Development of single input
polarization-sensitive optical coherence
tomography, towards local birefringence imaging
with high resolution and lower cost

Xiong, Qiaozhou

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**Development of single input polarization-sensitive
optical coherence tomography, towards local
birefringence imaging with high resolution and lower
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Qiaozhou Xiong

School of Electrical & Electronic Engineering

2019

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cost**

Qiaozhou Xiong

School of Electrical & Electronic Engineering

A thesis submitted to the Nanyang Technological University in
partial fulfillment of the requirement for the degree of Doctor of
Philosophy

2019

Statement of Originality

I hereby certify that the work embodied in this thesis is the result of original research, is free of plagiarised materials, and has not been submitted for a higher degree to any other University or Institution.

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XIONG QIAOZHOU

Supervisor Declaration Statement

I have reviewed the content and presentation style of this thesis and declare it is free of plagiarism and of sufficient grammatical clarity to be examined. To the best of my knowledge, the research and writing are those of the candidate except as acknowledged in the Author Attribution Statement. I confirm that the investigations were conducted in accord with the ethics policies and integrity standards of Nanyang Technological University and that the research data are presented honestly and without prejudice.

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27/07/2019

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LIU LINBO

Authorship Attribution Statement

This thesis contains material from 2 papers published in the following peer-reviewed journal where I was the first author.

Chapter 2 was published as Q. Xiong, N. Wang, X. Liu, et al, Single input state polarization-sensitive optical coherence tomography with high resolution and polarization distortion correction, Opt. Express 2019 10.1364/OE.27.006910

The contributions of the co-authors are as follows:

- AP. Linbo Liu suggested the initial direction of the project and helped review the manuscripts.
- I originated the idea and built the system, carried out experiments and numerical simulations.
- I wrote the first draft of the manuscripts. I and Mr. Nanshuo Wang revised it several rounds after reviewed by AP. Liu.
- Dr. Nanshuo Wang improved data visualization.
- Ms. Si Chen, Mr. Haitao Liang helped with the tissue preparation.
- Dr. Xinyu Liu, Ms. Sichen, and Mr. Haitao Liang helped review the draft.

Chapter 3 and part of chapter 4 and 5 were published as Q. Xiong, N. Wang, X. Liu, et al (2019). Constrained polarization evolution simplifies depth-resolved retardation measurements with polarization-sensitive optical coherence tomography. Biomedical Optics Express, 10(10), 5207. <https://doi.org/10.1364/boe.10.005207>

The contributions of the co-authors are as follows:

- AP. Linbo Liu helped review the manuscripts and led the project.
- Dr. Martin Villiger developed the theoretical explanation for the

constraint, edited the manuscripts and led the project.

- I built the system, carried out all experiments and numerical simulations. I helped edit and revise the manuscripts.
- Dr. Nanshuo Wang worked with data visualization. Also, he helped edit and revise the manuscripts and the theoretical deduction.
- Dr. Xinyu Liu was the first person to observe the mirror state constraint phenomenon. He helped with experiment and he helped edit and revise the manuscripts.
- Others helped with the tissue preparation or manuscripts proofreading.

27-July-19

27-07-2019

Xiong

XIONG QIAOZHOU

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When hesitating whether I should continue the Ph.D. study, Ph.D. was often ridiculed. as “permanent head damage”. It represents the reverence towards Ph.D. study. On the other hand, it’s a great opportunity to polish our creative thinking, critical reasoning, etc. Now the past four years is like the smoke through the keyhole to me. There were many struggles, but more happiness and growth.

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Summary

Optical coherence tomography (OCT), as a non-invasive imaging method, has been established as a standard diagnostic technology in clinics during the last 25 years. The current OCT can provide depth-resolved imaging, but lacks property resolved information and does not have enough spatial resolution to resolve micrometer scale structures. To address the former issue, polarization-sensitive OCT (PS-OCT) has been developed as a powerful technology to evaluate the distribution of collagen fibers, smooth muscle cells, nerve fibers, etc., which exhibit birefringence, an optical property leading to delay between light polarized in orthogonal directions. PS-OCT can be categorized into single input PS-OCT and multiple inputs PS-OCT according to the number of input polarization states. Single input PS-OCT has been widely applied in many fields such as ophthalmology, cardiology, and dermatology, due to its simplicity. To address the latter issue, ultrahigh resolution OCT and Micro-OCT have been developed to resolve cellular and subcellular structures relevant to disease diagnosis.

My research aims to develop theoretical frameworks and novel instrumental methods for the realization of single input PS-OCT with high resolution. Intuitively, it's straightforward to achieve ultra-high resolution in PS-OCT. However, broad bandwidth which is essential for ultra-high resolution magnifies the effects of imperfect polarizing elements and the fall-off imbalance of dual spectrometers for polarization diverse detection. In this thesis, based on Jones matrix formalism, the polarization distortions were modeled and calibrated. The proposed method yields lower polarization distortion and provides more reliable contrasts especially when the sample birefringence is weak. The polarization distortion correction was demonstrated with tissue phantoms as well as animal tissues.

On the other hand, single input PS-OCT usually cannot provide local birefringence imaging, which is more intuitive than its accumulative counterpart. Enabling local birefringence imaging using single input would alleviate the hardware requirements of PS-OCT and would enable more

widespread exploration of this compelling contrast mechanism. This simplification is possible with the mirror state constraint discovered in this work: the polarization state of backscattered or reflected light, when measured through identical illumination and detection paths, frequently evolved through the employed input polarization state but with reversed handedness, corresponding to the input state mirrored by the horizontal plane of the Poincaré sphere. We validated this constraint both theoretically and experimentally using technical phantoms of known birefringence. I further successfully demonstrated the local retardation imaging with single input PS-OCT both in free-space and fiber-based implementations with the mirror state constraint. Phantom imaging and animal ocular tissue imaging *ex vivo* were performed to validate the performance and clinic potential.

An important application of the mirror state constraint is to realize single input polarization-sensitive intravascular optical frequency domain imaging (OFDI), where the illumination polarization state changes when propagating through a rotating catheter which mandates two polarization inputs. Achieving reliable measurements of local retardation with single input polarization state will be of great commercial interest. We demonstrate the reliability of the single input processing with Bland Altman analysis when comparing the results with multiple input PS OFDI.

In conclusion, this thesis research advances the field in the following aspects. It provides working methods to correct the polarization distortions in the high-resolution PS-OCT for the first time; this thesis research also elucidated the polarization evolution trace along with the depth in the back-scattering system and established the mirror state constraint, a novel theoretical framework. This thesis further uses this constraint to enable local birefringence imaging using single polarization input in both free-space and fiber-based systems and demonstrates single input polarization sensitive intravascular OFDI with performances comparable to the dual inputs benchmark.

List of Abbreviations

ABS	Acrylonitrile Butadiene Styrene
AOM	Acousto-Optic Modulator
BS	Beam Splitter
CCD	Charge-Coupled Device
DFT	Discrete Fourier Transform
DOP	Degree of Polarization
FD-OCT	Fourier Domain Optical Coherence Tomography
FWHM	Full Width at Half Maximum
IVOCT	Intravascular Optical Coherence Tomography
OCE	Optical Coherence Elastography
OCT	Optical Coherence Tomography
OFDI	Optical Frequency Domain Imaging
ONH	Optical Nerve Head
PBS	Polarizing Beam Splitter
PDD	Polarization Diversity Detection
PMD	Polarization Mode Dispersion
POM	Polarization Modulator
PS-OCT	Polarization-Sensitive Optical Coherence Tomography
PS-OFDI	Polarization-Sensitive Optical Frequency Domain Imaging
PS- μ OCT	Polarization Sensitive Micro Optical Coherence Tomography
PSF	Point-Spread Function
QWP	Quarter Wave Plate
HWP	Half Wave Plate
SD-OCT	Spectral Domain Optical Coherence Tomography
SEES-OCT	Spectrally Encoded Extended Source OCT
SLD	Superluminescent Diode
SMF	Single Mode Fiber
SNR	Signal-to-Noise Ratio
SS-OCT	Swept Source Optical Coherence Tomography
UHR-OCT	Ultra-High-Resolution Optical Coherence Tomography
μ OCT	Micro Optical Coherence Tomography

Chapter 1 Introduction and background

1.1 Introduction

1.1.1 Optical coherence tomography background

Visualization of three-dimensional tissue structures *in vivo* is required to understand and diagnose human diseases. Conventional biomedical imaging methods, such as computed tomography (CT), ultrasound, and magnetic resonance imaging (MRI) are widely used in disease diagnosis and research. Although these techniques are able to generate three-dimensional images of the human body, their resolutions are limited to tens or hundreds of micrometers, which is not enough to capture cellular level images [1]. However, many diseases cannot be diagnosed easily by these technologies. In these cases, the cellular level resolution is vital for early diagnosis of several severe symptoms.

More than two decades ago, optical coherence tomography (OCT) was first proposed as a non-invasive, three-dimensional, high-resolution imaging modality. The spatial resolution of OCT is 10-15 μm , which improves the parameter of traditional imaging methods by one or two orders in magnitude, compared to MRI or ultrasonic image, etc [2], [3]. With such a high resolution and a penetration depth a few millimeters, OCT promises a technology of ‘optical biopsy’, to replace conventional excisional biopsy and histopathology [4]. **Figure 1.1(a)** shows the comparison of OCT and current image methods. It has been considered as a promising technology for visualizing cellular level fine structures ever since.

Figure 1.1. Current status of OCT and PS-OCT categorization. a. Diagram of comparison of the current image method. b. basic schematic of Fourier domain OCT. c. schematic of conventional single input PS-OCT. d. schematic of multiple input PS-OCT via polarization modulator. LS: laser source; BS: beam splitter; GV: galvanometers; L: lens; SAM: sample; RM: reference mirror; DU: detection unit; P: polarizer; QWP: quarter-wave plate; PBS: polarizing beam splitter; POM: polarization modulator.

The evolution of OCT devices from time domain (TD-OCT, the first generation technology) to Fourier domain OCT (FD-OCT, second generation technology), achieved a ~ 20 dB sensitivity improvement and ~ 100 times imaging speed boosting [5]–[8]. An exemplary Fourier-domain OCT (FD-OCT) setup is illustrated in **Figure 1.1(b)**. The setup is generally a Michelson Interferometer. FD-OCT can be categorized into two types: spectral domain OCT and swept source OCT based on the laser source and detection. Spectrometer domain OCT utilizes a continuing-wavelength broadband laser source and a grating-based spectrometer to acquire the signal while the swept source domain OCT uses a rapidly tunable broadband laser and a photodetector [5]–[8]. The output of a broadband light source or swept source is divided by a beam splitter into a sample arm and a reference arm. The sample light illumination is directed or guided to

the tissue sample through focusing optics. Backscattered light is generated through the interaction between the sample light and tissue sample of all depths. This backscattered light radiation is directed by the same focusing optics back towards the beam splitter. The reference light radiation is guided to a reference mirror and reflected towards the beam splitter. The light back reflected from the reference arm mirror and backscattered from the sample tissue is recombined through the beam splitter and guided to a spectrometer or a photodetector (PD). The spectral interference signal is acquired by the spectrometer or PD and processed by a computer.

The process of how OCT acquires a 3D image is illustrated in **Figure 1.2** (reproduced from [9]). The axial line profile (A-line) of the tissue can be retrieved by inverse Fourier transform of the spectral interference signal. A two-dimensional (2D) cross-sectional image can be obtained by transversely scanning the sample light radiation using a beam scanner while continuously acquiring axial line profiles. A three-dimensional (3D) image can be obtained by transversely scanning the sample light using 2-axis (X and Y) scanners [10].

Figure 1.2. OCT generating 3D image process. (reproduced from [9])

In these two decades, OCT has been established as a standard diagnostic device in ophthalmology [11]. It provides not only a detailed morphology inspection on ocular structures, such as corneal damage and retinal detachment but also quantitatively measures several important indicators

such as the thickness of layers and anterior chamber angle [12]–[14]. Besides its huge success in ophthalmology, hand-held scanning probe for skin imaging [15], endoscopy probes for porcine esophagus imaging [16] and coronary artery intravascular imaging [17] have been intensively investigated and yielded promising results. Based on the possibility of miniaturization of optics, OCT probe is promising to play a vital role in the diagnosis in important luminal structures in the human-like trachea, esophagus, blood vessel, bowel and pancreatic duct [18], [19].

One of the current hotspots of OCT is to improve the resolution. Recent advances in optics and laser technology has made it possible for OCT to achieve micrometer resolution even on sub-micrometer, named ultra-high resolution OCT (UHR-OCT) [20], [21] and micro-OCT (μ OCT) [22], by utilizing state-of-the-art lasers [23], adaptive optics [24], [25] and other novel techniques. Many attempts have been made to image single cells. Recently developed μ OCT is based on FDOCT and uses a super-continuum source with novel optics design to achieve a $\sim 2 \times 2 \times 1 \mu\text{m}$ spatial resolution. The application of μ OCT reveals the possibility and feasibility of using OCT to view and evaluate the cellular and subcellular structure on the cornea, retina [26], upper airway [27], coronary artery [22] and so on, providing invaluable information in diagnosis and treatment.

1.1.2 Functional OCT and polarization-sensitive OCT

One of the remaining limitations of conventional OCT was lacking in specific contrast. However, in functional OCTs, such as spectroscopic OCT, polarization sensitive OCT, etc., employing additional properties of light, specific qualitative contrast or quantitative measurement can be achieved. Spectroscopic OCT (SOCT) can reveal the wavelength-dependent attenuation of light traversing through the biological medium. So far, contrast enhancement has been demonstrated when SOCT is combined with the use of microspheres and nanoparticles in tissue phantoms [28], [29] and in excised breast tissue [30]. In addition, varying degrees of success have

been achieved in the investigation of assessment of hemoglobin absorption, which is a compelling target for any biomedical imaging technique [31].

Polarization-sensitive OCT, as the first functional extension, has been applied to many fields since its invention in 1992 [32]. The polarization state of light changes while propagating in some tissue, such as the aorta, cornea, airway muscle, retinal nerve fiber layer, retinal pigment epithelium (RPE) [33], etc. In a simplified model neglecting depolarization, polarized light is decomposed into orthogonally polarized components traveling at different group velocity when entering the birefringent sample. One component is thus retarded with respect to the other one depending on the amount of birefringence. Another phenomenon in some materials is diattenuation which seems to be negligible in tissues studied so far [34], [35]. Polarization properties including retardation, optic axis orientation, and degree of polarization uniform (DOPU) can be extracted by analyzing the backscattered light from the sample by PS-OCT.

Classified by the number of input polarization states, there are multiple input polarization states and single input polarization state PS-OCT. There are two main implementations for multiple inputs system. The first is using a polarization modulator to generate two successive A-lines with different polarization state on the same site [35] as shown in **Figure 1.1(d)**. The other is using depth multiplexing [36] or frequency multiplexing [37]. The advantages of multiple input polarization state PS-OCT are the capability for local birefringence imaging as well as compatibility with flexible fiber-based implementations [37]. But polarization modulation and multiplexing would increase the cost and complexity of the system.

Distinguished for simplicity, single input PS-OCT uses circularly polarized light for illumination and detects the back-scattered light with a polarization diversity detection module [32] as shown in **Figure 1.1(c)**. The configuration of single input PS-OCT can be divided into the bulk optics-based system and fiber-based system including single mode fiber (SMF) based and polarization maintaining fiber (PMF) based system or mixture

system [38], [39]. For SMF-based system, all the fibers should be carefully manipulated and fixed to mimic the function of the free-spaced bulk-optics system. PMF-based systems demonstrate reliable polarization stability but need a very careful alignment when splicing pieces of fiber together [40], [41]. Another issue is the “ghost image” due to the polarization crosstalk. To avoid the “ghost image”, long (20-30m) PMF should be added in the interference arm [42]. Also, the cost of the PMF-based system is higher.

Both implementations have their advantages. Conventionally, the local birefringence measurement provided by the multiple inputs system is more favorable to the clinical application due to its more intuitive and quantitative imaging information provided. But multiple-input PS-OCT involves more complexity in fabrication as well as signal processing. And it is more difficult to achieve polarization-sensitive contrasts with an ultra-high resolution with multiple polarization input. Since such broad bandwidth of light source required for ultra-high resolution makes it extremely difficult to achieve two polarization state inputs PS-OCT by polarization modulation and the ranging depth of the spectrometers leave little margin for depth multiplexing. Therefore, the development of high-resolution PS-OCT with local retardation with lower cost will be of great significance.

1.2 Major contribution and organization of this thesis

The major objectives of this thesis are to improve the performance of the current single input PS-OCT with high-resolution and to simplify the reconstruction of local birefringence imaging. My mission is to lower the barrier-to-entry of PS-OCT and foster the interests of developers and end-users in PS-OCT, especially in single input PS-OCT.

To fulfill this goal, my first effort was to improve the methods to fabricate and calibrate single input PS-OCT with lower cost and simpler procedures as described in Chapter 2. Specifically, I revised the conventional PS-OCT system configuration and investigated the polarization distortions in single input PS-OCT based on the Jones matrix modeling and developed a method to calibrate it. I found the effect of polarization distortion is inversely

proportional to the strength of sample birefringence. Since tissue birefringence is generally small such as local retardation of 0.05-0.2deg/ μm for RNFL, correcting polarization distortions becomes a must. The effectiveness of correction is demonstrated in resultant system performances predicted by simulations and obtained through experiments on artificial retarders, birefringence phantoms as well as swine retina.

In Chapter 3, we reported a phenomenon as well as a polarization constraint in a unitary reciprocal optic system, which is the basis for local retardation imaging in single input PS-OCT. In a reciprocal system, where there is little depolarization and diattenuation, the back-scattered light always tends to pass or gather around one specific polarization state. Presented on the Poincaré sphere, the polarization state usually is the mirrored polarization state of input polarization state by QU plane, named as mirror state. We explored the predisposition for this mirror state, and I demonstrated how it constrains the depth-dependent evolution of polarization states measured with PS-OCT.

In Chapter 4-5, I demonstrated the application of the constraint in single input PS-OCT with both free-space and fiber-based implementations. In the free-space system, I illustrated the geometric local retardation reasoning algorithm, which was validated by phantom imaging. The local retardation images of the tissue scanned in chapter 2 were reconstructed with this algorithm. Compared with the current accumulative retardation contrast, more intuitive birefringence contrasts were achieved without extra expense. I believe this report will be very meaningful to current researchers with single input PS-OCT system.

In the local retardation imaging reconstruction with the proposed method, one limitation is the mirror state artifact. The artifact appears when the polarization state becomes very near to the mirror state, making the local retardation calculation much more susceptible to the noise. This might not be an issue for the free-space system where meaningful birefringence tends to be small. But this might be a hurdle for the application in the fiber-based

system due to the intermediate illumination polarization state caused by bending of the sample fiber. To overcome this remaining limitation, I developed a local retardation reasoning algorithm for fiber-based implementations with spectral binning, which was conceived by Villiger *et al.* to overcome the effects of polarization mode dispersion (PMD) in fiber-based systems [43]. Firstly, I split the spectrum into several bins (here 9 bins were applied). Then, I introduced some PMD in the sample arm by bending the sample arm fiber to diversify the illumination polarization state of different bins. This method can avoid the situation where the polarization state aligns with the mirror state simultaneously for the 9 bins. I validated the reliability of this method with a phantom which consists of two layers of birefringence band with different fast axis orientations via a fiber-based spectrometer domain PS-OCT system. Also, the detailed calibration method is provided there including system diattenuation compensation and mirror state estimation. Animal tissue imaging was performed to demonstrate its capability.

To further reduce the complexity of the fiber-based single input PS-OCT and improve its sensitivity, I developed a fiber coupler based single input PS-OCT. In comparison, the system used in the previous demonstration still involves polarization state manipulation in free space, thus requiring light collimation and coupling from and to the fiber tips, which might result in sensitivity loss and involve crafty manipulation. The method does not require the sample arm fiber to be fixed which is common in other SMF based implementations. I also demonstrated the local retardation imaging capability with birefringence phantoms and tissues.

Last, I expanded the application of mirror state constraint to cardiovascular PS-OFDI. Previously, Villiger *et al.* evaluated the robustness and repeatability of imaging coronary tissue birefringence and depolarization in a clinical setting by the repeated PS-OFDI pullback imaging [44]. I used one of the two polarization states channels to reconstruct the local retardation images, which requires both channels in the current PS-OFDI intravascular polarimetry. Pearson correlation and Bland-Altman analysis

were performed to compare the processing results with those of the benchmark processing (two polarization states input). The results from the two experiments show a high correlation, with an average correlation coefficient over 0.7. A comparable limit of agreement was achieved compared to the results in the repeatability study. What's more, I developed a reliability metric to quantify the credible degree of each measurement. These results might be a good argument to motivate the replacement of two input intravascular polarimetry with single input ones by reducing one polarization modulator.

In the last chapter, I summarized my efforts in improving the function of single input PS-OCT, discussed the limitations of my work, and proposed some further path for the development of PS-OCT.

