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Biomedical Optical Applications of Liquid Crystal Devices

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Liquid crystals exhibit large electro-optic effects which make them useful for a variety of applications as fast, compact, and tunable spectral filters, phase modulators, polarization controllers, and optical shutters. They were largely developed for liquid crystal displays and in the last decade for optical telecommunications, however their application in the field of optical imaging just started to emerge. These devices can be miniaturized thus have a great potential useful in miniature optical imaging systems for biomedical applications. Using a collection of tunable phase retarders one can perform:
1. Stokes parameters imaging for skin and eye polarimetric imaging;
2. Tunable filtering to be used for hyperspectral imaging, fluorescence microscopy, and frequency domain optical coherence tomography;
3. Adaptive optical imaging and eye aberrations correction;
4. Phase shift interferometric imaging;
5. Variable frequency structured illumination microscopy. Basic optics of liquid crystals devices is reviewed and some novel designs are presented in more detail when combined to imaging systems for a number of applications in biomedical imaging and sensing.

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1. Introduction

Biomedical optical imaging [1] is noninvasive and able to create contrast not only by intensity, but also through several other properties, such as wavelength, polarization, coherence, lifetime, and nonlinear effects. Imaging methods that take advantage of one or more of these attributes can be combined for complementarity or even synergy. The light microscope, an icon of the sciences, is a highly versatile instrument with applications in fields as diverse as molecular biology, neuroscience, forensics, surgical pathology, silicon wafer inspection, or art conservation. The convergence of advances in hardware (e.g., video, solid-state cameras,

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micro-positioning, lasers and computers) and today's ability to manipulate living systems (e.g., to produce genetically encoded probes) has transformed what was previously a static, two-dimensional visualization instrument into a dynamic, four-dimensional research tool. Better light sources and detectors have enabled the introduction of such elegant methods as confocal scanning, optical coherence tomography (OCT), multiphoton microscopy, and digital data handling has allowed deconvolution and enhancement of complex images. Optical imaging is now capable of monitoring cellular and subcellular activities, all the way down to single molecular events, digitally and quantitatively. Indeed, the information which can be gathered with this vast range of intensities (about 12 orders of magnitude), of time (femtoseconds to years) and of space (nanometers to centimeters), as well as the resolution within these ranges of optical imaging is mind boggling.

Enabling technologies such as liquid crystal (LC) devices that can be integrated into imaging system can enhance different imaging modalities. Liquid crystals are birefringent materials that exhibit large electro-optic effects making them useful for variety of applications as fast, compact, and tunable spectral filters, phase modulators, polarization controllers, and optical shutters [2]. They can be incorporated into optical microscopes and other imaging tools to enhance their performance such as tunable filters for fluorescence and hyperspectral imaging, as polarization controllers for polarimetric imaging and as intensity or phase modulators for adaptive optical imaging. In this paper we give short overview of LCs as enabling technology for enhancement of different optical imaging modalities.

2. Basic LC devices

Liquid crystals are birefringent materials that exhibit strong response to an applied electric field via their large dielectric anisotropy or in some cases via the spontaneous dipole moment when ferroelectric LCs (FLCs) are used [2]. Figure 1a summarizes the important thermotropic LC phases usually used in LC devices. The dielectric coupling between the LC molecules and an applied electric field is such that the molecules tend to align parallel to the field when the dielectric anisotropy is positive and perpendicular to the field when it is negative. The ferroelectric coupling is such that the dipoles tend to align along the field direction. Many effects arise depending on the way the LC are anchored to the boundaries. Nonuniform structures can evolve during the field application or spontaneously due to the boundary conditions, for example the twisted nematic structure frequently used in displays.

The simplest LC device structure is shown in Fig. 1b when the LC is between two glass substrates coated with transparent conductive oxide (TCO) and alignment layers. In this figure a uniform nematic LC is shown with the molecules oriented at an average direction $\hat{n} = (\cos\theta\cos\phi, \cos\theta\sin\phi, \sin\theta)$ as described in Fig. 1c.

