

Diagnostic photomedicine: probing biological tissues with polarized light

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Extract, quantify, and interpret intrinsic tissue polarimetry characteristics using a novel Mueller matrix decomposition approach.

The polarization parameters of light scattered from biological tissue contains rich morphological and functional information of significant biomedical importance. Effectively probing optically-thick turbid media, such as tissues, is challenging due to multiple scattering and the simultaneous occurrence of many polarization effects. These include difficulties in obtaining accurate measurements as well as the extraction and correct interpretation of the constituent polarization parameters. A method that can account for the effects of multiple scatterings and decouple the contributions of polarization effects is needed for the practical application of these probing techniques in a biomedical setting.

Mueller calculus is a mathematical matrix method used to model the transformations of the polarization state of light in its interactions with an optical system. Therefore, a Mueller matrix description contains complete information about all the polarization properties of a given medium. However, when many optical polarization effects occur simultaneously (as is the case of tissues where the most common polarimetry effects are depolarization, linear birefringence, and optical activity), the resulting matrix elements reflect several 'lumped' effects, thus hindering their unique interpretation. Each of these, if separately extracted, holds promise as a useful biological metric. For example, chirality-induced optical rotation can be linked to the glucose concentration of the medium, and changes in tissue mechanical anisotropy (resulting from disease progression or treatment response) can be extracted by birefringence measurements. We have developed and validated an expanded Mueller matrix decomposition approach to delineate the individual intrinsic polarimetry characteristics in complex tissue-like turbid media.

Our method treats a 'lumped' system Mueller matrix \mathbf{M} as the product of three constituent 'basis' matrices,^{1,2}

$$\mathbf{M} = \mathbf{M}_{\Delta} \cdot \mathbf{M}_{\mathbf{R}} \cdot \mathbf{M}_{\mathbf{D}}$$

where a depolarizer matrix \mathbf{M}_{Δ} accounts for the depolarizing effects of the medium, a retarder matrix $\mathbf{M}_{\mathbf{R}}$ describes the effects of linear birefringence (or linear retardance) and optical activity, and a diattenuator matrix $\mathbf{M}_{\mathbf{D}}$ includes the effects of linear and circular dichroism.² Once calculated, these constituent matrices are further analyzed to derive individual polarization medium properties, namely, linear retardance (δ , and its orientation angle θ), optical rotation (Ψ), diattenuation (d), and the depolarization coefficient (Δ).²

In addition, we have also developed a polarization-sensitive forward Monte Carlo (MC) model capable of simulating all of the simultaneous optical scattering and polarization effects.³ This model is supplemented by a high-sensitivity polarization modulation/synchronous detection experimental system that is capable of measuring the complete Mueller matrix from tissues and tissue-like turbid media.^{2,3} These three methodologies form a comprehensive turbid polarimetry platform (Figure 1).

We experimentally validated our approach using optical phantoms that had controlled sample-polarizing properties.² To develop the phantoms, we used polyacrylamide as a base medium with polystyrene microspheres to create turbidity, sucrose to induce optical activity, and mechanical stretching to cause linear birefringence. Additional validation tests were performed using MC-generated Mueller matrices. The derived polarization parameters were in excellent agreement with the controlled inputs, showing self-consistency in inverse decomposition analysis and successful decoupling of the individual polarization effects.²

The initial biomedical application of this approach was monitoring myocardial tissue regeneration following stem-cell

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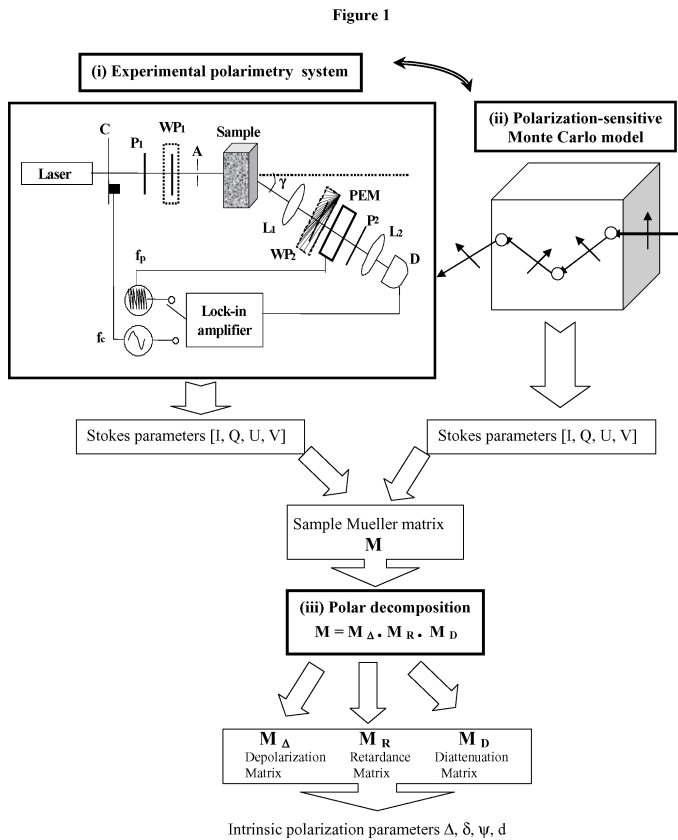


Figure 1. Schematic of the turbid polarimetry platform: (i) experimental system based on polarization modulation and phase-sensitive synchronous detection, (ii) polarization-sensitive Monte Carlo simulations for forward modeling of simultaneous polarization effects in the presence of turbidity, and (iii) the polar decomposition of the Mueller matrix to inverse calculate the constituent polarization contributions in a complex turbid media. See reference 2 for details.