Chapter 2 Single input PS-OCT with high resolution and distortion correction

2.1 Motivation and background

As introduced in last chapter, optical coherence tomography (OCT)[1], as a non-invasive cross-sectional imaging method, has been applied in many fields such as ophthalmology[14], [45], cardiology [22], [46] and dermatology [47]. But conventional OCT is lacking in specific contrast. To enable functional imaging, polarization-sensitive OCT has been developed to reveal depth-resolved birefringent information of tissue[32]. Polarization properties including retardation[32], [48], optic axis orientation [49], [50] and depolarization [51] can be extracted by analyzing the backscattered light from the sample by PS-OCT.

Single input polarization state PS-OCT has been favored due to the simplicity in comparison to its two inputs counterparts. It illuminates the sample with circularly polarized light and detects the back-scattered light with polarization diverse detections [32], [38], [41] Assuming the optic axis was constant, the accumulative birefringence could be extracted by one-shot measurement. Afterward, ultra-high-resolution OCT has demonstrated its great potential in revealing more details [22][45], compared to the conventional OCT. Single input PS-OCT with ultra-high resolution has been widely used in ophthalmology [13], [14], [52]–[54], dermatology [55], [56], brain micro-tractography [57], etc. Meanwhile, there are many technical publications dealing with dispersion compensation essential for ultra-high resolution [58]–[60], spectrometers alignment for birefringence artifacts removal [52], [61], [62], ghost images elimination in polarization-maintaining fiber-based system [40], [41]. Yet few discuss the polarization distortion caused by the polarizing components in the system and under a broad operating bandwidth.

In the current single input polarization state PS-OCT systems, the polarization state manipulation of the illumination light is achieved by

quarter-wave plates (QWPs) or single-mode fiber (SMF) [32], [38], [39], [41]. Ideally, a QWP oriented at 45° in the sample arm provides circularly polarized illumination and a QWP oriented at 22.5° in the reference arm provides 45° linearly polarized reference light after the double pass. This mechanism works well when the operating spectral bandwidth is not so broad that the retardance induced by the QWP is uniform over the whole spectrum. However, if the operating spectral bandwidth becomes so broad that the chromatic variations in the retardation induced by the QWP or SMF are no longer negligible. Take a commercially available achromatic QWP (AQWP10M-980, Thorlabs Inc.) as an example, the mean value and standard deviation of the induced retardance within the spectral band of 760-920 nm in single pass is 93° and 0.25° , making the illumination light deviated from the circular polarization state, and the double pass through the QWP amplifies the defects in the current setup configuration[38]. Moreover, in the spectrometer-based polarization diverse detection, the mismatch in the intensity roll-off between the two spectrometers also leads to polarization distortions. These polarization distortions become salient when the sample birefringence is weak.

In this work, we introduced a Jones matrix model on a single input PS-OCT system, considering the polarization distortions induced by the wavelength-dependent retardance of QWP and the intensity roll-off mismatch between the two spectrometers operating at a broad bandwidth. Based on the model, a correction method has been developed to tackle these distortions. Numerically, we investigated the impact of the polarization distortion caused by the QWP on scattering samples at different birefringence scale and validated the correction method. Furthermore, a sample with known birefringence was imaged to demonstrate the performance of the correction. Last, we imaged animal tissues such as swine retina and rat esophagus *ex vivo* to demonstrate potential clinical applications.

2.2 System description and routine calibration

2.2.1 System description

The detailed description of the ultra-high-resolution system we built is as follows. The light source from the supercontinuum laser (SCL: SC-5OEM, YSL Photonics) is clipped by a dichroic mirror (DMSP950 Thorlabs Inc., not shown in **Figure 2.1**) and collimated into the fiber coupler (90/10). The light exiting from the fiber coupler is collimated into free space. The free-space light becomes linearly polarized after passing through a linear polarizer (P1: LPNIRE100-B, Thorlabs Inc.). The quarter-wave plate (QWP, AQWP10M-980, Thorlabs Inc.) at the angle of 45° transforms the linearly polarized light into circularly polarized light. The beam splitter (50/50) splits the light into the sample arm and reference arm. The linear polarizer (P2) at an appropriate angle generates a reference beam of the same phase and amplitude regarding the two channels of the polarization diversity detections. The determination of the polarizer angle is described in the fabrication procedures below. The lens and the mirror in the reference arm are attached on a linear stage (LS: Newport M-423 linear stage). The LS can create a variable optical path length difference between the reference arm and the sample arm. In the sample arm, a dispersion compensator is used to compensate for the dispersion caused by the polarizer in the reference arm. The compensator is made of polarization independent BK7 glass, thus the illumination light at the sample surface is kept as circularly polarized light. In the interference arm of the interferometer, a half-wave plate (HWP: AHWP10M-980, Thorlabs Inc.) is placed before the light is coupled into a polarization maintaining fiber to rotate the polarization coordinates of the free-space light to match with that of the polarization maintaining fiber (PMF: P3-780PM-FC-2, Thorlabs Inc.). The polarization sensitive detection unit consists of a polarizing beam splitter and two spectrometers. The design of the spectrometers is illustrated in the dashed square. The custom spectrometer consists of transmission grating (Wasatch transmission grating: 1200 line/mm), camera lens (L9: Nikon AF 85mm f/1.8D), line scan CCD camera (E2V AVIIVA EV71YEM4CL2010-BA9, with 2048 pixels). The

operating center wavelength is 840nm, and bandwidth is ~160 nm. The custom preview and acquisition system are designed with LabVIEW 2015(National Instrument Inc.) and MATLAB 2016b (MathWorks Inc.).

Figure 2.1. The calibration of the single input PS-OCT. (a). The diagram of the PS-OCT system. BS, beam splitter; DC, dispersion compensator; HWP, half-wave plate; L1-9, lenses; LS, linear stage; M1-2, mirror; P1-2, polarizers; PBS, polarizing beam splitter; PM, power meter; PMF, polarization maintaining fiber; QWP, quarter-wave plate; SCL, super-continuum laser; SMF, single-mode fiber; SP, spectrometer, TG, transmission grating. (b). Remapping the interferogram from CCD detector space into the evenly sampled k -space process. (b-1). Remapping function $k = \Phi(n)$ extracted from interference fringes of a specular surface at two different optic path length difference Δz_1 , Δz_2 . The remapping function is obtained point to point (PSF) subtraction between the two extracted phases of two interferograms and normalized. (b-2). Raw interferogram recorded by the spectrometer. (b-3). Remapped interferogram in evenly sampled k -space. (b-4). Normalized point spread function with fwhm 2.3 μm in the air after dispersion calibration. (c). spectrometer alignment process after the remapping process in (b). (c-1). Normalized PSFs of the horizontal channel and vertical channel at different optical path length difference Δz_1 , Δz_2 before spectrometers alignment, encoded in different color and line style. (c-2). Normalized PSFs of the horizontal channel (ch1) and vertical channel(ch2) at different optical path length difference Δz_1 , Δz_2 after spectrometers alignment, encoded in different color and line style. The spectrum scale factor α is determined by the position of peaks' position of two channels. And after the interferograms of channel 2 is rescaled by α , the corresponding PSFs' peaks align together with that of channel 1. (c-3). K -space shift β determination by cross-correlation between interferograms of two channels at Δz_1 , Δz_2 , respectively. β corresponds to the maximum position of the two cross-correlation curves.

During construction, to facilitate the building process of the ultra-high-resolution PS-OCT system, a power meter is connected to the coupler. After completion, both coupler and power meter can be removed. The steps to place and adjust each polarization-changing element (polarizer, QWP, HWP) to the precise position and angle are as following:

1. Place polarizer P1 in the input arm. The angle of the polarizer is arbitrary since we can adjust our detection coordinate by rotating the HWP afterward.
2. Block the reference arm and place a reflector (e.g. a mirror) at the focus of the objective lens in the sample arm. Adjust the inclination and position of the reflector to harvest most back-reflected light judging by the highest possible reading on the power meter. This step ensures the reflector is placed exactly at the focal point.
3. Collimate the output free-space light into PMF as much as possible, then rotate the HWP until the highest extinct ratio between horizontal and vertical channels is achieved on the two spectrometers. This step guarantees that the horizontal and vertical polarization axes of free space light align with that of the PMF.
4. Place the QWP in the input arm (between polarizer P1 and the beam splitter) and rotate the QWP until the power meter detects the lowest light reflected from the reflector in the sample arm. This step ensures the orientation of the QWP is 45° . The imperfection of the QWP will be compensated in the calibration section.
5. Until now, the reference arm has been blocked. Remove the block and rotate polarizer P2 to make the amplitude of interference fringes in the two spectrometers equal. The angle of the polarizer is not critical since it does not induce phase difference but only brings an amplitude mismatch between horizontal and vertical channels which can be easily compensated afterward.
6. Remove the coupler at the input arm and connect SCL source fiber port directly to the collimation.

In the revised system configuration, the light beam is manipulated into a circularly polarized state before beam splitter, thus precluding the back-reflected and back-scattered light from passing QWP again, which provides convenience for the calibration of the imperfection of QWP. On the reference arm, the QWP at 22.5° is replaced by a more economical linear polarizer at 45° . The requirement on the orientation of the linear polarizer is

less strict than QWP since polarizer can enforce identical phase for the horizontal and vertical components of the reference light and only amplitude response on the two detection channels needs compensation. Compared to the traditional single-input PS-OCT system, our custom system is easier to construct and calibrate. The procedures take advantage that the position and angle of the polarization-changing items are self-consistent.

2.2.2 Dispersion calibration

For spectral domain ultra-high-resolution PS-OCT system, it is essential to remap the interferogram into k -space and compensate the dispersion mismatch between the sample arm and reference arm. The method to remap the interferogram into k -space can be characterized into two categories. The first is the hardware method. With novel design, the interferogram is detected in terms of wavenumber directly, which also has the advantage of longer ranging depth [60]. For software method, Park *et al.* introduced a mathematical model for the spectrometer according to its physical design to remap the interferogram into k -space [63]. Eom *et al.* used 5 fiber Bragg gratings to generate 5 reference peaks with specific wavenumber in the spectrum to remap the interferogram into k -space. Mujat *et al.* iteratively altered the index of interferogram between two surfaces of glass slides until the interferogram became ideally sinusoidal shape [61]. For dispersion compensation, the common hardware-based compensation is by inserting compensating material in reference arm or sample arm. But it's usually very labor-intensive to compensate dispersion completely via hardware-based method as far as we know. On the other hand, the software method is more flexible and can be divided into iterative method [64] and non-iterative method [23].

In this paper, the method I adopted has been described earlier by our group [59]. Briefly speaking, the compensation is based on the fact that the interference with a specular sample is ideally sinusoidal shape. First, we extract the instantaneous frequency of the interference by the Hilbert transform. By remapping the instantaneous frequency back into linearity, a

remapping function $k = \Phi(n)$ can be found to remap the interferogram into evenly-sampled k -space from CCD pixel space, where k is the k -space index, n is CCD pixel index, Φ is the remapping function. The second step is to calculate dispersion between the reference arm and the sample arm.

The detected interference can be expressed as $I(n) = S(n) \cdot \exp(-i(\Phi(n) \cdot \Delta z + D(\Phi(n))))$, where $S(n)$ is the amplitude response of n -th pixel, $D(\Phi(n))$ is the dispersion term, Δz is the optical path length difference. In the calibration, we recorded two interferograms $I_1(n)$ and $I_2(n)$ at different optical path length difference $\Delta z_1, \Delta z_2$. The difference $P_1(n) - P_2(n)$ between the instantaneous phase $P_1(n) = \Phi(n) \Delta z_1 + D(\Phi(n))$ $P_2 = \Phi(n) \Delta z_2 + D(\Phi(n))$ is proportional to the remapping function $\Phi(n)$ since $\Delta z_1 - \Delta z_2$ is constant. With $\Phi(n)$ shown in **Figure 2.1(b-1)**, $I_1(n) = S(n) \cdot \exp(-i(\Phi(n) \cdot \Delta z + D(\Phi(n))))$ (**Figure 2.1(b-2)**) can transform the interferogram into evenly sampled k -space $I_1(k) = S(k) \cdot \exp(-i(k \cdot \Delta z + D(k)))$ (**Figure 2.1(b-3)**). [65]

The next step is to calculate dispersion term $D(k)$ in $I(k)$. As $D(k)$ can be regarded as higher order distortion in terms of k . The first order term $P_{1st} = \Delta z \cdot k$ is obtained after performing the linear regression to the instantaneous phase $P(k) = k \cdot \Delta z + D(k)$. The dispersion term is obtained by $D(k) = P(k) - P_{1st}(k)$. The calibrated point spread function is shown in **Figure 2.1.(b-4)**.

It is worth mentioning that the interference we recorded for dispersion compensation can also be used in the next step of spectrometer alignment. To guarantee the same phase of calibration interferograms of the orthogonal polarization channels which is essential for spectrometer alignment, a polarizer was inserted between the beamsplitter and the HWP in the system. The polarizer was removed once the acquisition of calibration interferograms was finished.

2.2.3 Spectrometer alignment

The spectrometers used in SD-OCT are usually based on a grating and a line-scan camera. The grating disperses the light in terms of wavelength, and the lens before the line-scan camera focuses the light on camera pixels. According to [63], the j -th wavelength λ_j and pixel mapping on the spectrometer can be expressed by

$$\lambda_j = g \left\{ \sin \theta_i + \sin \left[\sin^{-1} \left(\frac{\lambda_c}{d} - \sin \theta_i \right) + \tan^{-1} \left(\frac{w \cdot j - x_c}{F} \right) \right] \right\} \quad (2-1)$$

where θ_i is the incident angle on the grating with spacing g , λ_c is the center wavelength of light transmitted unperturbed through the lens of focal length F , and x_c is the distance from the first pixel to the position of λ_c on the camera pixel array, which has a pixel width of w . According to this equation, for two spectrometers even subtle difference in incident angle θ_i , the grating spacing g or the pixel size w can result in discrepancy on the wavelength-pixel mapping of the two spectrometers.

Götzinger *et al.* [52] developed a guide for fabricating the spectrometers to eliminate the misalignment between two orthogonal polarization channels. Mujat *et al.* [61] proposed to use the autocorrelation of the surfaces of two microscope slides inserted into the sample arm for the wavelength assignment. Chen *et al.* [62] presented a calibration method for the wavenumber alignment using a series of interference fringes between the light reflected from a mirror in the sample arm and the reference arm, with different reference mirror locations.

We transform the interferograms recorded by the two spectrometers into evenly sampled in k -space, but there is no guarantee that the two interferences are exactly in the same k -space and perfectly overlap. The correspondence between the two spectra wavenumber can be modeled into a linear function: $k_2 = \alpha * k_1 + \beta$, Where k_1 , k_2 stands for the wavenumber of each pixel index of the two spectrometers, respectively, α and β are the stretching factor and offset to align the two spectrometers.

If the two fringes are well aligned, the stretching factor α is equal to 1, corresponding to the same peak position among the two spectrometers in depth z domain after Fourier transform. According to scaling properties of Fourier transform, the effects of stretching parameter α on depth z domain and on wavenumber domain can be revealed by Eq.(2-2), where I is the spectrum, k is the spectrum wavenumber, FT stands for the Fourier Transform, Γ is the depth profile, z is the depth in the sample.

$$FT(I(\alpha * k)) = \frac{1}{|\alpha|} FT\left(I\left(\frac{k}{\alpha}\right)\right) = \frac{1}{|\alpha|} \Gamma\left(\frac{z}{\alpha}\right) \quad (2-2)$$

Figure 2.1(c) shows the procedures to determine α and β for spectrometers alignment. The stretching factor α could be determined in depth z domain by simply aligning the peak positions since the changes of peak positions are absolute and identical among both channels (shown in **Figure 2.1(c-1,2)**). K -space shift β was determined by cross-correlation between the interference fringes of orthogonal polarization states (shown in **Figure 2.1(c-3)**).

2.3 Jones matrix model of polarization distortion calibration

2.3.1 Jones matrix modeling of the detected signals

In single input PS-OCT, the signal intensity $\vec{I}(k) = [I_{\perp}(k) \ I_{\parallel}(k)]^T$ of a single scattering sample detected by two orthogonal polarization channels can be expressed as a function in terms of wavenumber k .

$$\begin{bmatrix} I_{\perp}(k) \\ I_{\parallel}(k) \end{bmatrix} = \begin{bmatrix} E_{\text{ref}\perp} E_{\text{ref}\perp}^* \\ E_{\text{ref}\parallel} E_{\text{ref}\parallel}^* \end{bmatrix} + \begin{bmatrix} E_{\text{sam}\perp} E_{\text{sam}\perp}^* \\ E_{\text{sam}\parallel} E_{\text{sam}\parallel}^* \end{bmatrix} + \begin{bmatrix} E_{\text{ref}\perp} E_{\text{sam}\perp}^* \\ E_{\text{ref}\parallel} E_{\text{sam}\parallel}^* \end{bmatrix} + \begin{bmatrix} E_{\text{sam}\perp} E_{\text{ref}\perp}^* \\ E_{\text{sam}\parallel} E_{\text{ref}\parallel}^* \end{bmatrix} \quad (2-3)$$

where $\vec{E}_{\text{ref}} = [E_{\text{ref}\perp} \ E_{\text{ref}\parallel}]^T$, $\vec{E}_{\text{sam}} = [E_{\text{sam}\perp} \ E_{\text{sam}\parallel}]^T$ represent the Jones vectors of the light returned from the reference arm and sample arm, respectively. Subscript $\perp$ and $\parallel$ denote the vertical and horizontal detection channel, respectively. Superscript $*$ represents complex conjugate, and superscript T denotes matrix transpose.

In practice, the DC term $[E_{\text{ref}\perp} E_{\text{ref}\perp}^* \ E_{\text{ref}\parallel} E_{\text{ref}\parallel}^*]^T$ and $[E_{\text{sam}\perp} E_{\text{sam}\perp}^* \ E_{\text{sam}\parallel} E_{\text{sam}\parallel}^*]^T$ are subtracted as the background. The

complex electrical field interference vector could be obtained by Hilbert transform (H) as follows.

$$\vec{E}(k) = \begin{bmatrix} E_{\text{ref}\perp}^* E_{\text{sam}\perp} & E_{\text{ref}\parallel}^* E_{\text{sam}\parallel} \end{bmatrix}^T = \vec{I}(k) + i \cdot H(\vec{I}(k)) \quad (2-4)$$

Usually, the polarization dependent attenuation can be ignored, so the attenuation factors regarding the optical loss and sample reflectivity can be simply described as scalars $C_{\text{ref}}(k)$ and $C_{\text{sam}}(k)$. The optical path length traveled from the reference reflector and the sample back to the spectrometer were z_{ref} , z_{sam} , respectively. The reference signal detected on the spectrometer can be expressed as:

$$\vec{E}_{\text{ref}}(k) = \begin{bmatrix} \eta_{\perp}(k) & 0 \\ 0 & \eta_{\parallel}(k) \end{bmatrix} \cdot \begin{bmatrix} \cos^2 \phi & \frac{1}{2} \sin 2\phi \\ \frac{1}{2} \sin 2\phi & \sin^2 \phi \end{bmatrix} \cdot \vec{E}_{\text{in}}(k) \cdot C_{\text{ref}}(k) \cdot S(k) \cdot e^{ikz_{\text{ref}}} \quad (2-5)$$

where $\eta_{\perp}(k)$, $\eta_{\parallel}(k)$ are the quantum efficiency of vertical and horizontal polarization channels, respectively, ϕ is the polarizer orientation with respect to the horizontal direction, and $S(k)$ defines source power spectral density. $\vec{E}_{\text{in}}(k) = [1 \ e^{i\Psi(k)}]^T$ is the Jones vector defining the input polarization state after the QWP. For an ideal QWP, Ψ should be equal to $\pi/2$ over the spectrum, but in practice, k -dependent deviation of Ψ from $\pi/2$ should be considered. The detected sample arm signal can be expressed as Eq.(2-6).

$$\vec{E}_{\text{sam}}(k) = \begin{bmatrix} \eta_{\perp}(k) & 0 \\ 0 & \eta_{\parallel}(k) \end{bmatrix} \cdot \mathbf{J}_{\text{sam}}(k) \cdot \vec{E}_{\text{in}}(k) \cdot C_{\text{sam}}(k) \cdot S(k) \cdot e^{ikz_{\text{sam}}} \quad (2-6)$$

Combining Eq. (2-5), the complex electrical field $\vec{E}(k)$ could be described in Eq.(2-7) as the product of the input electrical field, a diagonal matrix which depicts the overall effects of the reference and the spectrometers' efficiency, and a Jones transmission matrix of the sample which is the objective of measurement. Note that $\Delta z = \Delta z_{\text{sam}} - \Delta z_{\text{ref}}$ is the optical path difference (OPD) between the sample arm and reference arm. For simplicity, $R_{\perp}(k)$ and $R_{\parallel}(k)$ represent the combined effects of quantum efficiency $\eta_{\perp}(k)$, $\eta_{\parallel}(k)$, and orientation of polarizer on the orthogonal

polarization channels. To simplify the analysis, we omit the power spectral density $S(k)$.