As a field is applied the polar and azimuth angle θ, ϕ can vary, however for the homogeneously aligned nematic LC and the field applied along z, the molecules

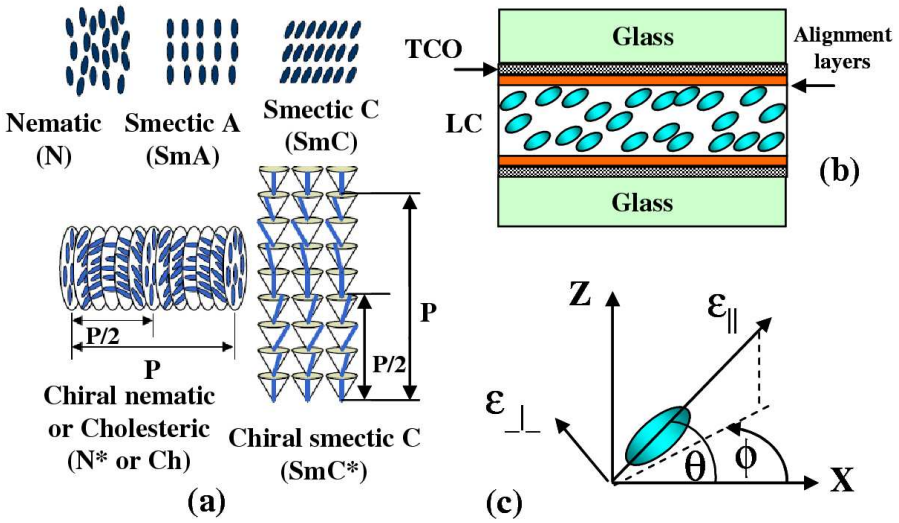

Fig. 1. Schematic of: (a) main thermotropic LC phases, (b) LC device, and (c) orientation of principal axis of the dielectric tensor.

rotate in the xz plane thus varying $\theta(z)$, while $\phi = 0$. The ordinary and extraordinary eigenwaves can be excited depending on the incident light polarization. The ordinary wave undergoes a constant phase variation $\varphi_{\mathrm{o}} = 2\pi n_{\mathrm{o}} d/\lambda$, where d is the LC thickness and λ is the wavelength. The extraordinary wave undergoes phase variation that depends on the applied electric field which in first approximation can be written as

$$\varphi_{\mathrm{e}} \approx \frac{2\pi}{\lambda} \int_0^d \frac{\sqrt{\varepsilon_{\parallel}\varepsilon_{\perp}}}{\sqrt{\varepsilon_{\perp} + (\varepsilon_{\parallel} - \varepsilon_{\perp}) \sin^2 \theta(z)}} \mathrm{d}z. \tag{1}$$

Hence if the incident light polarization is along the x axis, phase-only modulation is obtained while at any other polarization direction, a polarization modulation is obtained which can be converted into intensity modulation when the device is between two polarizers. This is the essence of the LC retarder upon which many devices are based such as phase, polarization and intensity modulators and tunable filters.

3. LC devices in biomedical optics

Liquid crystal devices can be incorporated in biomedical optical imaging systems in variety of ways for example as polarization controllers for polarimetric imaging, as tunable filters for hyperspectral imaging, by operation called frequency domain OCT (FD-OCT) [3], and fluorescence imaging, as phase masks for aberration corrections, as phase modulators for phase shift interferometric imaging, as adaptive lens, as shutters and variable fringe projection imaging. Figure 2 shows a good example of imaging system, the interferometric Linnik microscope [4, 5]. It

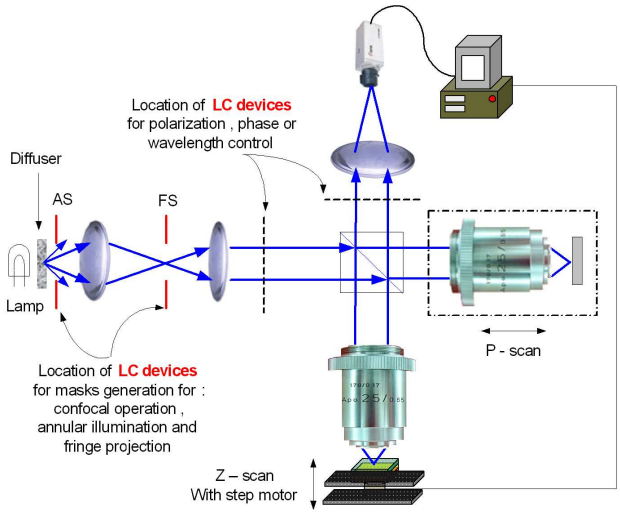

Fig. 2. Example of multi-functional optical imaging system enhanced by the incorporation of LC devices.

