomposition. Therefore, a direct relationship exists between the Mueller and Jones matrix of the retarder associated with the sample. The polar representation of the normalized Jones matrix obtained is

$$J_R = \begin{pmatrix} 1 & 0.0026 \cdot e^{j0.0306} \\ 0.0031 \cdot e^{j0.0306} & 1 \cdot e^{-j3.0804} \end{pmatrix}. \quad (14)$$

Comparing this matrix with the Jones matrix of the basic devices, it is clear that this matrix is very similar to that of a homogeneous linear retarder. Indeed, from the Lu-Chipman decomposition it is calculated that the linear retardance of the sample is 176.491° . The total retardance is the same, so it can be stated that this biological tissue does not show any elliptical retardance.

Birefringence consists of unequal retardance of orthogonal polarization components, which causes a phase shift between them. In skin, birefringence is caused mainly by the linear anisotropy shown by epidermis keratin and dermis collagen. These components are fibrous structures that are present in the extracellular matrix of connective tissue. Collagen fibers are arranged in an ordered way in the absence of pathologies, and this disposition shows a close relationship with the constituent parts of organic liquid crystals. Indeed, an analogy can be established between biological tissues and liquid crystals at a microstructural level, in terms of birefringence.

Due to the arrangement of collagen fibers, which are aligned in a parallel fashion in relation to the consecutive skin layers, the appropriate liquid crystal texture to work on an analogy basis is the planar texture. Biological fibrous structures are long cylindrical threads, which is in agreement with the typical liquid crystal constituents. Again, a direct correspondence is observed between both media [16]. The Jones matrix of the liquid crystal texture proposed here is, in its normalized expression, the following:

$$J = \begin{bmatrix} 1 & 0 \\ 0 & e^{-\frac{2\pi i}{\lambda}(n_e - n_o)d} \end{bmatrix}. \quad (15)$$

Comparing (14) and (15), we obtain that $-\frac{2\pi}{\lambda}(n_e - n_o)d = -3.0804$, and, particularizing for a wavelength of 550 nm, with which the measurement was performed, it is calculated that $(n_e - n_o)d = 2.696 \cdot 10^{-7}$. As it can be seen, in this equation it is necessary to fix whether the birefringence or the thickness. Given a value of $\Delta n = n_e - n_o = 1.5 \cdot 10^{-3}$ for the birefringence, which is in agreement with the typical values registered for porcine skin, it is obtained that the equivalent planar liquid crystal plate has a thickness of 0.09 mm. It has been taken into account the fact that the matrix has been measured in a backscattering configuration, so that the distance undergone by the light beam is twice the thickness. Therefore, it can be stated that the biological tissue microstructure responsible for the birefringent behaviour of the sample can be modelled by a liquid crystal plate that consists of long cylindrical particles arranged parallel to the plate surface. It is important to note that the extraordinary refraction index is higher than the ordinary refraction index, which

corresponds to a positive uniaxial medium. This corroborates the results, as the extraordinary index for liquid crystals with cylindrical particles is always higher than the ordinary index.

6. CONCLUSION

In this work, an innovative optical model of biological tissues has been presented. It is based on the analogy between the biological microstructures exhibiting anisotropy and the characteristics of liquid crystals. The main properties of liquid crystals have been revised, as well as the application of Jones calculus to their characterization in terms of polarization behaviour. Next, Mueller calculus and Lu-Chipman decomposition have been studied, as they are powerful mathematical tools that enable us to completely characterize and analyse biological tissues. Finally, we have presented a brief example of this model, in which an analogy between a porcine skin sample and a planar liquid crystal texture is based on the microstructural parallelisms between them.

The model presented in this work is useful as long as the changes affecting its structure could be used to make a diagnosis on the pathological or healthy state of the biological tissue under test. It is clear that polarization properties of light interacting with biological tissues strongly depend on tissue structure. As in conventional medical morphology diseases are diagnosed based on histological samples tissue structure alterations, the fact that this will be reflected in polarization information makes it a good diagnostic tool. Indeed, the differences in the structure, resulting from pathological processes and mainly due to the absence of regularity in collagen fibers, are reflected in the equivalent liquid crystals, in such a way that the lesion could be detected. The analysis could be applied to porcine skin, both healthy and damaged by optical radiation. The procedure, applied here to a Mueller matrix coming from a point, could also be extended to 2D surface Mueller matrix measurements or even to 3D tomographic techniques like PS-OCT, providing a complementary contrast parameter in tissue diagnosis.

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