$$\vec{\mathbf{E}}(k) = \begin{bmatrix} E_{\perp}(k) \\ E_{\parallel}(k) \end{bmatrix} = \begin{bmatrix} R_{\perp}(k) & 0 \\ 0 & R_{\parallel}(k) \end{bmatrix} \cdot \mathbf{J}_{\text{sam}} \cdot \vec{\mathbf{E}}_{\text{in}} \cdot e^{ik\Delta z} \quad (2-7)$$

In practice, there is OPD dependent roll-off in interference intensity. Therefore, the actual electrical field $\vec{\mathbf{E}}(k)$ should consider another diagonal matrix for the roll-off effect. In summary, for the single input state ultra-high-resolution PS-OCT, the detected complex electrical field is shown in Eq.(2-8), where $\beta(\Delta z)$ is the spectrometer roll-off coefficient.

$$\vec{\mathbf{E}}(k) = \begin{bmatrix} E_{\perp}(k) \\ E_{\parallel}(k) \end{bmatrix} = \begin{bmatrix} R_{\perp} \cdot \beta_{\perp}(\Delta z) & 0 \\ 0 & R_{\parallel} \cdot \beta_{\parallel}(\Delta z) \end{bmatrix} \cdot \mathbf{J}_{\text{sam}} \cdot \vec{\mathbf{E}}_{\text{in}} \cdot e^{ik\Delta z} \quad (2-8)$$

2.3.2 Polarization distortion calibration

According to the modeling above, the polarization distortion consists of two parts: the phase distortion mainly caused by the imperfection of QWP, and the roll-off difference between two orthogonal polarization channels. In this section, we calibrated the detected phase $\Psi(k)$ to be $\pi/2$ independent of k with a static mirror as the sample. The unbalanced roll-off coefficient $\beta_{\perp}(\Delta z)$, $\beta_{\parallel}(\Delta z)$ which depended on Δz was compensated using the interferograms obtained with different OPD. The electrical field detected from a specular surface can be expressed by Eq. (2-9), in which we assume that the k -dependent $R_{\perp}$ and $R_{\parallel}$ can be negligible because the spectral responses of the two cameras generally are the same. Therefore, the overall response difference was compensated by a vector factor indexed in the depth domain.

$$\vec{\mathbf{E}}_{\text{surf}}(k) = \begin{bmatrix} E_{\perp}(k) \\ E_{\parallel}(k) \end{bmatrix} = \begin{bmatrix} R_{\perp} \cdot \beta_{\perp}(\Delta z) & 0 \\ 0 & R_{\parallel} \cdot \beta_{\parallel}(\Delta z) \end{bmatrix} \cdot \frac{1}{\sqrt{2}} \cdot \begin{bmatrix} 1 \\ e^{i\Psi(k)} \end{bmatrix} \cdot e^{ik\Delta z} \quad (2-9)$$

The detected phase was compensated to the theoretical value by adding the offset point to point (**Figure 2.2** (a)). At the same time, the amplitude roll-off ratio curve was fitted at a series of the reference mirror positions within 0.8 mm from the DC (**Figure 2.2** (b)). Hence, the amplitude response of the two detection channels can be calibrated to be identical. To validate the polarization distortion calibration, we transformed the detected Jones

vectors recorded with a specular sample and different reference mirror positions into Stokes vectors and plotted them on the Poincaré sphere. The reference mirror was moved by steps of 100 μm over a series of OPDs up to 1200 μm . After polarization distortion correction, all the polarization states gathered around $[0 \ 0 \ 1]^T$, while the uncorrected spread out into an irregular line and deviates from $[0 \ 0 \ 1]^T$ (**Figure 2.2** (c)), which demonstrates that the illumination polarization states were calibrated to be circular polarization at all depths.

I further validated our system performance by measuring the transmission axis of a linear polarizer (LPNIRE100-B, Thorlabs Inc.), and the retardation of a QWP (AQWP10M-980, Thorlabs Inc.). The retardation and optic axis reasoning are introduced in the next section. First, a linear polarizer was inserted in the sample arm and rotated by 10 degrees for each measurement. The measured transmission axis orientation of the linear polarizer is shown in **Figure 2.2** (d). Then, the polarizer was replaced by a QWP, and the above rotation steps were repeated. The double-pass cumulative retardance of the QWP with different optic axis orientations is shown in **Figure 2.2** (e). The average and standard deviation of the measured cumulative retardation of the QWP were 171.5° and 5.5° , respectively. These results agreed well with the theoretical expectations, indicating the high reliability of the calibrated system.

Figure 2.2. Polarization distortion compensation process and measurement of a polarizer and a QWP. (a). Measured phase difference versus the k -space index, the compensated values were obtained by point to point subtraction between the measured values and theoretical values. (b). PSF peak ratios between two

spectrometers at different imaging depths. (c). Measured polarization states from the sample mirror with a series of OPDs, with (red points) and without (blue points) distortion correction. (d). the measured orientation of linear polarizer. The asterisk points are the measured data, the blue line is the linear-least-square fit of the measurements, and the red dashed line is the theoretical relation. (e). Measured phase retardation of QWP when placed at different orientations.

2.4 Extraction of sample polarization parameters

For non-depolarizing tissues, the Jones matrix of the sample $\mathbf{J}$ can be decomposed as $\mathbf{J}=\mathbf{R}^{-1}\cdot\mathbf{D}\cdot\mathbf{P}\cdot\mathbf{R}$, where $\mathbf{R}$ is a rotation matrix defining the optic axis orientation θ of the sample with $\mathbf{R} = [\cos\theta, -\sin\theta; \sin\theta, \cos\theta]$, and $\mathbf{D}$, $\mathbf{P}$ are diattenuation matrix and retardation matrix, respectively [35]. Diattenuation in biological tissue is usually negligible, and retardation matrix can be expressed as $\mathbf{P} = [e^{i\delta}, 0; 0, e^{-i\delta}]$ where δ could be considered to be linearly dependent on k considering the wavelength-dependent retardance of QWP so that the sample Jones matrix can be written as Eq. (2-10) [38].

$$\mathbf{J}_{\text{sam}} = \mathbf{R}^{-1} \cdot \mathbf{P} \cdot \mathbf{R} = \begin{bmatrix} e^{i\delta/2} \cos^2 \theta + e^{-i\delta/2} \sin^2 \theta & (e^{i\delta/2} - e^{-i\delta/2}) \cos \theta \sin \theta \\ (e^{i\delta/2} - e^{-i\delta/2}) \cos \theta \sin \theta & e^{-i\delta/2} \cos^2 \theta + e^{i\delta/2} \sin^2 \theta \end{bmatrix} \quad (2-10)$$

When the system is well calibrated following the procedures described above, measured complex field (Eq.(2-9)) can be rewritten as

$$\vec{\mathbf{E}}(k) = \sqrt{R(z)} \cdot \mathbf{J}_{\text{sam}} \cdot \frac{1}{\sqrt{2}} \cdot [1 \ i]^T \cdot e^{-i \cdot 2k \cdot \Delta z} \quad (2-11)$$

After the Fourier transform, depth information could be considered as the convolution of the transformed sample Jones matrix with a delta function which defines the depth-displacement. The depth-resolved information is shown in Eq. (2-12), where $\delta(z) = \Delta n \cdot k_0 \cdot z$ is the retardance between ordinary and extraordinary beams, and k_0 is the center wavenumber of the light source).

$$\begin{bmatrix} A_{\perp}(z) \\ A_{\parallel}(z) \end{bmatrix} = \sqrt{\frac{R(z)}{2}} \cdot \begin{bmatrix} \cos \delta(z) - \sin \delta(z) \cdot \sin(2\theta(z)) + i \cdot \sin \delta(z) \cdot \cos(2\theta(z)) \\ \sin \delta(z) \cdot \cos(2\theta(z)) + i \cdot (\sin \delta(z) \cdot \sin(2\theta(z)) + \cos \delta(z)) \end{bmatrix} \quad (2-12)$$

Furthermore, after we convert the Jones vector into the Stokes vector, a more simplified version of the depth-resolved information is shown as Eq. (2-13), where $\Delta\Phi$ is the phase difference between the two orthogonal polarization channels.

$$\mathbf{S} = \begin{bmatrix} I \\ Q \\ U \\ V \end{bmatrix} = \begin{bmatrix} A_{\perp}^2 + A_{\parallel}^2 \\ A_{\perp}^2 - A_{\parallel}^2 \\ 2A_{\perp}A_{\parallel}\cos\Delta\Phi \\ 2A_{\perp}A_{\parallel}\sin\Delta\Phi \end{bmatrix} = R(z) \cdot \begin{bmatrix} 1 \\ -\sin\delta(z) \cdot \sin 2\theta(z) \\ \sin\delta(z) \cdot \cos 2\theta(z) \\ \cos\delta(z) \end{bmatrix} \quad (2-13)$$

The intensity depth profile, retardation, optic axis, and DOPU could be calculated by Eq. (2-14). Of note, we used full Stokes averaging to reject speckle noise [33], [43], [66]. Compared with other complex averaging methods [67], [68], Stokes averaging is more intuitive and coincidentally makes retardation and optic axis calculation in the designed model more concise. In this paper, in brief, we transformed the Jones vectors into full Stokes vector first, and we averaged the full Stokes vectors defined by a 3D Gaussian kernel including pixels within 40 μm . Namely, the resolution of accumulative retardation and optic axis measurement in this paper is 40 μm .

$$\begin{aligned} I(z) &= |A_{\perp}(z)|^2 + |A_{\parallel}(z)|^2 \\ \delta(z) &= \cos^{-1}\left(\frac{V}{I}\right) \\ \theta(z) &= \frac{1}{2} \tan^{-1}\left(-\frac{Q}{U}\right) \\ \text{DOPU}(z) &= \sqrt{(Q/I)^2 + (U/I)^2 + (V/I)^2} \end{aligned} \quad (2-14)$$

2.5 Results

2.5.1 Simulations

To evaluate the influence of QWP's wavelength-dependent retardance (AQWP10M-980, Thorlabs Inc.) on the measurement of retardation and optic axis, we simulated a phantom with two scattering layers. Meanwhile, we demonstrated the performance of the correction method for correcting the imperfection of QWP. The first layer has homogeneous retardation and optic axis orientation, while the second layer is a non-birefringent scattering sample. The thickness of each layer is 280 μm . To compare the performance of the correction method under different amount of birefringence, we performed the simulation twice and set the retardance of the first layer to be 0.15 rad and 1.5 rad, respectively. Gaussian noise corresponding to average signal-to-noise ratio (SNR) of 20 dB was added to the interferogram. The simulated bandwidth was set to be consistent with the actual system (760-920 nm). In the simulation, the wavelength-dependent birefringence

properties of the QWP was set based on the data provided by the manufacturer (Thorlabs Inc.) and other optical elements were assumed ideal. The retardation and optic axis reasoning were performed according to the description in section 3. The area chosen for analysis was the second non-birefringent layer. The width of the lateral and axial averaging kernel with Gaussian shape were 10 A-lines and $16\text{ }\mu\text{m}$, respectively. The area of interest (AOI) was chosen from the second non-birefringent layer, from depth $350\text{ }\mu\text{m}$ to $380\text{ }\mu\text{m}$. For a comprehensive evaluation, each sample was imaged six times at different orientation. For each sample orientation angle, 5000 points within the AOI were evaluated.

Figure 2.3 (a) & (c) show the measured retardance value within the AOI without (blue boxes) and with (red boxes) the distortion correction where the first layer exhibits two different levels of birefringence and **Figure 2.3** (b) & (d) show the corresponding optic axis orientation measurement. To make the comparison better visualized, we present the optic axis measurements as the difference between the reconstructed values and corresponding ground truths. When the retardance of the first layer was set to be 0.15 rad , the mean value and the standard deviation of the measured accumulative retardation without the polarization distortion correction on different sample orientations were 0.1541 rad and 0.0383 rad , respectively, which became 0.1497 rad and 0.0072 rad , respectively, when polarization distortion correction was applied. The mean and the standard deviation of the optic axis error was 0.070° and 7.88° without the correction and becomes -0.13° and 1.24° with the correction, respectively. The polarization distortion caused by the QWP imperfection made the measurement noisy, while the corrected one yielded estimation close to the ground truth. When the accumulative retardation was set to be 1.5 rad , the difference in retardation measurements between the uncorrected and corrected method was almost negligible, while the corrected method still showed some improvement in the optic axis results. In general, the impact of the distortion on the measurement decreases as the sample birefringence increases, and the

optic axis measurement is more susceptible to the polarization distortion than accumulative retardation.

Figure 2.3. Simulation of the accumulative retardation and optic axis measurement without (blue box plot) and with (red box plot) calibration when imaging a two-layer phantom positioned at different orientation angles. (a-b). Demonstration of the effect of polarization distortion correction on accumulative retardation (a) and optic axis (b) measurement when the accumulative retardation of the first layer is set to be 0.15 rad; (c-d) Demonstration of the effect of polarization distortion correction on accumulative retardation and optic axis measurement when the accumulative retardation of the first layer is set to be 1.5 rad.

2.5.2 Experimental results

We developed a polarization-corrected single input PS-OCT system and validated its performance. The axial resolution was $\sim 2.3 \mu\text{m}$ in air, and the 6-dB roll-off depth was $500 \mu\text{m}$ in air. Based on the Jones matrix modelling of the system, we corrected the illumination polarization state to be circularly polarized across all depths. First, we imaged a phantom which consisted of two layers. The first non-birefringent layer was made by 1.0% polystyrene microspheres (Polysciences Inc., 300 nm in diameter) solution. The second layer was a tissue-like birefringent phantom which was fabricated following the procedures described in Ref.[69]. From the intensity image (**Figure 2.4** (a)), the two layers can be distinguished by a bright boundary. **Figure 2.4** (b) shows the accumulative retardation image without the polarization distortion correction, where the first non-birefringent layer shows some amount of accumulative retardation. In contrast, the corrected image is shown in **Figure 2.4** (c), where the upper

layer (microspheres solution) exhibits zero accumulative retardation and the second layer presents gradually increasing accumulative retardation along with the depth. We obtained differential retardance[70] image (**Figure 2.4** (d)), by axially differentiating the accumulative retardation (**Figure 2.4** (c)) with an interval set to be the kernel size of the averaging of Stokes vectors. In the differential retardance image (d), the boundary delineated by the distinct retardation difference accords well with the boundary seen in the intensity image (**Figure 2.4** (a)).

Figure 2.4. A demonstration of polarization distortion removal on a designed phantom. (a). Intensity image, scale bar 100 μm ; MS: microsphere solution (non-birefringent sample); AP: ABS phantom (birefringent sample made of acrylonitrile butadiene styrene (ABS)). (b) Accumulative retardation image without the polarization distortion correction; (c). Accumulative retardation image with polarization distortion correction; (d) Differential retardance image, which was obtained by point-to-point differentiation of the accumulative retardation presented in the image (c).

Figure 2.5. A comparison of birefringence imaging of swine retina near the macula with and without the polarization distortion correction. (a). Intensity image, scale bar: vertical 100 μm , horizontal 500 μm . RNFL: retinal nerve fiber layer, RPE; retinal pigment epithelium. (b) Accumulative retardation with polarization distortion

correction. (c) Differential retardance with polarization distortion correction. (d) Accumulative optic axis image. (e) DOPU image. (f)-(h) Accumulative retardation, differential retardance, accumulative optic axis image without polarization distortion correction, respectively. The white arrows indicate the area where RNFL is not highlighted as a high birefringence area.

Then, we imaged swine retina *ex vivo*. The swine eyeball was collected from a slaughterhouse within one hour after harvesting. We removed the cornea and vitreous body of the eye, thus exposing the retina directly to the air within two hours after the eyeball was harvested. The scanned area centered at the optic nerve head and spanned to the macular area. Note that swine retina does not have fovea shape at the center of the macular area, which is different from that of human[71]. **Figure 2.5(a)** shows the cross-sectional intensity image of the retinal structure, where layer structures such as the retinal nerve fiber layer (RNFL) and the retinal pigment epithelium (RPE) can be clearly visualized. **Figure 2.5 (e)** shows the DOPU contrast of the retina. The low DOPU value at the RPE indicates strong depolarizing effects and can be used to differentiate RPE and choroid for the diagnosis of drusen[54], [72]. **Figure 2.5 (b)** shows that the accumulative retardation increases gradually along with depth within the RNFL, especially on the right side of the image. The birefringence distribution in the retina is better visualized in **Figure 2.5 (c)** after differentiation on accumulative retardation image (b), from where highly birefringent RNFL can be easily distinguished. In contrast, in the uncorrected retardation images **Figure 2.5 (g)**, the birefringence distribution does not accord well with the RNFL, especially in the area indicated by the white arrows. While in the uncorrected optic axis image, the change of the measured optic axis is more toneless than the corrected one, the difference will be more evident in the *en face* image shown in **Figure 2.6**.

Figure 2.6 shows a set of cross-sectional images and *en face* projections of the optic nerve head area of the swine retina, where the RNFL is much thicker than the macular area. The *en face* projections were obtained by averaging the corresponding results along with depth within the RNFL. Fiber structures are clearly seen in the *en face* intensity projection in **Figure**

2.6 (f). The accumulative retardation at the lower boundary of RNFL is mapped as an *en face* image illustrated in **Figure 2.6** (g). **Figure 2.6** (h)-(i) demonstrate *en face* projections of optic axis with and without the polarization distortion calibration: the calibrated optic axis image (**Figure 2.6** (i)) reveals the radial pattern of the nerve fiber orientation, while the uncorrected one (**Figure 2.6** (h)) shows an indistinct pattern.

Figure 2.6. Birefringence imaging of swine retina near the optical nerve head. (a) Intensity image, scale bar: vertical 100 μm , horizontal 500 μm . (b) Accumulative retardation with polarization distortion correction. (c). Differential retardance with polarization distortion correction. (d) Accumulative optic axis image. (e) DOPU image. (f). Intensity projection, scale bar 400 μm . (g) The *en face* projection accumulative retardation at the bottom of the retinal nerve fiber layer. (h). *En face* projection of the optic axis without polarization distortion correction. (i). *En face* image of optic axis after polarization distortion correction

Figure 2.7 shows cross-sectional images of rat esophageal tissue scanned along the circular direction after polarization distortion correction. To mitigate surface reflection, we placed a cover glass gently on the tissue surface to keep in contact with it, meanwhile inserted an identical cover glass in the reference arm to balance the dispersion. In the intensity image (**Figure 2.7** (a)), layered structures are clearly visualized with high resolution. In accumulative retardation image (**Figure 2.7** (c)), the top five layers (keratinized layer to submucosa layer) do not present significant birefringence, while the muscularis propria (MP) layer shows a rapid

accumulation of phase retardation. The amount of birefringence in each layer can be better visualized in the differential local retardation image (Figure 2.7 (d)). In Figure 2.7 (b), the distinct optic axis orientation difference between the internal circular layer (ICL) and outer longitudinal layer (OLL) of muscularis propria agrees well with the orientation of the muscle fibers shown in the histology image (Figure 2.7 (e)).

Figure 2.7. Birefringence imaging of rat esophagus. (a) Intensity image; (b) Optic axis orientation image; (c) Accumulative retardation image. (d) Differential retardance image. (e). Histology of rat esophagus (transverse section). KL: keratinized layer; EP: epithelium; LP: lamina propria; MM: muscularis mucosa; SM: submucosa; MP: muscularis propria; ICL: internal circular layer; OLL: outer longitudinal layer; AD: adventitia. Scale bar: vertical 100 μm , horizontal 200 μm .

2.6 Discussion and conclusion

According to the simulation, the calibration is crucial for the determination of the accumulative optic axis of the sample when the sample birefringence is weak. This might be why the optic axis contrast of the retina was obscured without this polarization distortion correction. Moreover, the retardation was also biased to its ground truth when the initial polarization state is not circular polarization, and this might be why some parts of retinal nerve fiber layer do not present a gradual increase in accumulative retardation. In contrast, the measurement of strong retarder seems far less affected by the polarization distortion. This implies a negative correlation between the impact of the polarization distortion and strength of the retarder. Thereby, it is crucial for the measurement of low birefringence tissue such as retina to correct this polarization distortion.

It is worth mentioning that the system configuration of our single input PS-OCT setup also provides some convenience for the polarization distortion correction over the existing ones. The light beam is manipulated to be circularly polarized before entering the beam splitter, thus precluding the back-reflected and back-scattered light from passing QWP again, which provides a convenience for the calibration of the imperfection of QWP. In the reference arm, the QWP at 22.5° is replaced by a more economical linear polarizer at 45° . The requirement on the orientation of the linear polarizer is less strict than a QWP since a polarizer ensures identical phase inherently for the horizontal and vertical components of the reference light so that only the amplitude responses of the two detection channels need compensation. Compared with the traditional single-input PS-OCT system, our customized system theoretically has lower polarization distortion caused by polarizing components. In the sample arm, the double pass through the imperfect QWP exacerbates the defect of wavelength-dependent characterization. In the reference arm, double pass through the imperfect QWP cannot ensure identical reference light beam for the orthogonal polarization detections, especially the phase. These modifications also provide convenience in the correction of the polarization distortion induced by the roll-off difference of the two spectrometers.