can be used as standard microscope when the reference path is blocked and it can be used as full field OCT system for deep imaging of biological tissue. Possible incorporation of LC devices is shown in the figure where for phase masks the LCD can be placed in the aperture plane of the illumination system. Similarly intensity mask can be placed in the plane of the field stop for structure light illumination and fringe projection imaging. For polarization and wavelength control two devices should be placed, one in the illumination path and one in the imaging path in planes where the beam is collimated to minimize aberrations. For FD-OCT one tunable filter is adequate either in the illumination or in the imaging paths. For phase shift imaging one phase modulator will be placed either in the reference or in the sample path. In what follows we give some more details on the integration of LC devices into imaging systems.

3.1. LC tunable filters applications in biomedical optical techniques

Polarization birefringent filters existed since the beginning of the 19th century since they allowed very narrow-band (sub-Angstrom) filtering useful for studies of solar and astrophysical spectra. The best known of these are the Lyot–Ohman (L–O), the folded-Solc (FoS), and the fan-Solc (FaS) configurations [6–8]. Leroy [9] has shown that with some arrangement of the orientations of the wave plates in folded Solc filter one obtains transfer function equivalent to that of L–O filter. Yeh [10] proposed to use iso-index materials with these filters to increase the angular field of view. Lyot [6] and Evans [11] proposed an L–O type filter with wider angular field of view. Lately [12] the present author has proposed a reflective type filter with polarization conversion based on Solc structure combined with one-dimensional photonic crystal. He also generalized [13] the fan-Solc filter

and found that several different twist configurations can lead to the same transfer function. Unique optical properties of helicoidal LCs were found to arise when the LC is inside a Fabry–Perot cavity including polarization independence of the transfer function [14]. The interest in liquid crystal tunable filters (LCTFs) using the above concepts was stimulated from their potential use in displays [15, 16] and telecommunications [17]. The integration of LCTFs into imaging systems has emerged recently [18].

The addition of a LCTF to such system will add additional dimension, the spectral dimension that will enrich the information content of the images and help optimize the wavelengths used for the specific application. One of the recently incorporated modes of operation is FD-OCT where the partially coherent light is decomposed spectrally and Fourier transformed to reveal the depth section of the object. The use of LCTF with FD-OCT is more compact and cheaper than a spectrometer.

LCTFs can be incorporated into hyperspectral imaging (HSI) system with properties designed to be optimum for the specific application [19]. For example, one medical area not fully exploited with hyper-spectral imaging is in the eye research where images of the retina with large information content can have advantage over present retinal techniques. In other medical applications HSI is emerging as a new means of early or more sensitive detection of changes in tissue that can be used to define pathology, predict clinical outcomes and adapt therapy. Figure 3 demonstrates one example of multi-spectral imaging combined with some image processing. The difference image shows clear details of blood vessels.

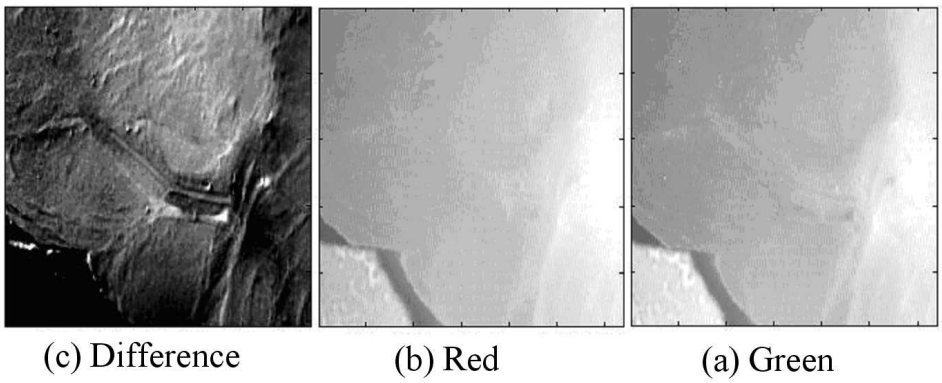

Fig. 3. Demonstration of the advantage of using different spectral filters for biological imaging. The images taken are for scattered light from chicken thigh at nearly 40 deg incidence angle with polarizer in front of the light source and crossed polarizer in front of the camera.