therapy. The anisotropic organized nature of myocardial tissues stemming from their fibrous structure leads to linear birefringence. Upon suffering an infarction, a portion of the myocardium is deprived of oxygenated blood and subsequently cardiomyocytes die, replaced by disorganized isotropic scar tissue. Recently, stem-cell-based regenerative treatments for myocardial infarction have been shown to reverse these trends by increasing the muscular constituents and decreasing the scar tissue components.⁴ These remodeling processes likely affect tissue structural anisotropy, and the newly developed Mueller matrix decomposition method may offer a sensitive probe into the small birefringence alterations that are signatures of regenerative treatments.⁵ Using the experimental setup, polarized light measurements through 1mm thick ex vivo myocardial samples from Lewis rats after myocardial infarction, both with and

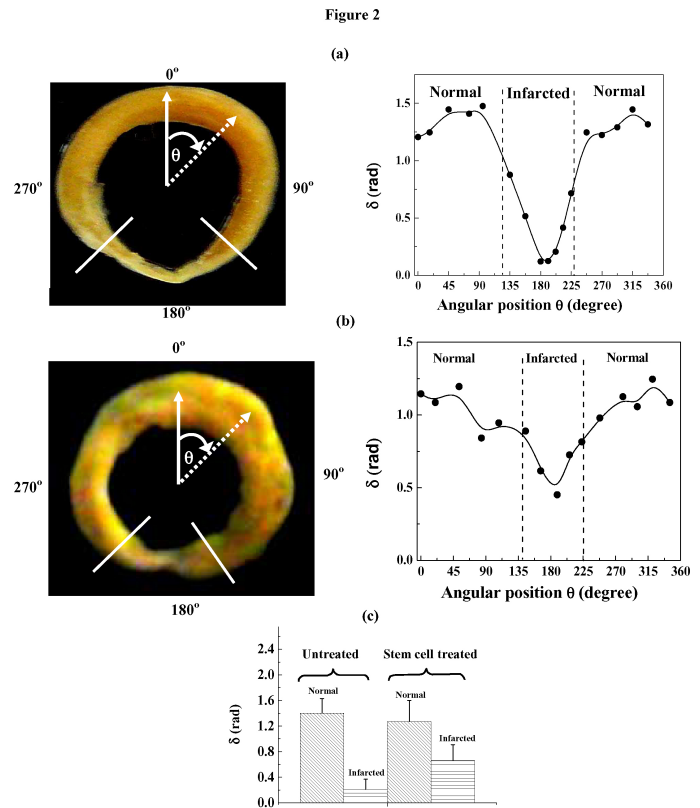


Figure 2. Linear retardance (δ) derived from transmission polarization measurements in 1mm-thick sections from Lewis rat hearts following myocardial infarction. (a) Untreated tissues and (b) tissues following stem-cell treatments (two weeks after treatment). The marked sector around $\theta = 180^\circ$ indicates the infarcted region. The derived birefringence parameters from the controls and the stem-cell treated groups of infarcted hearts are shown in the histogram (c).

without stem-cell treatments, yielded the measured Mueller matrices. These were analyzed using polar decomposition to obtain linear retardance (δ) values as shown in Figure 2. As expected, a large decrease in δ was seen in the infarcted region of the untreated myocardium (Figure 2a). An increase in δ towards native levels was seen in the infarcted region after stem-cell treatment (Figure 2b), indicating regrowth and reorganization of the myocardium. Statistically significant ($p < 0.05$) differences in derived retardance values were observed between normal and infarcted regions and between infarcted regions with and without stem-cell treatments (Figure 2c). These results show significant promise for polarized light monitoring of stem-cell-based treatments following myocardial infarction.

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To conclude, a novel method for polarimetry analysis of turbid media based on polar Mueller matrix decomposition has been developed and validated. The ability to isolate individual polarization properties in complex turbid media (such as tissues) provides a valuable noninvasive tool for their characterization. In the biological domain, quantification of tissue structural anisotropy and concentration determination of optically active molecules, such as glucose, are two potential applications that have been initially explored, with early indications showing promise and warranting further studies. We are currently expanding our investigations in these biomedical directions, including extending this novel method towards clinical application.

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References

1. S. Yau Lu and R. A. Chipman, *Interpretation of Mueller matrices based on polar decomposition*, *J. Opt. Soc. Am. A* **13**, pp. 1106–1113, 1996.
2. N. Ghosh, M. F. G. Wood, and I. A. Vitkin, *Mueller matrix decomposition for extraction of individual polarization parameters from complex random media exhibiting multiple scattering, optical activity and linear birefringence*, *J. Biomed. Opt.* **in press**, 2008.
3. M. F. G. Wood, X. Guo, and I. A. Vitkin, *Polarized light propagation in multiply scattering media exhibiting both linear birefringence and optical activity: Monte Carlo model and experimental methodology*, *J. Biomed. Opt.* **12**, p. 014029, 2007.
4. D. Orlic, J. Kajstura, S. Chimenti, I. Jakoniuk, S.M. Anderson, B. Li, J. Pickel, R. McKay, B. Nadal-Ginard, D.M. Bodine, A. Leri, and P. Anversa, *Bone marrow cells regenerate infarcted myocardium*, *Nature* **410**, pp. 701–705, 2001.
5. N. Ghosh, M. F. G. Wood, S.H. Li, R. D. Weisel, B. C. Wilson, R. K. Li, and I. A. Vitkin, *Mueller matrix decomposition for polarized light assessment of complex turbid media such as biological tissues*, *Journal of Biophotonics* (accepted).