In conclusion, I introduced a high-resolution single input PS-OCT with self-consistent fabrication procedures and detailed calibration procedures. The cost of the system was reduced by replacing one QWP with a less expensive linear polarizer. I investigated the effect of polarization distortion induced by the imperfection of QWP on the measurement of birefringence. And I developed a polarization distortion correction method based on the Jones matrix modeling of the PS-OCT system. Correspondingly, an algorithm for retardation, optic axis, and DOPU reasoning was formed. To demonstrate the performance of the polarization distortion correction method, we performed a numerical simulation. Moreover, images of the swine retina and rat esophagus demonstrated the capability of resolving the birefringence property of real tissues.

Chapter 3 Polarization mirror state constraint

3.1 Background

In biological optics, polarimetry sensing and imaging via back-scattering signal show immense potential especially in revealing birefringence properties of tissue [73]–[76]. Currently, due to the complexity of light-matter interaction [77], considerable efforts have been made to reliably resolve local birefringence information of the target via back-scattering, where usually more than one state of polarization is needed for light illumination and detection [77], [78]. In this Chapter, we report the mirror state constraint in reciprocal unitary back-scattering measurement, which enables reconstruction of local birefringence in media with only one state of polarization illumination in back-scattering polarimetry. This constraint could also be applied in other areas where a reciprocal unitary back-scattering optical path is employed [79].

3.2 Discovery of the mirror state phenomenon

Reciprocity is a fascinating property of wave propagation and states that in reciprocal media a forward propagating wave can be exactly reversed, to trace back the exact same path in reverse direction. Reciprocity has been closely investigated [80], as the underlying principle enabling focusing of light in complex media [81], and strategies for breaking it enable unexpected physical behavior [82], [83]. Reciprocity also governs the polarization of light, with the consequence that the Jones matrix describing the polarization transformation of light illuminating a sample with symmetric dielectric tensor and detected within the coherent backscattering peak is transpose symmetric [84]. Furthermore, we found in a reciprocal unitary system, the polarization states of an ensemble of sample realizations with sufficient retardation variation tend to bunch around a specific polarization state, corresponding to a point on the Poincaré sphere. It corresponds to the polarization state of the illumination light, but ‘mirrored’

by the horizontal QU-plane of the Poincaré sphere, thus named as mirror state. Although previously reported [85]–[87], this phenomenon has not been discussed in detail, especially in back-scattering polarimetry.

To demonstrate the existence of the polarization mirror state, an optical system was constructed, containing a polarization controller which changes birefringence in the reciprocal system, shown in **Figure 3.1(a)**. Two flip mirrors were added in the reference arm and sample arm, respectively, to quickly switch between pure free space configuration and fiber-based configuration. The redirected beams were coupled into two 1.5 meters long single-mode fiber patches (Thorlabs 780HP) and reflected by mirrors. Two 3-paddle polarization controllers (PC1, PC2) were applied to each fiber, numbers of fiber loops coiled in the paddles are 1, 2 and 1, respectively.

To measure the initial polarization state of the incident light, we toggled the flip mirrors (FM1, FM2). In this configuration, the system was a free-space polarization sensitive Michelson interferometer, the initial polarization state after beam splitter can be measured and recorded.

Then we inserted the flip mirrors to the light circuit, switch the system to fiber-based configuration. To maximize the light passing polarizer P2, we tuned PC1 to maximize the intensity received by the spectrometers. We took the sample arm (from beam splitter BS to M5 back to BS) as the reciprocal unitary backscattering circuit under investigation. To observe the light polarization state evolution, we randomly moved the paddles of P2 while recording the polarization states. This experiment was conducted three times with incident light of different polarization states created by rotating the quarter wave plate (Q1) in the input arm.

We plotted the measured polarization state with different PC paddles position as a time trace on the Poincaré sphere in **Figure 3.1(b)**. For different polarization states coupled into the SMF (indicated by yellow arrows in **Figure 3.1(b)-(d)**), the polarization state evolution on the Poincaré sphere clearly passes a specific point multiple times, which we termed the polarization mirror state (marked with red arrows), as it corresponds to the

mirror state point of input polarization state (indicated by blue arrows) by the QU-plane.

Figure 3.1 Demonstration of polarization mirror state. (a) Schematic of the optical circuit of the demonstration experiment. SCL: super-continuum laser. P1,2: Polarizer. Q1: Quarter-wave plate, H1: Half-wave plate. BS: Non-polarizing beam splitter (50/50). PBS: Polarizing beam splitter (50/50). DC: Dispersion compensation, BK7 glass plate. M1-5: Mirrors. FM1-2: Flip mirrors. PC: Polarization controller. Three-paddle polarization controllers, with 1, 2 and 1 fiber loops in the three paddles, respectively. (b)-(d) Polarization state evolving trace on the Poincaré sphere with circularly, elliptically and linearly polarized input light, respectively.

3.3 Theoretical explanation of the polarization mirror state phenomenon

Of note, the rotation effect of a linear retarder in the double pass can be expressed in the axis-angle representation as $\mathbf{r} = \omega^*[\cos\alpha, \sin\alpha, 0]^T$, where α is the azimuth angle with respect to the Q-axis and ω is the rotation angle. The corresponding rotation matrix is to rotate input polarization state $\mathbf{s} = [s_1, s_2, s_3]^T$ to any polarization state $\mathbf{s}' = [s'_1, s'_2, s'_3]^T$ can be represented by a Mueller matrix:

$$\mathbf{R}(\alpha, \omega) = \begin{bmatrix} \cos^2(\alpha) + \cos(\omega)\sin^2(\alpha) & \cos(\alpha)\sin(\alpha) - \cos(\alpha)\cos(\omega)\sin(\alpha) & \sin(\alpha)\sin(\omega) \\ \cos(\alpha)\sin(\alpha) - \cos(\alpha)\cos(\omega)\sin(\alpha) & \cos(\omega)\cos^2(\alpha) + \sin^2(\alpha) & -\cos(\alpha)\sin(\omega) \\ -\sin(\alpha)\sin(\omega) & \cos(2\alpha)\sin(\omega) & \cos(\omega) \end{bmatrix} \quad (3-1)$$

For a general case, the rotation matrix $\mathbf{R}(\alpha, \omega)$ maps the input polarization state $\mathbf{s} = [s_1, s_2, s_3]^T$ to some state $\mathbf{v} = [s'_1, s'_2, s'_3]^T$ other than the mirror state ($\mathbf{s}' = \mathbf{D} \cdot \mathbf{s}$, $\mathbf{D} = \text{diag}(1, 1, -1)$). Solving equation $\mathbf{v} = \mathbf{R}(\alpha, \omega) \cdot \mathbf{u}$ for angles α and ω , a unique set of solutions could be found as shown in Eq. (3-2) where $A = s_2 \cdot \cos(\alpha) - s_1 \cdot \sin(\alpha)$, $B = s_3$, $C = s'_3$, and $\arctan 2$ denotes four quadrant inverse tangent.

$$\begin{aligned} \vartheta &= \arctan 2 \left(-\left(s'_1 - s_1\right), \left(s'_2 - s_2\right) \right) \\ \omega &= \cos^{-1} \left(\frac{AB - C\sqrt{A^2 + B^2 - C^2}}{A^2 + B^2} \right) \end{aligned} \quad (3-2)$$

This means there exists only one rotation vector in the QU plane that rotates the input state $\mathbf{s}$ to an arbitrary state $\mathbf{v}$. Geometrically, this rotation vector aligns with the intersection between the QU plane and the bisecting plane of vectors $\mathbf{s}$ and $\mathbf{v}$.

When the arbitrary polarization state $\mathbf{s}''$ coincides with the mirror state $\mathbf{s}'$, equation $\mathbf{s}' = \mathbf{R}(\alpha, \omega) \cdot \mathbf{s}$ holds for all values of α . The rotation angle is

$$\text{solved as } \omega = \cos^{-1} \left(\frac{s_3^2 - \left(s_1 \sin(2\vartheta) - s_2 \sin(2\vartheta)\right)^2}{s_3^2 + \left(s_1 \sin(2\vartheta) - s_2 \sin(2\vartheta)\right)^2} \right) \text{ for any given } \alpha. \text{ This means}$$

the rotation vector of a linear retarder that rotates the input state $\mathbf{s}$ to the mirror state $\mathbf{s}'$ can be found for any azimuth direction within the QU plane. Such rotation vectors would trace out a continuous curve if they are represented by their equivalence with a rotation angle $\omega \in (-\pi, \pi]$ considering the 2π -ambiguity (shown as the red curve in **Figure 3.2(b)**).

Figure 3.2 The relationship between the trace of the rotation vector that maps the input state to the mirror state and the position of the input state. (a) The maximum and minimum rotation angle α, β and the corresponding rotation axis orientations $\vec{\tau}_{An}$, $\vec{\tau}_{Bn}$ shown on a Poincaré sphere. (b) How $\vec{\tau}_{An}$ and $\vec{\tau}_{Bn}$ define the orientation and curvature of the trace of the rotation vector that maps the input state to the mirror state (red line). The largest rotation angle ω_A corresponds to the rotation vector $\vec{\tau}_A$ that aligns with the projection of input state on the QU plane. Thus, the azimuth angle of the input states determines the orientation of the trace. The smallest rotation corresponds to the rotation vector $\vec{\tau}_B$ which is perpendicular to $\vec{\tau}_A$. The smallest rotation angle ω_B equals to twice the elevation angle of the input state and determines the curvature of the trace.

The shape and orientation of the trace of rotation vectors which map input state $\mathbf{s}$ to mirror state $\mathbf{s}'$ are determined by the location of $\mathbf{s}$. Assume the azimuth and elevation angles of $\mathbf{s}$ are α and ε , respectively ($\alpha \in [0, 2\pi)$, $\varepsilon \in [-\frac{\pi}{2}, \frac{\pi}{2}]$). Then the largest rotation angle appears when the rotation vector aligns with the projection of $\mathbf{s}$ on the QU plane ($\theta = \alpha$, the orientation of the rotation axis is indicated by $\vec{\tau}_{An}$ in **Figure 3.2**). The rotation angle ω_A is π if $\mathbf{s}$ is rotated around $\vec{\tau}_{An}$ to reach $\mathbf{s}'$. The smallest rotation angle appears when the rotation axis $\vec{\tau}_{Bn}$ is perpendicular to $\vec{\tau}_{An}$. In this case, the rotation trajectory coincides with a longitude of the sphere and corresponds to a radius angle of $\omega_B = 2|\varepsilon|$ (ε is the elevation angles of $\mathbf{s}$). According to 3b, the orientation of the trace is aligned with the azimuth angle of input state $\mathbf{u}$, the curvature of the trace is determined by the elevation angle of $\mathbf{s}$.

For a randomly given input polarization state $\mathbf{s}$, endpoints of all the rotation vectors that map $\mathbf{s}$ precisely to its mirror state $\mathbf{s}'$ compose a curve $\mathbf{r} = \omega(\theta)$ shown by the thick red line in **Figure 3.2(b)**. Curve $\mathbf{r}$ intersects with the π -circle at two points symmetric about the origin because of the 2π folding effect. In contrast, for any polarization state $\mathbf{s}''$ other than mirror state $\mathbf{s}'$, there exists only one rotation vector lying in the π -circle of QU plane that rotates $\mathbf{s}$ to $\mathbf{s}''$. So, the infinite possible linear retarder which can rotate a randomly given input polarization state $\mathbf{s}$ to its mirror state makes the possibility of polarization state gathering around its mirror state highest when twisting the polarization controller paddles in the sample arm.

3.4 Polarization mirror state constraint and its significance

First, consider a birefringent medium whose single-trip transmission can be described by a Mueller matrix $\mathbf{M}(x)$, with its retardation varying as a parameter x , e.g. the depth within. Assuming the polarization state of the illuminating light to be $\mathbf{s}$, the polarization state of the output light at the other side of the medium would be $\mathbf{t}_s = \mathbf{M} \cdot \mathbf{s}$. Without considering the effects of depolarization and diattenuation, the transmission matrix is in the rotation group $\text{SO}(3)$. Geometrically, $\mathbf{M}$ can be represented by its rotation vector $\boldsymbol{\beta}_s$. The polarization state $\mathbf{t}_s$ is obtained by rotating $\mathbf{s}$ around the $\boldsymbol{\beta}_s$ for a rotation angle $|\boldsymbol{\beta}_s|$. Take derivative for both sides of equation $\mathbf{t}_s = \mathbf{M} \cdot \mathbf{s}$ and substitute $\mathbf{s}$ as $\mathbf{M}^T \cdot \mathbf{t}_s$, and we have

$$\frac{\partial \mathbf{t}_s}{\partial x} = \frac{\partial \mathbf{M}}{\partial x} \cdot \mathbf{s} = \frac{\partial \mathbf{M}}{\partial x} \cdot \mathbf{M}^T \cdot \mathbf{t}_s = [\boldsymbol{\beta}_s]_{\times} \cdot \mathbf{t}_s \quad (3-3)$$

Because $\mathbf{M} \cdot \mathbf{M}^T$ is the identity matrix, $(\partial \mathbf{M} / \partial x) \cdot \mathbf{M}^T = -\mathbf{M} \cdot (\partial \mathbf{M}^T / \partial x)$ is skew-symmetric and can be expressed as the cross-product operator $[\boldsymbol{\beta}_s]_{\times}$. $[\boldsymbol{\beta}_s]_{\times}$ is termed as the differential Mueller matrix and corresponds to the rotation vector of the rotation matrix $\mathbf{M}$, $\boldsymbol{\beta}_s = [\text{LB}, \text{LB}', \text{CB}]^T$ [88]

$$[\boldsymbol{\beta}_s]_{\times} = \begin{pmatrix} 0 & \text{CB} & -\text{LB}' \\ -\text{CB} & 0 & \text{LB} \\ \text{LB}' & -\text{LB} & 0 \end{pmatrix} \quad (3-4)$$

where CB, LB and LB' denote three elementary birefringence components of the transmission matrix, which are the circular birefringence, the linear birefringence with respect to the X and Y laboratory axes, and the linear birefringence with respect to the $\pm 45^\circ$ axes, respectively.

In a round-trip propagation, the transmission equation can be written as $\mathbf{t} = \mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D} \cdot \mathbf{M} \cdot \mathbf{s}$, where $\mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D}$ is the reverse transmission (see Appendix for more details), and $\mathbf{D} = \text{diag}(1, 1, -1)$. Take the derivative of both sides of the equation and substitute the input state as $\mathbf{s} = \mathbf{M}^T \cdot \mathbf{D} \cdot \mathbf{M} \cdot \mathbf{D} \cdot \mathbf{t}$, we have

$$\begin{aligned} \frac{\partial \mathbf{t}}{\partial \mathbf{x}} &= \left(\mathbf{D} \cdot \frac{\partial \mathbf{M}^T}{\partial \mathbf{x}} \cdot \mathbf{M} \cdot \mathbf{D} + \mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D} \cdot \frac{\partial \mathbf{M}}{\partial \mathbf{x}} \cdot \mathbf{M}^T \cdot \mathbf{D} \cdot \mathbf{M} \cdot \mathbf{D} \right) \\ &\cdot \mathbf{t} = [\boldsymbol{\beta}]_{\times} \cdot \mathbf{t} \end{aligned} \quad (3-5)$$

Where the differential Mueller matrix $[\boldsymbol{\beta}]_{\times}$ can be further expressed as

$$\begin{aligned} [\boldsymbol{\beta}]_{\times} &= \mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D} \cdot \left(\mathbf{D} \cdot \mathbf{M} \cdot \frac{\partial \mathbf{M}^T}{\partial \mathbf{x}} \cdot \mathbf{D} \right) \cdot \mathbf{D} \cdot \mathbf{M} \cdot \mathbf{D} + \mathbf{D} \cdot \mathbf{M}^T \\ &\cdot \mathbf{D} \cdot \left(\frac{\partial \mathbf{M}}{\partial \mathbf{x}} \cdot \mathbf{M}^T \right) \cdot \mathbf{D} \cdot \mathbf{M} \cdot \mathbf{D} \\ &= \mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D} \cdot (-\mathbf{D} \cdot [\boldsymbol{\beta}_s]_{\times} \cdot \mathbf{D} + [\boldsymbol{\beta}_s]_{\times}) \cdot (\mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D})^{-1} \end{aligned} \quad (3-6)$$

If we denote $\mathbf{Q} = -\mathbf{D} \cdot [\boldsymbol{\beta}_s]_{\times} \cdot \mathbf{D} + [\boldsymbol{\beta}_s]_{\times}$ it can be shown that $\mathbf{Q} =$

$$\begin{pmatrix} 0 & 0 & -2 \cdot \text{LB}' \\ 0 & 0 & 2 \cdot \text{LB} \\ 2 \cdot \text{LB}' & -2 \cdot \text{LB} & 0 \end{pmatrix}$$

is both linear and skew-symmetric. By re-

integrating the derivative of $\mathbf{t}$ we have the first-order approximation to the evolution of $\mathbf{t}$:

$$\begin{aligned} \tilde{\mathbf{t}} &= \exp([\boldsymbol{\beta}]_{\times} \cdot \Delta \mathbf{x}) \cdot \mathbf{t}(\mathbf{x}_0) \\ &= (\mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D} \cdot \exp(\mathbf{Q} \cdot \Delta \mathbf{x}) \cdot \mathbf{D} \cdot \mathbf{M} \cdot \mathbf{D}) \cdot \mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D} \cdot \mathbf{M} \cdot \mathbf{s} \\ &= \mathbf{D} \cdot \mathbf{M}^T \cdot \mathbf{D} \cdot \exp(\mathbf{Q} \cdot \Delta \mathbf{x}) \cdot \mathbf{M} \cdot \mathbf{s} \\ &= \mathbf{D} \cdot \mathbf{L}^T \cdot \mathbf{C}^T \cdot \mathbf{D} \cdot \exp(\mathbf{Q} \cdot \Delta \mathbf{x}) \cdot \mathbf{C} \cdot \mathbf{L} \cdot \mathbf{s} \\ &= \mathbf{L} \cdot \exp(\mathbf{C}^{-1} \mathbf{Q} \mathbf{C} \cdot \Delta \mathbf{x}) \cdot \mathbf{L} \cdot \mathbf{s} \\ &= \mathbf{L} \cdot \exp(\mathbf{Q}' \cdot \Delta \mathbf{x}) \cdot \mathbf{L} \cdot \mathbf{s} \end{aligned} \quad (3-7)$$

Here $\mathbf{M}$ is decomposed as the product of a linear element $\mathbf{L}$ and a circular element $\mathbf{C}$ ($\mathbf{M} = \mathbf{C} \cdot \mathbf{L}$). Left-multiplying Eq. (3-7) with $\mathbf{M}^T$ gives the relationship of transformed $\mathbf{t}$ and $\mathbf{s}$:

$$\tilde{\mathbf{t}}' = \exp(\mathbf{Q}' \cdot \Delta \mathbf{x}) \cdot \mathbf{s}' \quad (3-8)$$

where $\tilde{\mathbf{t}}' = \mathbf{L}^T \cdot \tilde{\mathbf{t}}$ and $\mathbf{s}' = \mathbf{L} \cdot \mathbf{s}$. Owing to the linearity of $\mathbf{Q}'$, we can always find a suitable Δz that rotates $\mathbf{s}'$ onto $\mathbf{t}'$ (see section 3.3 for the proof):

$$\tilde{\mathbf{t}}' = \mathbf{D} \cdot \mathbf{s}' \quad (3-9)$$

Under this circumstance, the corresponding $\mathbf{t}$ would be:

$$\begin{aligned} \tilde{\mathbf{t}} &= \mathbf{L} \cdot \tilde{\mathbf{t}}' = \mathbf{L} \cdot \mathbf{D} \cdot \mathbf{L} \cdot \mathbf{s} = \mathbf{D} \cdot \mathbf{D} \cdot \mathbf{L} \cdot \mathbf{D} \cdot \mathbf{L} \cdot \mathbf{s} = \mathbf{D} \cdot \mathbf{L}^T \cdot \mathbf{L} \cdot \mathbf{s} \\ &= \mathbf{D} \cdot \mathbf{s} \end{aligned} \quad (3-10)$$

Hence, the first order approximation to the evolution of the polarization state varying with some argument x lies on a circle evolving through the mirror state $\mathbf{m} = \mathbf{D} \cdot \mathbf{s}$.