3.2. LC devices with applications for polarimetric imaging

Tissue optical properties at the visible and near infrared wavelengths are dominated by multiple scattering that greatly complicates biomedical optics studies. Polarimetric imaging involves grabbing images at different polarization states to enhance contrast of images especially when the imaged medium is a scattering medium such as tissue that partially depolarizes the incident light beam. Ideally for complete description of the polarization state four images are required corresponding to the four Stokes parameters [20], $S^{\mathrm{T}} = (S_0, S_1, S_2, S_3)$. In polarimetric imaging one image or more of the Stokes parameters S_1, S_2, S_3 are grabbed. When S_1, S_2, or S_3, alone are measured, it is called polarization difference imaging (PDI). The incident and scattered light Stokes vectors are related through the 4×4 Müeller matrix M, which depends on the sample: $S_{\mathrm{out}} = MS_{\mathrm{in}}$.

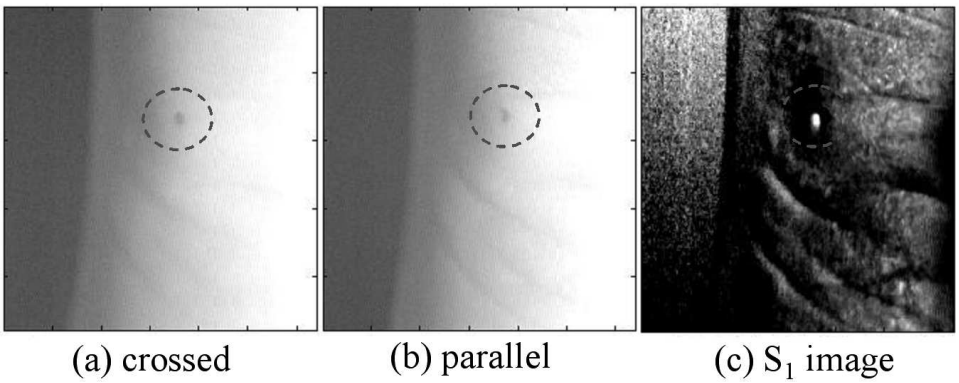

Fig. 4. Polarimetric images of human finger with a strange body (circled) under the skin polarizers (a) crossed, (b) parallel, and (c) Stokes image S_1.

There are several techniques for achieving images of the Stokes parameters that usually involve the use of passive or active polarization components. The polarization manipulation can be done with the addition of 2–3 components to the imaging system such as polarizer, analyzer, and compensator or retarder. The configuration of polarizer–compensator–analyzer (PCA) has been used for Müeller matrix determination with null ellipsometry from scattering media [21]. The two polarizers scheme was improved recently [22], to determine the Müeller matrix elements. It was shown that 49 intensity measurements with various orientations of polarizer and analyzer allow the determination of the 16 elements of the Müeller matrix of scattering media. The two rotating quarter wave plates technique is based upon an operational principle, which involves the modulation of a polarization state for both probing and outcoming light beams as suggested earlier by Azzam [23]. The time-resolved polarimetric imaging technique uses short pulses and time gating to distinguish between multiply scattered and weakly scattered photons where each has a different degree of polarization [24]. Several techniques

have been studied to differentiate between weakly scattered and multiply scattered photons. Because multiply scattered photons usually have greater path lengths, they can be rejected with time gating [25]. The complete determination of the Müeller matrix elements or the 4 Stokes parameters in OCT was demonstrated using a polarizer, half-wave plate, and quarter-wave plate in the illumination while using a variable wave plate in the reference channel [26]. Lately [27], determination of Stokes parameters was done with FD-OCT using polarizer and polarization modulator in the illumination and a polarizing beam splitter at the output. In Fig. 4 we present polarimetric images of human finger with an under skin body showing that the Stokes image gives the best result with a 3D tomographic view of the skin. This can be achieved fast and reliably with LC retarders combined with a scatterometric imaging system, a work that is planned to be published in the near future [28].

Acknowledgments

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