Another explanation of the constraint

Further, in a more general case, let's consider a simple reciprocal unitary optical system model with continuously changing linear birefringence $\mathbf{M}(x)$ preceded by static layers described by single-trip transmission matrix $\mathbf{P}$ as shown in **Figure 3.3(a)**. The system is illuminated by light with polarization state $\mathbf{s}$ and the detected backscattered polarization state is $\mathbf{v}$. According to Mueller-Stokes formulism, the system transmission equation can be expressed as

$$\mathbf{t} = \mathbf{D} \cdot \mathbf{P}^T \cdot \mathbf{M}^T(x) \cdot \mathbf{D} \cdot \mathbf{M}(x) \cdot \mathbf{P} \cdot \mathbf{s} = \mathbf{T}(x) \cdot \mathbf{s} \quad (3-11)$$

Part of the system described by round-trip transmission matrix $\mathbf{M}$ varies in the response of argument x which represents either time t in the demonstration experiment when one paddle of the polarization controller is being twisted, or depth z in typical birefringence imaging when the light is reflected at increasing depth within a homogenous retarding sample. The light passes through the static path described by $\mathbf{P}$ prior to $\mathbf{M}$. In the

backward propagation, the transmission matrix of the static part is described by $\mathbf{D}\mathbf{P}^T\mathbf{D}$ where $\mathbf{D} = \text{diag}(1, 1, -1)$. From Eq. (3-11) we know that $\mathbf{s} = \mathbf{P}^T \cdot \mathbf{M}^T(x) \cdot \mathbf{D} \cdot \mathbf{M}(x) \cdot \mathbf{P} \cdot \mathbf{D} \cdot \mathbf{t} = \mathbf{T}^T(x) \cdot \mathbf{t}$. As $\mathbf{M}$ is changing with x , take the derivative of both side of the equation and substitute $\mathbf{s}$ with $\mathbf{t}$, we have

$$\frac{\partial \mathbf{t}}{\partial x} = \frac{\partial \mathbf{T}}{\partial x} \cdot \mathbf{T}^T(x) \cdot \mathbf{t} = [\boldsymbol{\beta}(x)]_x \cdot \mathbf{t} \quad (3-12)$$

By nature of a rotation matrix, we know that $\mathbf{T} \cdot \mathbf{T}^T = \mathbf{I}$ and take the derivative of both sides, we have $\partial \mathbf{T} / \partial x \cdot \mathbf{T}^T + \partial \mathbf{T}^T / \partial x \cdot \mathbf{T} = \mathbf{0}$, implying that $\partial \mathbf{T} / \partial x \cdot \mathbf{T}^T$ is a skew-symmetric matrix. A skew-symmetric matrix is a cross product operator, ensuring that the trajectory of $\mathbf{t}$ should always be a circular arc on the Poincaré sphere.

It should be noted that since the system is unitary reciprocal, its round-trip transmission can be described as a pure linear retarder, whose overall effect on an input Stokes vector can be described by a rotation vector lying on the QU plane of the Poincaré sphere. Furthermore, rotation around a rotation axis by an angle θ is equivalent to a series of rotations along the same rotation axis by angles $(n \cdot 2\pi - \theta)$ (n is an integer). If such 2π folding effect is considered, rotation vectors corresponding to all linear retarders can be represented equivalently by their endpoints located within a circle of radius π on the QU plane (shown by the dashed circle in **Figure 3.3(b)**).

Figure 3.3. Theoretical explanation of the polarization mirror state. (a) Model of the round-trip propagation through a reciprocal sample, comprising $\mathbf{R}(x)$ with varying retardation and a static element $\mathbf{P}$. (b) The rotation vectors of all linear retarders localize within a circle of radius π within the QU-plane of the Poincaré sphere. The orange curve represents the endpoints of the rotation vectors mapping the randomly chosen input polarization state $[\cos(-\pi/6) \cdot \cos(\pi/3), \cos(-\pi/6) \cdot \sin(\pi/3), \sin(-\pi/6)]^T$

exactly to its mirror state. The green trace represents the simulated rotation vector evolution for a synchronous movement of the polarization controller paddles. The purple curves represent the rotation vectors of $\mathbf{D} \cdot \mathbf{P}^T \cdot \mathbf{M}^T(x) \cdot \mathbf{D} \cdot \mathbf{M}(x) \cdot \mathbf{P}$, where $\mathbf{M}(x)$ is a linearly increasing linear retarder, for three representative sets of distinct $\mathbf{P}$ and $\mathbf{M}(x)$.

In the case of birefringent sample imaging where the birefringence of matrix $\mathbf{M}$ is increasing linearly along with depth x , the rotation vector of the system described by Eq.(3-11) would trace out a similar curve across the π -circle (Some rotation vector traces with randomly generated rotation axis orientations are drawn by blue lines in **Figure 3.3**). These traces also intersect with the π -circle at two points symmetric about the origin, which ensures themselves an intersection with curve $\mathbf{r}$, implying that the circular trajectory of $\mathbf{t}$ always passes the mirror state $\mathbf{s}'$.

Figure 3.4 shows experimental validation of the existence of mirror state when round-trip transmission matrix $\mathbf{M}$ varies in the response of the depth of x . We prepared a scattering phantom consisting of three linearly birefringent layers with distinct optic axis orientations (**Figure 3.4(a)**). The birefringent phantom is custom made by ABS and has homogeneous birefringence with constant optic axis[69]. The phantom was probed three times with light of different polarization states (circular in **Figure 3.4(b)**, elliptic in **Figure 3.4(c)** and linear in **Figure 3.4(d)**). Backscattered light was recorded by polarization diversity detectors. Applying PS-OCT techniques, the coherence gate was used to differentiate the light backscattered from different depths.

Figure 3.4 Mirror state effect validation using a three-layer retarder phantom. (a) Schematic sketch of the three-layer phantom sample. Each layer has a different optic axis orientation. (b)-(d) Polarization state evolving trace (color-coded corresponding to (a)) for each layer on the Poincaré sphere with different input polarization state ((b) circularly polarized input light; (c) elliptically polarized input light; (d) linearly polarized input light). Purple lines are the fitting circles of the polarization state

evolution of each retarder layer. Mirror state and input polarization state are indicated by red and blue arrows, respectively. It can be noticed that the mirror state and input point are symmetric with respect to the QU plane.

Figure 3.4(b)-(d) show the polarization state evolution along with the depth, color-coded for different birefringent layers according to **Figure 3.4(a)**. We fitted a circle (purple circles in **Figure 3.4(b)-(d)**) to the measured polarization state evolution for every sample layer. Matching our prediction, the circles all crossed the polarization mirror state $\mathbf{s}'$ (blue arrows in **Figure 3.4 (b)-(d)**), which is exactly the QU plane mirror state of the input polarization state $\mathbf{s}$, confirming $\mathbf{s}' = \mathbf{D} \cdot \mathbf{s}$.

An apparent application of the mirror state constraint is resolving local birefringence with a single state of polarization illumination via back-scattering signal. As described above, that polarization state $\mathbf{t}$ and its derivative are related by multiplication with a skew-symmetric matrix, which corresponds to a cross-product of a rotation vector $\boldsymbol{\beta}$ and $\mathbf{t}$:

$$\frac{\partial \mathbf{t}(x)}{\partial x} = \begin{bmatrix} 0 & -\tau_v & \tau_u \\ \tau_v & 0 & -\tau_\phi \\ -\tau_u & \tau_\phi & 0 \end{bmatrix} \cdot \mathbf{t} = \boldsymbol{\beta} \times \mathbf{t} \quad (3-13)$$

Convert Eq.(3-13) into scalars, we have $\left| \frac{\partial \mathbf{t}}{\partial x} \right| = |\boldsymbol{\beta}| |\mathbf{t}| \sin \alpha$, where α is the angle between the rotation axis and the polarization state $\mathbf{v}$. With the knowledge that the mirror state $\mathbf{s}'$ lies in the same plane with $\mathbf{t}$ and $\frac{\partial \mathbf{t}}{\partial x}$, it can be inferred that the difference between the current state and the mirror state $(\mathbf{t} - \mathbf{s}')$ as well as the derivative of $\mathbf{t}$ have to be orthogonal to the rotation axis. Hence, the direction of the rotation axis can be obtained by the cross product $\boldsymbol{\beta}_0 = \frac{\partial \mathbf{t}}{\partial x} \times (\mathbf{t} - \mathbf{s}')$. Then angle α can be resolved by $\sin \alpha = \frac{|\mathbf{t} \times \boldsymbol{\beta}_0|}{|\mathbf{t}| \cdot |\boldsymbol{\beta}_0|}$.

Hence, the norm of $\boldsymbol{\beta}$ is calculated by

$$\boldsymbol{\beta} = \frac{\frac{\partial \mathbf{t}}{\partial x} \times \mathbf{s}' - \mathbf{t}}{1 - \mathbf{t}^T \cdot \mathbf{s}'} \quad (3-14)$$

3.5 Conclusion

In conclusion, we demonstrated the peculiar properties of the mirror polarization state when measuring backscattered light along identical illumination and detection paths free of polarization-dependent loss. The mirror state constrains the evolution of the depth-dependent polarization state and can enable local retardation imaging, which previously has not been available to PS-OCT or other polarimetry without substantially more complex measurements using multiple input states. And its application in single input OCT will be demonstrated in Chapter 4.

3.6 Appendix: Mueller matrix of reverse transmission through a reciprocal medium

In this appendix, we derive the deterministic (i.e. non-depolarizing) Mueller matrix of the reverse transmission through a reciprocal element from its corresponding Jones expression. If A and B denote the front and rear interface of this element, the Jones matrix $\mathbf{J}_{AB}$ describes the forward propagation through this element (as shown in **Figure 3. 5**). The reverse transmission is given by the transpose of this matrix $\mathbf{J}_{BA} = \mathbf{J}_{AB}^T$, when maintaining the orientation of the spatial xy-coordinates irrespective of the propagation direction[89].

Figure 3. 5 Schematic diagram of the transmission through an element from A to B and in the reverse direction, described by the Jones and Mueller matrices, respectively.

A matrix $\mathbf{J}$ in the Jones formalism can be converted into its corresponding Mueller matrix $\mathbf{M}$ using[90]

$$\mathbf{M} = \mathbf{U} \cdot (\mathbf{J} \otimes \mathbf{J}^*) \cdot \mathbf{U}^\dagger \quad 3-15$$

$$\mathbf{U} = \frac{1}{\sqrt{2}} \begin{bmatrix} 1 & 0 & 0 & 1 \\ 1 & 0 & 0 & -1 \\ 0 & 1 & 1 & 0 \\ 0 & i & -i & 0 \end{bmatrix}$$

where $\otimes$ is the Kronecker tensor product, $\mathbf{J}^*$ is the complex conjugate of $\mathbf{J}$, and $\mathbf{U}^\dagger$ represents the conjugate transpose of $\mathbf{U}$, corresponding also to its inverse. Using the fact that the transpose is distributive for the Kronecker product $((\mathbf{A} \otimes \mathbf{B})^\top = \mathbf{A}^\top \otimes \mathbf{B}^\top)$, we find

$$\begin{aligned} \mathbf{M}_{BA} &= \mathbf{U} \cdot (\mathbf{J}_{BA} \otimes \mathbf{J}_{BA}^*) \cdot \mathbf{U}^\dagger \\ &= \mathbf{U} \cdot (\mathbf{J}_{AB}^\top \otimes \mathbf{J}_{AB}^\dagger) \cdot \mathbf{U}^\dagger \\ &= \mathbf{U} \cdot (\mathbf{J}_{AB} \otimes \mathbf{J}_{AB}^*)^\top \cdot \mathbf{U}^\dagger \\ &= \mathbf{U} \cdot \mathbf{I} \cdot (\mathbf{J}_{AB} \otimes \mathbf{J}_{AB}^*)^\top \cdot \mathbf{I} \cdot \mathbf{U}^\dagger \\ &= \mathbf{U} \cdot (\mathbf{U}^\top \cdot \mathbf{U}^*) \cdot (\mathbf{J}_{AB} \otimes \mathbf{J}_{AB}^*)^\top \cdot (\mathbf{U}^\top \cdot \mathbf{U}^*) \cdot \mathbf{U}^\dagger \\ &= (\mathbf{U} \cdot \mathbf{U}^\top) \cdot \mathbf{U}^* \cdot (\mathbf{J}_{AB} \otimes \mathbf{J}_{AB}^*)^\top \cdot \mathbf{U}^\top \cdot (\mathbf{U}^* \cdot \mathbf{U}^\dagger) \\ &= (\mathbf{U} \cdot \mathbf{U}^\top) \cdot \mathbf{M}_{AB}^\top \cdot (\mathbf{U}^* \cdot \mathbf{U}^\dagger) \end{aligned} \tag{3-16}$$

Evaluating the outermost expressions, we find $\mathbf{U} \cdot \mathbf{U}^\top = \mathbf{U}^* \cdot \mathbf{U}^\dagger = \text{diag}(1,1,1,-1)$. The transpose of a Jones matrix corresponds to the transpose of its corresponding Mueller matrix, with the sign of the last row and column, excluding the on-diagonal element, inverted. It represents the reverse transmission through a reciprocal element. For a pure retardation matrix $\mathbf{R}$ in the SO(3) formalism, this results in $\mathbf{R}_{BA} = \mathbf{D} \cdot \mathbf{R}_{AB}^\top \cdot \mathbf{D}$, where $\mathbf{D} = \text{diag}(1,1,-1)$

Chapter 4 Free-space single input PS-OCT with local retardation measurement modality

4.1 Background and innovation

Polarization-sensitive OCT(PS-OCT), as a functional extension to conventional OCT, has showed enormous potential in ophthalmology [14], [91]–[93] cardiology [94], [95] etc. Among the polarization contrasts obtained by PS-OCT, retardation imaging is the most popular and accessible. Generally, retardation contrast can be divided into two types: accumulative retardation and local retardation.

Local birefringence imaging provided by two polarization state input PS-OCT is more intuitive in revealing the distribution of birefringence in tissues[33][96]. Meanwhile, Micro-OCT with subcellular resolution can show more details which were not resolvable by convention OCT [22]. However, such a broad band of the light source required for ultra-high resolution makes it extremely difficult to achieve two polarization state inputs PS-OCT by polarization modulation [35] and the ranging depth of the spectrometers leave little margin for depth multiplexing [36], [97]. In the last chapter, a polarization mirror state constraint was introduced. The mirror state can be an additional constraint to determine the polarization state evolvment trace. Namely, it makes imaging the local retardation possible even with single polarization state input. In this chapter, I report a single input PS-OCT with high resolution and local retardation measurement.

4.2 System description and method

The system used here is the same as that in our previous report [98]. Briefly, we used a super-continuum light source and two customized, pixel-aligned spectrometers. The detected bandwidth was about 160 nm centered at 840 nm, providing a measured axial resolution of 2.3 μ m in the air. We used an achromatic 50 mm focusing lens as the objective of the system, resulting in a lateral resolution of $\sim$ 13 μ m. The polarization state of light was

manipulated by a polarizer and a quarter-wave plate before directed into the Michelson interferometer, making the polarization state of sample illumination was fixed as circularly polarized.

For reconstruction of local retardation, we employed the pre-calibrated polarization mirror state $\mathbf{u}'$, and implemented Eq.(4-1) by approximating $\mathbf{v}(z) = \mathbf{s}[z]$ and $\partial\mathbf{v}/\partial x = (\mathbf{s}[z+\Delta z] - \mathbf{s}[z-\Delta z])/\Delta z$, where Δz is the axial sampling distance, and we take Δz as the half of the axial filtering width used. To avoid high-frequency noise introduced by taking the difference between adjacent points, we axially averaged the reconstructed rotation vector $\boldsymbol{\tau}(z)$ with a rectangular Gaussian window of 10×10 speckle ($20 \times 80 \mu\text{m}$), before computing its norm as the local retardation image, scaled to degrees of retardation per depth ($^\circ/\mu\text{m}$). Then double pass rotation angle α caused by the birefringence in the sample slice in the interval $2\Delta z$ can be resolved by $\sin\alpha = \frac{|\mathbf{v} \times \boldsymbol{\tau}_0|}{|\mathbf{v}| \cdot |\boldsymbol{\tau}_0|}$. Hence, the norm of $\boldsymbol{\tau}$ is calculated by

$$\boldsymbol{\tau} = \frac{\frac{\partial\mathbf{v}}{\partial x} \times (\mathbf{u}' - \mathbf{v})}{\mathbf{v}^T \cdot \mathbf{v} - \mathbf{v}^T \cdot \mathbf{u}'} \quad (4-1)$$

The reasoning is clearer in geometric representation, shown in **Figure 4.1(b)**. On the Poincaré sphere, A and B correspond to the polarization states $\mathbf{s}(z - \Delta z)$ and $\mathbf{s}(z + \Delta z)$ and P corresponds to mirror state. The rotational axis can be calculated from $\mathbf{r} = \overrightarrow{\text{PA}} \times \overrightarrow{\text{PB}}$. Once $\mathbf{r}$ is known, the double-pass retardation can be solved as the angle δ between vectors $\text{O}'\text{A}$ and $\text{O}'\text{B}$, where O' is the center of the polarization evolving circle. And the projection of $\mathbf{r}$ on QU plane is the relative optic axis.

For comparison in the imaging results session, cumulative retardation was computed by evaluating the angle between $\mathbf{s}(z)$ at each depth and $\mathbf{s}(z_{\text{surf}})$, where z_{surf} is the axial location of the sample surface.

Figure 4.1 (a) The schematic of the PS-OCT system and (b) demonstration of local birefringence reasoning. SCL, super-continuum laser; C, collimation; P, polarizer; QWP, quarter-wave plate; BS, Beam Splitter; DC, dispersion compensator; L, lens; S, sample; M, mirror; LS, linear stage; HWP, half-wave plate; PMF, polarization maintaining fiber; SMF, single-mode fiber; PBS, polarization beam splitter; SP, spectrometer, G, grating.

4.3 Imaging results

4.3.1 Phantom imaging

Figure 4.2 (a) shows the structure of the designed phantom with birefringence at the range of normal biological tissue [69]. The first layer consists of four elements with distinct birefringence levels, and the second layer is a long birefringent band. The mixture of beads solution and ultrasonic gel serves as the embedding matrix of the phantom, providing a non-birefringent background. The angle of the optic axis orientations of the first and second layer is nearly 45 degrees. During the phantom imaging process, we scanned the phantom from the side of the short ABS band first. Then we flipped the phantom and scanned it again with the short ABS band on the bottom. **Figure 4.2** (b) shows the retardation measurement comparison between conventional cumulative birefringence image and our local birefringence image. In **Figure 4.2** (c), the relative optic axis of the phantom is shown. Compared to the conventional method, our method is more straightforward to distinguish films with different birefringence. And **Figure 4.3** shows the numerical analysis of the accuracy of the measurement. The birefringence results of the four pieces of ABS films prove consistent measurement between the two scans. This result

demonstrates the high consistency of the retardation in the two measurements.

Figure 4.2. Phantom Imaging. (a) Structure sectional view of the phantom image; (b) the retardation measurement comparison between the conventional and our method. (c) Optic axis measurement comparison.

Figure 4.3. The numerical comparison between the two scans of opposite orientation. (a) local retardation image of the phantom from the top-to-bottom scan; (b) local retardation image of the phantom from the bottom-to-top scan; (C) the local retardation measurement comparison of the selected region between the two scans in the box plot.

4.3.2 Animal tissue imaging *ex vivo*

Next, we imaged the swine retina *ex vivo*. The preparation of the retina is the same as what we did in chapter 2. **Figure 4.4** demonstrates the local retardation imaging of swine retina. The intensity image visualizes the layered structure of the retina (**Figure 4.4(a-b)**). The local retardation reveals the birefringence of the retinal nerve fiber layer (RNFL), clearly differentiating it from the less birefringent subsequent layers (**Figure 4.4(c-**

d)). RNFL birefringence is being investigated for its potential in diagnosing early degeneration of the RNFL associated with glaucoma[14], [99].

Figure 4.4. Swine retina imaging. (a-b). Intensity cross-sectional images corresponding to the location marked in *en face* intensity projection (e). (c-d). The corresponding local retardation image. (f). the *en face* local retardation projection at depth 40 μm under the retina surface. Scale bar in figure (a), horizontal 400μm, vertical 100μm. Scale bar in figure (f), 100μm. Areas, where SNR is below 10, were grey out.

Figure 4.5. Swine trachea imaging. (a). Intensity cross-sectional image of the trachea, scale bar horizontal 400μm, vertical 100μm. (b). Degree of polarization uniform image. (c). Accumulative retardation. (d). local retardation. Areas, where DOPU is below 0.5, is gray out in figure (c) & (d).

Figure 4.5 shows the local retardation imaging in swine trachea. In the intensity image (a), the layered structure was highly visualized in the high-resolution image. Compared with accumulative retardation image (c), the distribution of the high birefringent is more visualized in local retardation images. Especially, submucosa appears higher birefringent than lamina propria, which indicates higher collagen content in the submucosa. Also, depolarization becomes more obvious in the submucosa according to the DOPU image (b).

4.4 Discussion and conclusion

Based on the polarization mirror state constraint, we can determine the rotation axis between two polarization states of adjacent points. Of note, the constraint exists only in a unitary and reciprocal system. The requirement makes PS-OCT as an ideal application for this constraint, where depolarizing and diattenuation are negligible in most cases. Previous strategies to reconstruct local birefringence from single-input-state PS-OCT rely on the intrinsic symmetry of the imaging system [100], [101]. Crucially, the evolution of $\mathbf{t}$ through the mirror state persists also in an imaging system with additional system components in only the illumination or the detection path, as frequently the case in fiber-based systems, equivalent to left-multiplying both sides of Eq.(3-11) with an additional matrix $\mathbf{B}$. While this breaks the overall D -transpose symmetry, it simply alters the location of the circular evolution of the polarization states on the Poincaré sphere to go through the actual mirror state to $\mathbf{B} \cdot \mathbf{m}$. This part will be described in the next session, fiber-based implementation.

Another remaining challenge manifests whenever the measured polarization state aligns with even getting close to the mirror state, which makes the reconstruction of local retardation susceptible to noise, the cyan arrowed area in phantom imaging results (**Figure 4.2**). First, using circularly polarized input light requires a half wave of retardation to realize this alignment, which is uncommon in many biological samples. Second, in the fiber-based system, where the polarization state on the sample surface is not

fixed, the artifacts can be avoided by introducing a modest amount of polarization mode dispersion in sample arm fiber and using spectral binning for reconstruction[43], which is the topic in next session.

In summary, we demonstrated a single polarization state input free-space PS-OCT system with local birefringence measurement modality. We reconstructed the local retardation and relative optic axis images of the designed phantom, swine retina as well as swine trachea *ex vivo* and validated the capability of high-resolution birefringence imaging using proposed modality.

Chapter 5 Fiber based single input PS-OCT with local retardation measurement modality

5.1 Background and motivation

Polarization-sensitive optical coherence tomography (PS-OCT) [32], [33], [102], as a functional extension to conventional OCT[1], has been applied in many areas, such as ophthalmology [91], dermatology [55], cardiology [94], etc. It detects the change of polarization state of light back scattered from the tissue. The polarization contrast could be very useful in locating the well-arranged fiber structure, such as elastic fiber, collagen fiber, etc. For example, in ophthalmology, the polarization contrast provided by PS-OCT could be useful in more comprehensive retinal layer characterization [14]. In dermatology, the degree of burn is correlated with the loss of birefringent signal [103]. In cardiology, collagen content in aortic plaques can be a predictor of the vulnerability of plaques [95].

As we introduced in chapter 1, local birefringence imaging is more intuitive in revealing the distribution of birefringence in tissues [32], [39], [41]. However, local birefringence imaging needs multiple states of polarization input illumination, which highly increases the cost and complexity of the system [96]. What's more, fiber-based PS-OCT is much more flexible and is more fit to the clinical application [37]. However, single-mode fiber usually cannot preserve the polarization when light transmits through it. Except for multiple input implementations, manipulating fiber and fixing it were employed in fiber-based single input PS-OCT [38], [39]. These methods need calibration when sample arm was moved. Development of single input fiber-based PS-OCT with local birefringence imaging is still challenging.

Recently, we have found in the reciprocal unitary backscattering light circuit, the polarization state evolvement of backscattered light always tends to pass a circular arc if all the polarization states are presented by the points on Poincaré sphere. And the circle on which the circular arc lies always pass a

certain state, a mirror state of the input polarization state by QU plane on Poincaré sphere, named as mirror state. This constraint can be used to reconstruct the polarization evolution in depth even with only one polarization state input, thus enabling local birefringence reasoning even with an SMF based system.

In this work, I report two fiber-based single input PS-OCT systems. In the first system, polarization manipulation is achieved in the free space of a fiber bench (FT-51X60, Thorlabs Inc.). While another system is implemented all with fibers. Both systems operate at 840 nm with bandwidth 160 nm and the axial resolution is around 2.5 μm . The organization of this work is as follows: we started with a description of the fiber-bench-based systems. In this session, the mirror state constraint in the system and the method to extract mirror state were introduced, and geometrical reasoning and spectral binning method for the artifact-free image were presented [43]. Last, imaging on a sample with known birefringent and animal tissues *ex vivo* were performed to demonstrate its local birefringence measurement capability. In the second session I introduce the system operating fully with fibers. In this section, I present the system description and system diattenuation calibration, followed by experimental measurement of a polarizer and a QWP and imaging a phantom and the human nail and skin.

5.2 System based on fiber bench

5.2.1 System description

The fiber-based single-input system is derived from the free-space single input PS-OCT system we reported before [98]. The light source from the super-continuum laser (SCL, SC-50EM, YSL Photonics) is clipped by a dichroic mirror (DMSP950, Thorlabs Inc., not shown in the figure) and coupled into single-mode fiber. The other side of the fiber is connected to a fiber bench (FT-51X60, Thorlabs Inc.). The fiber bench can provide stable coupling and allows light beam polarization manipulation inside the bench. On the input port of the fiber bench, a linear polarizer (P1: LPNIRE050-B,

Thorlabs Inc.) and a quarter-wave plate (QWP, FBR-AQ2, Thorlabs Inc.) at the angle of 45° is cascaded to transform the linearly polarized light into circularly polarized light. After a beam splitter (BS 50/50, BS008, Thorlabs Inc.), light is split into a sample beam and a reference beam.

Figure 5.1. (a) The diagram of a single input fiber-based PS-OCT setup. BS, beam splitter; DC, dispersion compensator; HWP, half-wave plate; L1-13, lenses; LS, linear stage; M1-2, mirror; P1-2, polarizers; PBS, polarizing beam splitter; PMF, polarization maintaining fiber; QWP, quarter-wave plate; SCL, super-continuum laser; SMF, single-mode fiber; SP, spectrometer, TG, transmission grating. (b) Geometric reasoning for local retardation and relative optic axis. Δz is the birefringence resolved resolution we defined. The polarization states A: $\mathbf{S}_{z-\frac{\Delta z}{2}}$ and B: $\mathbf{S}_{z+\frac{\Delta z}{2}}$ from reflection at the top and bottom interface, respectively. $P(S_{MP})$ is the mirror state of the system. On the Poincaré sphere, A, B, and P determines a circle how the polarization state evolves from depth A to B.

In the reference arm, light is coupled into a single-mode fiber after transmitting through a linear polarizer (P2: LPNIRE050-B, Thorlabs Inc.). The light passes through the same linear polarizer again on the back reflected trip. The linear polarizer ensures the reference has an identical phase for orthogonal polarization components. So, only the amplitude response of the reference on orthogonal polarization detections needs calibration. It is worth noting that environmental disturbance on the reference fiber would not impact the stability of the reference once the polarizer P2 is fixed.

In the sample arm, a BK7 plate is inserted to balance the dispersion caused by the polarizer P2. A piece of single-mode fiber connects the output port of the fiber bench and a bench-top scanner. The focal length of the objective lens L7 is 30 mm, providing a transverse resolution around 8 μm . Also, a polarization controller (PC, Thorlabs Inc.) is installed with 1-2-1 coils on

the sample fiber for mirror state determination as well as the illumination state of polarization manipulation during imaging.

After the light from reference and sample arms are combined, it is coupled into a polarization maintaining fiber, and a half-wave plate (HWP, FBR-AH2, Thorlabs Inc.) is inserted between the beam splitter and coupling lens L8. The HWP could rotate the polarization coordinate of the free-space light to match with that of the PMF. The polarization diversity detection consists of the polarizing beam splitter and two custom-designed spectrometers [98]. The spectral fringes are acquired by image grabber (PCle, National Instruments). And the custom previous and acquisition interface is developed with LabVIEW 2015 (National Instruments) and MALAB 2016(MathWorks Inc.). The image acquisition speed of the system is 20K A-lines/s.

For the single polarization state input fiber-based system, the circular polarization of the light before entering the sample fiber is not necessarily required, which is different from the requirement of the conventional single polarization state input PS-OCT. In case the orientation of the linear polarizer in the reference arm was not strictly 45° , we can adjust it to balance the amplitude of reference detected by the two spectrometers. The calibration procedures are the same with our previous report in chapter 2.

5.2.2 Reciprocity of the system and mirror state determination

The sample arm of the system can be regarded as a unitary reciprocal system, and the round-trip Jones transmission matrix can be expressed as $J_s = J_f^T \cdot J_{sam}^T \cdot J_{sam} \cdot J_f$, where J_{sam} , J_f represent the Jones matrix of the sample and the fiber, respectively. So, according to the polarization mirror state constraint, the polarization evolution trace in the sample is composed of arcs and each circle on which each arc lies would pass the mirror state of the system.

Thereby, the determination of the mirror state of the system becomes the first step for local birefringence reasoning. Different from the free space

single input PS-OCT system, the input state of polarization determination could not be measured directly. Moreover, because of the imperfection of QWP in the system, the input state of polarization might vary depending on the wavelength. However, the birefringence of SMF could be manipulated by a polarization controller, thus making mirror state determination possible. What's more, to mitigate the polarization distortion, the spectral fringes was divided into 9 bins by multiplying a Hanning window of different center wavelengths. Therefore, 9 separate mirror states corresponding to different spectral bins could be found. And the 9 mirror states can be used for latter local birefringence reasoning via spectral binning [43], which is described in the next section.

During the mirror state determination, a specular sample (a mirror e.g.) was placed on the focal plane of the objective lens L7. Hence, the Jones matrix of the sample arm was $J = J_f^T \cdot J_f$. We recorded around 400k interference fringes consecutively while twisting the paddles of the polarization controller installed on the sample fiber. Then, the polarization state evolvment extracted from the fringes was plotted on the Poincaré sphere. The mirror state was the point where the traces of the polarization evolvment passed most. We could pick out the point manually.

5.2.3 Geometric local birefringence reasoning and spectral binning

After the raw data was acquired during scanning the sample, the first processing step was dispersion compensation and spectrometer alignment after background subtraction. Then, the tomogram could be obtained after Fourier transforms on the fringes. And the polarization state of each depth could be described as a Stokes vector.

Geometric local birefringence reasoning

The knowledge of the mirror state enables the reconstruction of the evolvment trace of the polarization states in the sample. The geometrical method to resolve local retardation was described in last chapter. In short, to retrieve the local birefringence, a depth interval Δz is defined, usually

several times larger than the OCT axial resolution (Δz corresponded to 10 μm in the studies of this chapter). The sample slice in the interval Δz is treated to be a pure linear retarder. For this retarder, the polarization states A: $\mathbf{s}_{z-\frac{\Delta z}{2}}$ and B: $\mathbf{s}_{z+\frac{\Delta z}{2}}$ from reflection at the top and bottom interface, respectively, are known. Both points lie on a circle passing through the mirror state P, as shown in **Figure 5.1(b)**. This allows calculating the rotation axis $\mathbf{r} = \overrightarrow{PA} \times \overrightarrow{PB}$. Once $\mathbf{r}$ is known, the double-pass retardation can be solved as the angle δ between vectors O'A and O'B[66], where O' is the center of the circle describing the polarization evolution. It is worth noting that if point A or B is too close to the mirror state P, the circle fitted would be very susceptible to the noise, thus making the $\mathbf{r}$ deviated from its ground truth. In this circumstance, the relative optic axis and local retardation measured results are not trustworthy and it was named as the mirror state artifact, as shown in **Figure 4.2**. To mitigate or even eliminate the mirror state artifact, a method based on spectral binning was developed as described below.

Spectral binning

The original purpose of spectral binning is to mitigate the detrimental effects of polarization mode dispersion (PMD) in fiber-based PS-OCT systems where the optical circulator induces considerable PMD [43]. The main idea of the spectral binning is dividing the fringe of the full spectrum into several spectral bins. Rotation vectors between two polarization states are calculated separately in each bin. And finally, vectorially averaging among vectors composed by rotation axis and arc after the vectors of all the bins are aligned with that of the central bin. Evading mirror state artifacts is to avoid the circumstance that polarization state of each spectral bin is close to its corresponding mirror state simultaneously. The distance between polarization state and mirror state can be treated as a confidence coefficient during vectorially averaging via spectral binning. A mirror state calculating threshold M_{th} is defined to filter out the unreliable area where the polarization state is too close to the mirror state. To achieve mirror state

artifact-free imaging, pre-induced system PMD is key to get enough diverse polarization state of each bin. And the analysis of how many systems PMD should be induced was discussed in the section of discussion and conclusion below.

The steps for geometric local birefringence reasoning via spectral binning are illustrated in Table 1. To mask out the unreliable area of the processed image, several thresholds were set, including the DOPU threshold DOP_{th} , signal to noise ratio threshold I_{th} , and M_{th} . These unreliable areas were not involved in the estimation of the correction matrix in step 6.

The procedures to extract local retardation with spectral binning was almost the same with that in the previous report by Villiger *et al* [43]. The main difference lies in the calculation of rotation vector which composes multiplication of rotation axis and rotation angle. We used the geometrical reasoning described above for the rotation vectors.

In the first 3 steps, the fringes of horizontal and vertical channels were split into $2N-1$ bins by Hanning window with identical width $\Delta k / N$ but centered at $m \cdot \Delta k / (2N - 1)$ where m starts from 1 to $2N-1$. Then after the Fourier transform, Stokes vectors were constructed, filtered with Gaussian window $h(z, x)$ corresponding to kernel size $20 \times 80 \mu\text{m}$ and normalized. In step 4, we used the geometric reasoning for the determination of rotation axis and rotation angle. In step 5, we masked out the area where the measurement was not reliable based on the defined threshold. In the next step, we used the least-square-maximum algorithm to determine the rotation matrix corresponding to each spectral bin. Last, we averaged the rotation vector among each bin after all the rotation vector of spectral bins were aligned with that of the central bin. Of note, as we mentioned in last chapter, when polarization state is nearer to the mirror state, rotation vector reasoning becomes more vulnerable to the noise. To overcome this problem, we took the product of the distance between mirror state and polarization states and intensity SNR as the weight $w(z, x, m)$ in the weighted averaging. The length

and direction of the averaged rotation vector correspond to the retardation and rotation axis, respectively. The relative optic axis mapping is the projection of the rotation axis $\vec{\mathbf{r}}$ on the QU plane.

Table 1. Spectral multiplexing in single input PS-OCT for artifact-free imaging

Parameters	$N, h(x), S_m(m), D_{th}, I_{th}, Dz, M_{th}$
Input	Spectral fringes $f_{h,v}(x, k)$
Output	local retardation $\mathcal{A}(x, z)$, the relative optic axis $b(x, z)$
1	Reconstructions of Jones vector with $2N-1$ spectral bins $t_{h,v} = FT(f_{h,v} \odot W(k, N, m))$ $W: \text{Hanning window with width } \Delta z/N \text{ centered at } m \cdot \Delta k / (2N - 1), \text{ with } m = 1, 2, 3 \dots 2N-1$
2	Construction of Stokes vector and spatial filtering $\mathbf{S}(z, x, m) = \begin{bmatrix} t_h \bar{t}_h + t_v \bar{t}_v & t_h \bar{t}_h - t_v \bar{t}_v & 2\text{Re}(t_h \bar{t}_v) & -2\text{Im}(t_h \bar{t}_v) \end{bmatrix}^T = \begin{bmatrix} S_I & S_Q & S_U & S_V \end{bmatrix}$ $\tilde{\mathbf{S}}(z, x, m) = \mathbf{S}(z, x, m) \otimes h(z, x), \quad h(z, x) \text{ is the gaussian filter}$
3	SNR, DOPU calculation and Stokes vector normalization $SNR = 10 \cdot \log_{10}(\tilde{S}_I)$ $DOPU = \frac{1}{2N-1} \sum_{m=1}^{2N-1} \left(\sqrt{(\tilde{S}_Q)^2 + (\tilde{S}_U)^2 + (\tilde{S}_V)^2} / (\tilde{S}_I)^2 \right)$ $\hat{\mathbf{S}} = \begin{bmatrix} \tilde{S}_Q & \tilde{S}_U & \tilde{S}_V \end{bmatrix}^T / \sqrt{(\tilde{S}_Q)^2 + (\tilde{S}_U)^2 + (\tilde{S}_V)^2}$
4	Rotation axis and rotation angle determination $\mathbf{r} = \left(\hat{\mathbf{S}} \left(z + \frac{\Delta z}{2}, x, m \right) - S_M \right) \times \left(\hat{\mathbf{S}} \left(z - \frac{\Delta z}{2}, x, m \right) - S_M \right)$ $\delta = \angle \left\{ \hat{\mathbf{S}} \left(z + \frac{\Delta z}{2} \right) - \frac{r}{ r } \cdot \cos \left(\angle \left(\hat{\mathbf{S}} \left(z + \frac{\Delta z}{2} \right), r \right) \right), \hat{\mathbf{S}} \left(z - \frac{\Delta z}{2} \right) - \frac{r}{ r } \cdot \cos \left(\angle \left(\hat{\mathbf{S}} \left(z - \frac{\Delta z}{2} \right), r \right) \right) \right\}$
5	Reliable area determination and averaging weight $x_{rel}, z_{rel}: (DOPU > D_{th}) \& (SNR > I_{th}) \& \left(\left\ \hat{\mathbf{S}} - S_M \right\ > M_{th} \right)$ $w(z, x, m) = \left\ \hat{\mathbf{S}} - S_M \right\ $
6	Estimation of the correction matrix $\mathbf{\Omega}(x, z, m) = \delta \cdot \mathbf{r}$

$$\min_{\mathbf{P}_{\text{corr}}(m)} \sum_{z_{\text{ref}}, x_{\text{ref}}} \left\| \mathbf{\Omega}(z, x, N) - \mathbf{P}_{\text{corr}}(m) \cdot \mathbf{\Omega}(z, x, m) \right\|^2$$

7 Estimation of local retardation

$$\text{Rotation vector: } \bar{\mathbf{r}} = \frac{1}{2N-1} \sum_{m=1}^{2N-1} \mathbf{P}_{\text{corr}}(m) \cdot \mathbf{\Omega}(z, x, m) \cdot w(z, x, m)$$

$$\text{Local retardation: } \vartheta(x, z) = \left\| \bar{\mathbf{r}} \right\| \frac{1}{dz}$$

Figure 5.2 demonstrated the process of removing artifacts with spectral binning. The polarization state of the 9 bins was diversified by introducing a modest amount of PMD with the polarization controller. Following the steps described above, the rotation vector, as well as the reliability maps, were derived as shown in (d)-(g). Averaging the rotation vector with the reliability as the weight penalized the artifact results. Comparing the results with full spectrum (h) and spectral binning (g), the removal of the artifact with spectral binning was demonstrated.

Figure 5.2. The process of spectral binning. (a) Schematic drawing of the fiber-based sample arm, where the PC introduces modest PMD. (b) Principle of spectral binning: The spectrum is divided into 9 overlying bins by multiplication with a shifted Hanning window. (c) Polarization state for each spectral bin measured by placing a mirror at the sample location, visualizing the PMD induced by the PC. (d)-(i) Cross-sectional images of a two-layer phantom. (d) Local retardation reconstructed using only the 1st spectral bin. (e) Local retardation reconstructed using only the 9th

spectral bin. (f,g) Reliability metric maps of the 1st and 9th spectral bin, respectively.
 (h) Local retardation reconstructed using the entire spectrum without spectral binning.
 (i) Local retardation image reconstructed with spectral binning combining all bins.
 Scale bars in (h) measure 100 μm (vertical) and 400 μm (horizontal) and apply to (d)-(i).

5.2.4 Phantom imaging

To demonstrate the modality of the fiber-based system, we first imaged a custom-made phantom. The structure of the phantom is shown in **Figure 5.3**. The phantom consists of two layers, and the first layer is a long ABS band with homogeneous birefringence. The second layer is made up of four short ABS bands with gradient birefringence. The orientation of the second layer is about 45° to the first long band layer. We scanned the phantom twice from both long band side and short band side. The results are shown in **Figure 5.3**. To further investigate the reliability of the local retardation imaging of the system, quantitative analysis was performed on the short bands of gradient birefringence. We made a comparison of the two measurements on the same location. The results indicate high reliability of the system and method.

Figure 5.3. Phantom Imaging. (A). imaging the phantom with the long band on the top. (B) imaging the phantom with the long band bottom. Scale bar: 100 μm axially, 400 μm transversely. Color bar: 0-2 $\text{deg}/\mu\text{m}$. (C). mean of the retardation and standard deviation comparison between the two measurements in corresponding regions.

5.2.5 Animal tissue imaging

Further, we applied the fiber-based system on swine trachea imaging *ex vivo* as shown in **Figure 5.4**. The layer structure can be easily discriminated from the intensity image. Lamina propria showed some birefringence while

substantial birefringence was found in the submucosa, where elastin is rich. Areas where SNR is below 8 dB and DOPU is smaller than 0.7 is greyed-out. High depolarization was found in the hyaline cartilage, which is the same with the results as in the imaging with free-space implementation.

Also, imaging on swine retina *ex vivo* with the fiber-based system was performed as shown in **Figure 5.5**. As illustrated in **Figure 2.5** & **Figure 4.4** in the free-space system, the retinal nerve fiber layer (RNFL) is birefringent and retinal pigment epithelium (RPE) is highly depolarizing. The consistent results demonstrate the reliability of the measurement with the fiber-based system. Of note, image (D) shows the degree of relative optic axis uniformity (DROAU). The concept of the DROAU is derived from the degree of polarization uniformity. This concept utilized the fact that the orientation of the retinal nerve fiber is changing gradually, resulting in high uniformity of the relative optic axis in that layer. For the extraction of DROAU, the averaging kernel to the relative optic axis is the same with the kernel applied for Stokes filtering (20*80 μ m, axially and transversely). Interestingly, the area with high DROAU coincides with RNFL.

Figure 5.4. Swine trachea imaging *ex vivo*. (A). Intensity image, layer-structure can be visualized with high resolution, scale bar 400 μm . (B). Local retardation image, color bar 0-1deg/ μm . (C). Degree of polarization uniformity image with color bar 0.2-1.

Figure 5.5. Swine retina *ex vivo* imaging with the fiber-based system. (A) Intensity imaging, RNFL, retinal nerve fiber layer, where demonstrates some birefringence as shown in (C), RPE, retinal pigment epithelium where demonstrates depolarization, as shown in (B). (D). degree of relative optic axis uniformity, which indicates the uniformity of the rotation axis of the birefringence regarding the locations.

5.3 Fully fiber-based system

5.3.1 System description

Figure 5.6 depicts the configuration of the single-mode fiber-based PS-OCT system. Light from a super-continuum laser (NKT Photonics) is coupled into single-mode fiber after passing through a linear polarizer. On the reference arm, a linear polarizer (LP) is inserted between the collimation and reference mirror to mitigate the polarization mode dispersion on the reference signal. The orientation of LP is with respect to the orthogonal detection to ensure equivalent amplitude response. On the sample arm, a polarization controller is placed to find the mirror state during calibration and adjust the illumination state of polarization on the sample surface during image acquisition. The polarization diverse detection is made up of two grating-based spectrometers (which was described above). The axial resolution of the system in the air is $2.5\ \mu\text{m}$ and transverse resolution is $13.5\ \mu\text{m}$. The measured sensitivity is 106 dB with illumination power 7 mW.

Figure 5.6. Schematic of fiber-based single input PS-OCT system. SCL, Super-continuum laser; PC, polarization controller; LP, linear polarizer; SMF, single-mode fiber; Galvo, galvanometer; PBS, polarizing beam splitter; G, grating.

5.3.2 System calibration

To measure the polarization state correctly, we need to ensure the reference light is in the same amplitude between the orthogonal polarization channels. The unbalanced reference light might induce polarization distortions which behave like diattenuation.

To illustrate the impact of the unbalanced reference, we modelled the system with Jones formalism. The detected Jones vector of the sample can be written as $\mathbf{E}_s = \mathbf{J}_{out} \mathbf{J}_{sam}^T \mathbf{J}_s \mathbf{J}_{sam} \mathbf{J}_{in} \mathbf{E}_{in}$, where the superscript T stands for transpose operation, $\mathbf{J}_{in} \mathbf{J}_{sam} \mathbf{J}_{out}$ is the Jones matrix of input arm, sample arm, and spectrometer arm, respectively. After system fabrication, input arm, sample arm, and spectrometer arm fiber of the coupler can be fixed, so $\mathbf{J}_{in} \mathbf{E}_{in}$ can be written as $\mathbf{E}_{in}'$, namely $\mathbf{E}_s = \mathbf{J}_{out} \mathbf{J}_{sam}^T \mathbf{J}_s \mathbf{J}_{sam} \mathbf{E}_{in}'$. For the reference signal, the detected reference can be written as $\mathbf{E}_R = [a \quad e^{j\phi}]^T$ where ϕ is retardance induced by the fiber at the reference arm as well as spectrometer arm. The detected complex fringe $\mathbf{f}(k)$ by polarization diverse detection after background subtraction can be written as

$$\mathbf{f}(k) = \mathbf{E}_R^\dagger \mathbf{E}_s = \begin{bmatrix} a & 0 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} 1 & 0 \\ 0 & e^{-j\phi} \end{bmatrix} \mathbf{E}_s = \begin{bmatrix} a & 0 \\ 0 & 1 \end{bmatrix} \mathbf{E}_s' \quad (5-1)$$

Where $\dagger$ is conjugate transpose operation, k is wavenumber of the spectrum. The objective of system diattenuation calibration is to determine the value of a for each spectral bin.

Figure 5.7. System deattenuating correction. (a) Stokes vector of bin 1 before correction. (b). Measured angle of polarizer rotation before correction. (c) Stokes vector of bin 1 after correction. (d). Measured angle of polarizer rotation after correction.

While calibrating the system diattenuation, we placed a polarizer above a mirror as the sample. We rotated the polarizer in the step of 10° for 18 times and recorded the interference fringes correspondingly. After converted into Stokes vector, the polarization states could be represented by the points on the Poincaré sphere. Due to the unbalanced reference light amplitude, the angle between the polarization states of two contiguous measurements would be varied from 10° . Iterations were performed to extract the correction factor until the variation of angles between polarization states of two contiguous measurements is minimized as shown in **Figure 5.7**.

Of note, after the calibration, the system becomes unitary again. Employing the same method used in the experiment of the discovery of the mirror state phenomenon in chapter 3, we can extract the mirror states of the 9 bins of the system. Briefly speaking, we randomly twisted the paddles of the

polarization controller in the sample arm and recorded the polarization state evolution on the Poincaré sphere. As a result of the polarization mirror state constraint, we can get a pattern shown in **Figure 5.8**. The polarization evolution trace would pass a certain polarization state, corresponding to the mirror state.

Figure 5.8 The polarization evolution during twisting fiber polarization controller paddles of spectral bin 2, 5, 8. The blue arrow points at the mirror state of each bin.

5.3.3 Measurement on polarizer and QWP

We measured the transmission axis of a linear polarizer (LPNIRE100-B, Thorlabs Inc.), and the retardation as well as the orientation of a QWP (AQWP10M-980, Thorlabs Inc.). The retardation and optic axis reasoning were introduced in the last section. First, a linear polarizer was inserted in the sample arm and rotated by 10 degrees for each measurement. The measured transmission axis orientation of the linear polarizer is shown in **Figure 5.9** (a). Then, the polarizer was replaced by a QWP, and the above rotation steps were repeated. The double-pass cumulative retardance of the QWP with different optic axis orientations is shown in **Figure 5.9** (b). The results show the high reliability of the system.

Figure 5.9. Measurement on polarizer and QWP. (a) the measured orientation of a linear polarizer. (b) the measured retardation as well as the orientation of a QWP.

5.3.4 Phantom imaging

To further validate the performance of the system, we imaged the custom-made phantom as shown in **Figure 5.10**. During the process, we split the spectrum into 9 bins by spectral binning. The detailed processing procedures are the same as the description above in section 5.2. The averaging kernel for mitigating the effect of speckles are $40 \times 40 \mu\text{m}$. We scanned the phantom twice, from the long band and short band. The two measurements indicate the high consistency of the method and system.

Figure 5.10. Phantom Imaging. (a-b) intensity images. Scale bars: horizontal 400 μm , vertical 100 μm . (c-d) local retardation images.

5.3.5 Imaging on human tissue

Last, we imaged the human nail, finger, and forearm skin. As shown in **Figure 5.11**, strong birefringence is visualized in the nail plate and corneum of a finger, which is made up of tightly keratinized epidermal cells. But the birefringence of the corneum is weaker than that of the nail plate. This might because the keratinized cells in snail plate are much more tightly

packed in the nail plate. In the images of forearm skin, where there is little corneum, the dermis is highly birefringent with a large amount of collagen content there.

Figure 5.11. Imaging results in human tissue. (a-c). intensity images of the nail, index finger, and forearm skin, respectively. (d-f). the corresponding local retardation images. Scalebar in the intensity images: horizontal 400 μ m, vertical 100 μ m.

5.4 Discussion and conclusion

We demonstrate the local retardation imaging with two fiber-based systems. Phantom imaging and tissue imaging experiments were performed to demonstrate the reliability. The imaging results show high consistency with those of the free-space systems. Of note, in the fiber-based system, the relative optic axis of the RNFL is obscure due to the accumulative nature of the measurement, so that its orientation cannot be clearly determined. But borrowing from the concept of DOPU, we were able to discriminate the layer of RNFL with the degree of relative optic axis uniformity. The results indicate the potential of the technology for improving RNFL segmentation.

As mentioned in Chapter 4, the mirror state artifact arises when the polarization state in the sample coincides with mirror state simultaneously, which is the shortcoming of local retardation reasoning utilizing the mirror state constraint. Our strategy is to diversify the polarization state of illumination of each spectral bin on the sample surface. Evading mirror state artifacts is to avoid the circumstance that polarization state of each spectral bin is close to its corresponding mirror state simultaneously. The apparent method to diversify the polarization state of each bin is introducing some PMD in the sample arm fiber. On the other hand, the resolution would sacrifice consequently.

To evaluate how much PMD should be induced and how much resolution would sacrifice statistically, we counted illumination polarization state diversity as well as resolution versus different amount differential group delay (DGD), which is altered by different paddles' position of a polarization controller in the fiber-based reciprocal system. To quantify the illumination polarization state diversity, Stokes variation is introduced which is the mean distance between the polarization Stokes of each spectral bin to that of central bin on Poincaré sphere as shown in, where N is the total spectral bin number and equal to 9 in this work.

$$d' = \sqrt{\frac{1}{N} \sum_{i=1}^N \left(\mathbf{s}(i) - \mathbf{s}\left(\frac{N+1}{2}\right) \right)^2} \quad (5-2)$$

Using a fiber-based single input PS-OCT, we recorded ~200k interference fringes while twisting paddles using a mirror as the sample. The fiber in the sample arm is 1m long. The twisted fiber was modeled as a pure retarder, and the double pass Jones matrix of the fiber $\mathbf{J}_{\text{sam}}$ can be reconstructed of a specific wavelength (840nm in this study). And differential group delay (DGD) could be calculated by $DGD = 2\sqrt{\det\left(d(\mathbf{J}_{\text{sam}})/d(\lambda)\right)}$ where det is the determinant of a matrix and λ is wavelength[87]. We calculated the DGD during the fiber twisting process and the distribution of DGD is plotted in the figure. The distribution of measured DGD shows an ideal Rayleigh distribution (p-value = 0.0418 with χ^2 test) which agrees well with theory [87] and the mean value is 8.7fs. The measured mean value is similar to the measured results in a previous report[104].

Figure 5.12. DGD versus resolution and stokes variation analysis. (A). the distribution of PMD is in Rayleigh distribution. (B). 2D histogram versus DGD and Stokes variation. (C) 2D histogram versus Stokes variation and resolution. (C) 2D histogram versus DGD and resolution.

Further, we plotted the Stokes variation and resolution versus DGD in the figure. And the relationship between Stokes and resolution is shown in **Figure 5.12**. Stokes variation is not necessarily proportional to DGD induced by twisted fiber. The highest probability of Stokes variation larger than 0.7 locates at the around 10 fs DGD. Resolution is proportional to Stokes variation statistically. According to our experience, Stokes variation larger than 0.4 can be safe for evading mirror state artifacts in most circumstances. In the worst case, to get 0.4 Stokes variation, still, less than 20% sacrifice is needed to result in resolution increase to $3.0\mu\text{m}$ from $2.6\mu\text{m}$.

And during the process to introduce a modest amount of PMD, we can observe the state of polarization on the sample surface in real time and twisted the paddles to make Stokes variation of spectral bins maximized. The process just takes less than 30 seconds before the image acquisition.

Usually, one of the main concerns of single input PS-OCT with fiber-based implementation is the immunity to environmental disturbances. In the system reported before, the sample arm fiber needs to be fixed which cause some inconvenience for clinical application[38], [39] While in the system based on fiber bench, the polarizer in the reference arm enforces the reference signal with the identical phase and amplitude on the two spectrometers. And the birefringence induced by the sample arm fiber is in the reciprocal system where the mirror state constraint holds though it would change due to environment disturbance. Therefore, the system is free from the environment perturbation, such as mechanical vibration or temperature changes. For the system based on SMF coupler, there is also no requirement for fixing the sample arm fiber. And the SMF coupler-based system could achieve less coupling loss.

In summary, we presented fiber-based single input PS-OCT systems based on fiber bench and SMF coupler. Based on mirror state constraint, we can obtain local birefringence imaging which usually requires multiple polarization illumination inputs. We validated the local birefringence measurement modality with a tissue-like phantom and performed imaging on the tissue.

Chapter 6 Reliable single input polarization state intravascular polarimetry

6.1 Background and motivation

Currently, intravascular optical coherence tomography (OCT) and optical frequency domain imaging (OFDI) have demonstrated the potential in the diagnosis of the vulnerable plaques and guiding the percutaneous artery interventions [105], [106]. With the high spatial resolution, intravascular OCT and OFDI have been able to visualize the fibrotic cap morphology both in disruption and erosion, and the accumulation of macrophage [4], [22], [107], [108].

However, the improvement in imaging method is still desirable for novel insight into the mechanism of thrombotic complication [109], and to the accurate evaluation of the rupture plaques [110]. It has been reported that polarization contrast provided by intravascular polarization sensitive (PS) OFDI with the capability to detect depth-resolved birefringence had been proved promising in the evaluation of plaques [95]. Changes in the content of collagen and smooth muscle cells which exhibit birefringence usually occur simultaneously with intravascular lesion [111]. Currently, to obtain depth-resolved birefringence, at least two input polarization states are needed [32], [33], [112]. To implement multiple input polarization states, different approaches have been proposed, such as adding a polarization modulator into the source arm [48], [113], generating different polarization states in a sequential manner, and by frequency multiplexing [37] or depth multiplexing [36], [97] encoding different polarization states at different depth or frequency. Nevertheless, these methods add complexity to the setup and higher the admittance threshold of intravascular PS OFDI.

We have previously reported a polarization mirror symmetry constraint which enables local retardation measurement with single input polarization state. The constraint elucidated that the polarization evolution of the back-scattered signal always tends to pass a specific polarization state (mirror

state) if presented on the Poincaré sphere. Great simplification of the system could be achieved by using this constraint in intravascular PS OFDI. Polarization of the illuminating light is impacted by the rotating catheter when propagating through it. To evaluate the robustness of imaging local retardation with single input polarization state in the intravascular PS OFDI, we performed the comparison of the results between the proposed method and current benchmark multiple input counterpart in 30 patients [44].

To achieve reliable local retardation imaging reconstruction with the proposed approach, we first demonstrated the extraction of mirror state according to the aggregation of the polarization state from the signal with sufficient SNR. And we assessed the performance of the method with a comparison with benchmark dual inputs processing.

6.2 Method

6.2.1 Dataset description

We used the same dataset as the previous reports[44], where the patient is imaged with a dual input PS-OFDI. To validate the proposed method, we only used one of the input polarizations channels. To ensure fairness, we did not apply any processing related to another channel when we were extracting the local retardation images. To examine the reliability of the single input processing, the results of the benchmark dual input processing was regarded as the ground truth.

6.2.2 Technical method

Polarization mirror state constraint in OFDI

The intravascular polarimetry imaging system was the conjunction of the commercial intravascular catheters (FastView, Terumo) and the home-made state-of-the-art PS-OFDI system. The detailed system description was in the previous report [44]. In brief, a polarization modulator was employed to generate light of linear polarization and circular polarization in a successive manner. The commercial catheter was pulled back at a speed of 20mm/s. The back-scattered signal was recorded by a set of polarization diverse detection.

Figure. 6.1. Schematic of the PS-OFDI. Two polarization states are generated by the polarization modulator. The polarization state before entering the coupler is denoted at $s_{1,2}$. P represents the Mueller matrix of sample arm fiber and catheter. And the $R(x)$ denotes the Mueller matrix of the sample in a single trip. A denotes the asymmetry part of the system.

Assuming the input polarization state of the coupler are $s_{1,2}$, the system transmission can be expressed as

$$t_{1,2} = A \cdot D \cdot P^T \cdot R^T(x) \cdot D \cdot R(x) \cdot P \cdot s_{1,2} = T(x) \cdot s_{1,2} \quad (6-1)$$

Where D is equal to $\text{diag}(1, 1, -1)$. If we take the derivative of the Stokes vector, as $T \cdot T^T = I$, the Mueller matrix differential is a skew-symmetry matrix and can be written as rotation vector $\beta(x)$ in Eq(6-2)

$$\frac{\partial t_{1,2}}{\partial x} = \frac{\partial T(x)}{\partial x} T^T(x) \cdot t_{1,2} = [\beta(x)]_{\times} \cdot t_{1,2} \quad (6-2)$$

knowing the polarization evolvement of the back-scattering light would always tend to pass the polarization mirror state m , we can determine the direction of the rotation vector $\beta(x)$:

$$\left(\frac{\partial t_{1,2}}{\partial x} \times (m - t_{1,2}) \right) \parallel \beta(x) \quad (6-3)$$

After some algebra manipulation, as described in chapter 5, we can calculate the rotation vector as

$$\beta(x) = \frac{\frac{\partial t_{1,2}}{\partial x} \times (m_{1,2} - t_{1,2})}{t_{1,2}^T \cdot t_{1,2} - t_{1,2}^T \cdot m_{1,2}} \quad (6-4)$$

Mirror state extraction

Mirror state estimation is the key for employing polarization mirror state constraint in single input PS-OCT for local retardation imaging. Estimating mirror state from the recorded data instead of pre-calibrating before the acquisition can provide great convenience of the Application of mirror state. According to the mirror state constraint, the polarization state of the back-scattered signal always tends to pass the mirror state, making the polarization state aggregating around the mirror state with enough back-scattered signal taken into consideration.

In practice, we remapped the polarization state of the areas where $\text{SNR} > 8\text{dB}$, $\text{DOPU} > 0.8$ into a Cartesian coordinate with horizontal axis azimuth angle and vertical axis elevation angle. The mirror state is chosen from the point with peak density from the polarization. To validate the feasibility of this method, we calculated the atlas of error when comparing the rotation vectors computed from dual input processing and single input processing with different mirror state. The ground truth of the mirror state should be the point with least error. The comparison is shown in **Figure. 6.2**, which indicate the reliability of the mirror state estimation.

Figure. 6.2. Histogram of the measured polarization state for input polarization state $s_{1,2}$ for various bins. Est. and G.T. denote estimation and ground truth, respectively. The red circle indicates the estimated mirror state, determined as the most frequently realized polarization state, while the black circle represents the calculated mirror state ground truth based on two polarization states.

Single input processing with spectral binning

As reported before, when the polarization state of the signal is close to the mirror state, the local retardation reasoning becomes susceptible noise. We employed spectral binning to avoid the scenario where the polarization state of all bins become close to its mirror states simultaneously. For a better estimation of the ground truth, a weight metric is to be developed to quantify the reliability of the measurements of each bin.

Reliability metric

First, let's consider a general case, how to determine the weight a and b when averaging two measurement $\mathbf{X}$ and $\mathbf{Y}$ with Gaussian distribution $P_x(\mathbf{X})$, $P_y(\mathbf{Y})$ and variance σ_x and σ_y , respectively.

$$\mathbf{Z} = a \cdot \mathbf{X} + b \cdot \mathbf{Y} \quad (6-5)$$

The distribution of $\mathbf{Z}$ can be derived after some integration and derivation:

$$P_z(\mathbf{Z}) = \text{Conv} \left(P_x \left(\frac{\mathbf{X}}{a} \right), P_y \left(\frac{\mathbf{X}}{a} \right) \right) = \frac{1}{\sqrt{2\pi} \sqrt{a^2 \sigma_x^2 + b^2 \sigma_y^2}} e^{\frac{(X - (a\mu_x + b\mu_y))}{2(a^2 \sigma_x^2 + b^2 \sigma_y^2)}} \quad (6-6)$$

where μ_x , μ_y denote the mean of the two distributions. To make the compound variance minimized, the weight a and b can be determined as Eq.(6-7)

$$\begin{aligned} a &= \frac{1/\sigma_x^2}{1/\sigma_x^2 + 1/\sigma_y^2} \\ b &= \frac{1/\sigma_y^2}{1/\sigma_x^2 + 1/\sigma_y^2} \end{aligned} \quad (6-7)$$

According to this model, the weight is proportional to the inverse of the variance of the measurement. To determine the variance under varied SNR and polarization state, we simulated the process of rotation vector reasoning with mirror state constraint. Before computing the variance of the measured rotation vector, to ensure the uniformity the measured rotation vector was subtracted by the rotation vector ground truth. Of note, the dispersion of the measured rotation vector was decomposed into 3 scalar parameters, which

was assumed in Gaussian distribution. Except for SNR, another parameter we chose to model the rotation vector variance is the distance between mirror state and polarization state of the signal, denoted as Dis.

In the simulation, we used 10 frames from the acquired data. First, we marked the area with SNR larger than 25dB, $DOPU > 0.9$, and $Dis > 1.4$ where the rotation vectors can be calculated with very high reliability using single input processing. Based on the results, we determined the limit of the rotation vector magnitude as 0.8rad. Next, a set of two polarization states were generated corresponding to rotation vectors with rotation axis random and magnitude in uniform distribution from 0 to 0.8 rad. And the two polarization states were transformed into Jones vectors. After added noise with certain SNR, the two Jones vectors were transformed into Stokes vectors. The mirror state was randomly selected on the circle determined by the two polarization states and the rotation vector. 1000 polarization states and rotation vectors were repeated for each specific SNR. And the SNR was set from 0 to 25 dB in the step of 0.62 dB. We calculated the standard deviation and errors with varied SNR and Dis, which is shown in **Figure. 6.3**. We found the distribution error of the retardation which was decomposed into QUV parameters was symmetric and unbiased in **Figure. 6.3** (A-B). The higher the Dis, the smaller is the error, which agrees with our expectation. In **Figure. 6.3** (C-D), we could find that the standard deviation is inversely proportional to SNR and Dis. Fitting the standard deviation versus Dis and SNR, we obtained the reliability metric $w(z, l, n)$ for the rotation vector weighed average in spectral binning (described in next section).

Figure. 6.3 reliability metric extraction. (a) The error distribution when the SNR is set as 12 dB. (b) The distribution of the error when SNR is 12 dB and Dis is in the range [0.39, 0.41] is close to Gaussian distribution. (c)-(d) The standard deviation under selected SNR and Dis.

Local retardation reasoning with spectral binning

We multiplied the pre-processed spectra with Hanning window resulting in the 9 spectral bins as the previous report [43]. The reconstructed Stokes vector was transversely averaged with 9 adjacent A-lines, same as dual input processing. Following the method provided above, the rotation vectors $\beta(z, l, n)$ of the 9 bins were computed. To remove the offset induced by the system polarization mode dispersion, a required rotation matrix can be determined to align each bin to the central bin $\beta(z, l, N)$, in a least-square manner:

$$\max_{\mathbf{G}(n)} \text{Tr} \left(\mathbf{G}(n) \sum_{z,l} \boldsymbol{\beta}(z, l, n) \cdot \boldsymbol{\beta}^T(z, l, N) \cdot w(z, l) \right) \quad (6-8)$$

Where $w(z, l, n)$ denotes the reliability metric derived above, z and l are points indices in the axial and lateral directions, respectively. The rotation vector estimation yields the weighted averaging of the 9 rotation vectors with its reliability.

$$\bar{\beta} = \sum_{n=1}^{2N-1} \mathbf{G}(n) \cdot \beta(z, l, n) \cdot w(z, l, n) \cdot w(z, l, N) \quad (6-9)$$

6.2.3 Statistical method

In the previous report [44], there were 274 pairs of comparison carried out. We chose 274 cross sections from the dataset. All the cross sections were remapped to Cartesian coordinate.

First, a pixel to pixel comparison was exercised. Pearson correlation coefficients between individual cross-sections by single input processing and benchmark dual input processing were computed. We also investigated whether the Deming regression slope is equivalent to one with two one-sided t-tests for significance 5%.

To examine the reliability of the single input polarimetry with the dual input processing repeatability, the same comparing strategy was employed [44] for Bland-Altman analysis. Namely, the signal was averaged among the circular region of interest (ROI) of diameter D , iterated across the entire frame in the step of $D/2$. Data from ROI where more than half of the pixels with a depolarization larger than the threshold will be excluded from the comparison. The 95 % limits of agreement (LoA) were applied, ranging from the 2.5th and 97.5th percentile of all the signal from 274 cross sections.

6.2 Results

For each cross-section in the 274-cross-section dataset, we generated three birefringence figures with benchmark dual inputs processing and single input processing with its mirror state. First, we employed pixel to pixel comparison within the area defined by $DepTh=0.2$, area with depolarization smaller than 0.2. Pearson correlation analysis and Deming regression were applied to compare the measurement resulting from single input processing with benchmark dual input processing. Meanwhile, we compute the estimated reliability of each measurement based on its SNR and distance between polarization state to its mirror state. The estimated variance is the inverse of the square root of the reliability. Next, the averaged retardation in the defined ROI was computed, taking the reliability as weight. The

corresponding compound reliability of the averaged retardation is the mean of the reliability of the qualified points in the ROI.

6.3.1 Pixel to pixel comparison

Figure 6.4 shows the comparison of the results between benchmark two input processing and single input processing by one channel with the mirror state. A-C show the figures compounding intensity and birefringence of the mixed plaque from one patient. We applied Pearson correlation and Deming regression on the birefringence measurements where DOP is larger than 0.8. Of note, the color in the scatter plot denotes the estimated variance of the measurement of each pixel. The estimated variance is the inverse of the sum of the reliability of 9 bins when we calculate the retardation in spectral binning [43]. Most points far from the Deming regression coincide with high estimated variance. G-I shows the Bland-Altman plot comparing birefringence map from a channel 1, channel 2 and dual channels.

Figure 6.4. Single input processing and two inputs processing comparison. (A-C) show the results of retardation imaging with two channels, channel 1, and channel 2, respectively. Scalebar in A represents 500 μm . (D-F) shows the Pearson correlation and Deming regressing between each other, where Δn_{12} denotes the results from benchmark two inputs processing, and Δn_1 Δn_2 represents results from single input

processing by channel 1 and 2, respectively. (G-I) show Bland-Altman plots comparing the different birefringence signals.

6.3.2 Bland-Altman analysis

To assess the overall performance of the single input processing, we conducted a Bland-Altman plot of the compound measurement from the *ROI* of the dataset. Considering a large number of data points from the 274 cross-sections, 2D-histograms were generated binned with the difference between the mean retardation from corresponding ROIs against their differences as shown in **Figure 6.5**. Table 2 summarized the computed parameters and compared them with the parameters of birefringence measurement in the repeatability study [44]. The limit of agreement was computed with 2.5% to 97.5% of the difference signal. And the contrast in the birefringence images was defined by the ratio between the LoA of average signal and LoA of the difference signal. The Bland-Altman plot between channel 1 and benchmark dual inputs processing delivered the best limit of agreement and contrast. Even the results of the two single input processing revealed comparable agreement as that in [44].

Table 2 Parameters extracted from Bland-Altman analysis

	Δn in ref. [44]	Δn_1 vs Δn_{12}	Δn_2 vs Δn_{12}	Δn_1 vs Δn_2
Median difference	1.37×10^{-6}	5.5×10^{-6}	1.5×10^{-5}	1.00×10^{-5}
LoA(-)	0.25×10^{-3}	0.2×10^{-3}	0.22×10^{-3}	0.23×10^{-3}
LoA(+)	0.24×10^{-3}	0.19×10^{-3}	0.22×10^{-3}	0.24×10^{-3}
Range: 2.5% to 97.5%	0.83×10^{-3}	0.81×10^{-3}	0.80×10^{-3}	0.76×10^{-3}
Contrast: Range/2/LoA($\pm$)	1.68	2.07	1.82	1.62

Δn in ref. [44]: the parameters from ref. [44]. Δn_1 : results from single input processing with channel 1. Δn_2 : results from channel 2. Δn_{12} : benchmark two inputs processing. LoA(-) is the 2.5% to 50% and LoA(+) the 50% to 97.5% of the difference signal. LoA($\pm$) is their mean.

Figure 6.5. Bland-Altman analysis of the 274 compound cross-sections in areas with

a depolarization ≤ 0.2 . All panels show mean offsets and the limits of agreement (LoA), as well as the 95 % confidence interval on the mean average signal.

6.3.3 Pearson correlation analysis and Deming regression

Figure 6.6 A-B shows the histogram of the Pearson correlation and Deming regression of the single cross-section. We set the benchmark dual inputs processing as the ground truth, and it was found that the Pearson correlation coefficients between results single channel and ground truth centered around 0.7 ($r = 0.7068$, 95% confidence interval (CI) 0.7058-0.7079 and $r = 0.6943$, 95% CI 0.6933-0.6954 for channel 1 and 2, respectively). And the correlation between the results from two single channel was lower, gathering around 0.5 ($r = 0.4813$, 95% CI 0.4801-0.4824) as shown in **Figure 6.6** (A). The lower correlations might result from the slight transverse shift between two channels while scanning the sample. And we could find the Deming regression slope distribution for the three pair comparisons concentrated near 1 ($a = 1.0312$ 95% CI 1.0186-1.0439 for channel 1, and $a = 1.0421$ 95% CI 1.0225-1.0598 for channel 2). To assess the overall agreement between benchmark dual inputs processing and single input processing with the proposed method, we calculated the retardation defined by the ROI with diameter $300\mu\text{m}$ with threshold $DepTh=0.2$, the same as in Ref. [44]. While computing the retardation average weighted by the reliability in the ROI within a circle with diameter $300\mu\text{m}$, we also calculated the estimated variance of the measurements which is represented by the inverse of the mean reliability within the ROI. In **Figure 6.6** (C-D), we could find the measurements with high errors coincide with high estimated variance. In **Figure 6.6**(E), to calculate the estimated relative variance when measurement with each channel, we first took the mean of the reliability weight of the two channels' measurement, and then took the inverse of the mean reliability. The comparison in compound results of the 274 cross-sections between the benchmark and single channel indicated high linearity of the regression with high correlation coefficients.

Figure 6.6. Pearson correlation and Deming regression results. A. Histogram of Pearson Correlation coefficient of the 284 cross-sections. B. Histogram of Deming regression slope. C. The Pearson correlation analysis and Deming regression on the compound results of the 274 cross-sections. The color bar indicates the estimated variance which is the square root of the inverse of averaged reliability within the ROI.

6.3.4 Dependence on varied estimated variance cut-off

As described above, we attached the estimated reliability to each measurement. And the reliability was also averaged while computing the compound birefringence in *ROI*. Hence, except for the measured value, we also provide the confidence level of the measurement. To validate the reliability (or the estimated variance) of the measurement, we iterated the Bland-Altman analysis, Pearson correlation, and Deming regression of the compound signal with different cutoff percentage. **Figure 6.7** demonstrates the changes of LoA and compound Pearson correlation coefficients and Deming regression slope after a varied percentage of the signal were excluded from analysis according to the estimated variance. The LoA was

inversely proportional to the cutoff percentages. And the Pearson correlation coefficients were increasing with higher cutoff percentage. The Deming regression slope was insensitive to the percentage cutoff. The relation between LoA and Pearson correlation coefficients and cutoff percentage verified the effectiveness of the reliability.

Figure 6.7. The improvement with varied variance cutoff. A. LOA evolution with different cutoff percentage according to the estimated variance. B. Compound Deming regression slope evolution. C. Pearson correlation coefficients' evolution.

6.3.5 The effect of subsampling

Compared with two inputs processing which employs the signal of two channels, single input processing with the single channel only utilized the half data volume. Hence, part of the error calculated with single input processing was attributed to the lower sensitivity of the subsampling. To investigate the effect of the subsampling, we reprocessed the 274 cross-sections with two input processing using the half-sampled signal. When computing the birefringence image in polar coordinate, two adjacent A-lines were treated as a pair of polarization (S_1 , S_2), and only odd-index pairs of polarization state were utilized. The birefringence images were remapped

into Cartesian coordinate with the same size as conventional dual input processing by bilinear interpolation. We compute the compound retardation by averaging the measurements within the *ROI* and compared it with the corresponding measurement by conventional dual inputs processing. **Figure 6.8(A)** shows the Deming regression and Pearson correlation analysis of the compound results from half subsampled signal and benchmark. Coincidentally, regression slope was smaller than 1 and overestimation occurred when birefringence was small, which is more visualized in the Bland-Altman plot **Figure 6.8(B)**.

Figure 6.8. Analysis of the effect of using half of the data in two inputs processing. A. Pearson correlation and Deming regression. B. Bland-Altman plot.

6.3 Discussion

Polarization-sensitive OFDI has been established as reliable technology in cardiology. Utilizing illumination with polarization alternating between radial scans and measuring the polarization state change along with the depth in tissue, it can provide additional contrast except for the backscattering intensity, enabling more detailed characterization of atherosclerotic plaques. On the other hand, reducing the system complexity would make this contrast more attractive. The knowledge of mirror state enables reconstruction of birefringence map with single input polarization, which was challenging considering that fiber motion would change the polarization of light transmitted through an optical fiber.

To reconstruct the birefringence map with a single channel, we extracted the mirror state from the existed dataset. We plotted the polarization

distribution with the signal from several cross-sections where we set depolarization threshold $DepTh=0.2$ to exclude meaningless signal. The overlap between the mirror state extracted from the aggregation of polarization and the computed mirror state ground truth indicates the reliability of this method. In the previous study, the mirror state was determined from the signal by twisting fiber with a polarization controller, realizing substantial birefringence variation. And in the case of catheter based OFDI, the round-trip retardation through the spinning catheter and the birefringent sample would ensure aggregation near the mirror state. The method does not rely on the pre-calibration before the imaging acquisition, without adding any complexity of the mirror state processing implementation.

Bland Altman analysis is a kind of evaluation on whether current measurement can be replaced by a novel method. In the previous report [44], Villiger *et al* validated the robustness of birefringence imaging which has a better agreement and higher contrast than intensity imaging in the repeated scanning. Compared with results in the repeatability study as shown in Table 2, the less measurement discrepancy in single input processing and benchmark dual inputs processing with the same dataset was achieved, which indicates the robustness and reliability of single input processing using a single channel.

Another advantage of the proposed processing method is the reliability quantification of each point. We derived the reliability metric model from Monte Carlo experiment with calculating the measurement variance with a series of SNR and mirror state location. To fully simulated the scenario of cardiovascular birefringence, the retardation setting in the simulation was derived from the signal where SNR and distance were sufficient with SNR threshold 25dB, and distance threshold 1.2. The effectivity of the metric was confirmed in the single frame comparison, where high estimated variance coincides with the high discrepancy. We further validated the reliability metric by excluding the data in the compound comparison. The increase in

the cutoff of high variance points led to an increase in agreement and Pearson correlation.

SNR always plays a vital role in the birefringence measurement especially when the birefringence is weak. As visualized in **Figure 6.5**, prominent overestimation was observed when the retardation is small. Part of this estimation was attributed to the fact that half fewer data were employed compared with dual inputs processing. The overestimation occurred when dual inputs processing was implemented with the half subsampled signal as shown in **Figure 6.8**. The biggest practical benefit of the method is the simplicity of the system, saving one polarization modulator at least. The increase of the sampling A-lines would further improve the performance of the single input intravascular polarimetry.

Limitations of this work include the inability to construct the absolute optic axis of the tunica media. The absolute optic axis imaging would rely on the reconstruction of the system, where at least two input polarization states are needed.

6.4 Conclusion

This study demonstrated that single input PS-OFDI intravascular polarimetry can generate a comparably reliable and robust map of tissue birefringence properties as benchmark dual inputs PS-OFDI intravascular polarimetry. We extracted the mirror state from the histogram of polarization states of meaningful signal in the existent datasets. Reliability metric was derived to quantify the retardation reconstruction reliability and serve as a weight for rotation vectors average in spectral binning. The two single input processing with single channel both demonstrated high agreement with the results from dual input processing. In conclusion, these results support the replacement of benchmark dual inputs PS-OFDI by single input one when only local retardation was considered. The replacement permits simplification in hardware, stimulating higher interest in this compelling contrast.

Chapter 7 Discussion and future work

Discussion and conclusion

Single input PS-OCT with ultra-high resolution can achieve depth-resolved polarization contrast and sub-cellular intensity images. But the operating broad bandwidth of light magnifies the imperfection of QWP, resulting in the inconsistent phase modulation among different wavelengths. The roll-off imbalance of the broad-bandwidth spectrometers also cause distortions to the polarization measurement. First, we redesigned the setup configuration of the system, replacing the QWP at reference arm with a polarizer, and placing the QWP at the input arm to avoid double pass through it. And we calibrated the residual polarization distortions based on the Jones formalism. Next, we illustrated a polarization mirror state constraint in a reciprocal unitary system, namely the system we calibrated in Chapter 2.

The mirror state constraint reveals the aggregation of the back-scattered polarization state after double pass through a birefringence medium on one specific polarization state, which relates to the input polarization state, but mirrored by the QU plane if presented on Poincaré sphere. After a theoretical explanation of this constraint, we verified it experimentally.

The constraint simplifies the reconstruction of local retardation, which usually needs multiple polarization state inputs. Using the polarization mirror state $\mathbf{m}$, we can determine the trace between polarizations ($\mathbf{S}_1, \mathbf{S}_2$) of two consecutive locations. Employing the free-space system in Chapter 2, we demonstrated the local retardation measurement modality. Importantly in the free space system, the mirror state and input polarization state are mirrored by the QU plane. The selection of the polarization state input becomes critical, refraining the input polarization state from linear polarization state. Of note, in the previous single input PS-OCT configuration, the input state of the sample arm is horizontally linear polarization. Hence, the polarization state of the sample surface coincides with the mirror state, making the local retardation vulnerable to noise,

which we termed as mirror state artifact. However, employing a circular input polarization state is the optimized option, and it takes half circle (π rad retardation) to rotate the polarization state to its mirror state. As shown in **Figure 4.2**, the regions suffered from mirror state artifacts were greyed-out. On the other hand, spectral binning was utilized to mitigate the mirror state artifact in fiber-based implementations. Removal of the artifact in free-space imaging becomes possible with spectral binning as shown in Figure. The artifact was largely mitigated after employing spectral binning.

Figure 7.1. Employing spectral binning to the local retardation imaging with the free-space system. (A). the imaging results without spectral binning, where white arrows mark the mirror state artifact region. (B) The imaging results after spectral binning.

As the relative locations of the polarization states and mirror state and the SNR would affect the local retardation reconstruction, careful manipulation of the polarization state on the surface by twisting the paddles of polarization controller is needed the imaging with fiber-based system, making sure the polarization state is far from its mirror state as much as possible. However, in a catheter-based system, such manipulation is not viable since the transmission matrix of the sample arm is changing when the catheter is rotating. The need to quantify the reliability of the measurement by the proposed method becomes pronounced. We derived a reliability metric to estimate the variance of each measurement based on the SNR and the distance between polarization state and mirror state. Moreover, the compound reliability after spectral binning was derived. The cardiovascular cross-section retardation imaging comparison between results from single

input polarization state and benchmark dual input polarization states confirmed the feasibility of the method.

In conclusion, this thesis deals with the implementation of mirror state constraint from the hardware configuration and calibration to local retardation imaging reconstruction with single input polarization state. Compared to the conventional single input PS-OCT, the proposed method for polarization distortion calibration, the system replaces QWP with a polarizer which is more premium. Compared to the multiple input PS-OCT, the proposed method would save polarization modulation or multiplexing module. Overall, the work would decrease the complexity of the system for local retardation imaging and attract more attention to the compelling contrast.

Future work

As highlighted many times, the biggest limitation of PS-OCT might be attributed to the system complexity. PS-OCT needs to involve at least one more spectrometer or one polarization modulator. In contrast, OCT angiography, another functional OCT, becomes the standard function in ophthalmology OCT, without adding any extra system component. Though this thesis provides a method to save a polarization channel, the cost and complexity are still higher than the conventional OCT. Here, I present another two proposals which would further simplify the system, lowering the entering barrier of PS-OCT with depth-resolved birefringence contrast.

PS-OCT with a single spectrometer

In this thesis, we demonstrated the method via mirror state constraint to save one polarization channel. However, polarization-diverse detection is still needed, which means two spectrometers in SD-OCT. Hence, reducing one spectrometer will reduce the cost a lot.

Considering the case of dual inputs PS-OCT with polarization-diverse detection. The transmission matrix could be expressed as

$$[\mathbf{v}_1(z, k) \quad \mathbf{v}_2(z, k)] = \mathbf{P}(k) \cdot \mathbf{J}_{fb}^T(k) \cdot \mathbf{J}_{sam}(k) \cdot \mathbf{J}_{fb}(k) \cdot [\mathbf{u}_1 \quad \mathbf{u}_2] \quad (7-1)$$

Where $\mathbf{u}_1 \mathbf{u}_2$ denotes the Jones vector of the input polarization state, and $\mathbf{J}_{sam} \mathbf{J}_{fb} \mathbf{P}(k)$ denotes the Jones matrix of the sample, sample arm fiber, and asymmetry part of the system, respectively. $\mathbf{v}_1 \mathbf{v}_2$ represents the two Jones vectors received by the polarization-diverse detection with different polarization input at the same spot. Taking a single detection channel into account, the transmission matrix was left multiplied with a filtering matrix $[1 \ 0; 0 \ 0]$.

$$\begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix} \mathbf{V} = \begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix} \mathbf{P}(k) \cdot \mathbf{J}_{fb}^T(k) \cdot \mathbf{J}_{sam}(k) \cdot \mathbf{J}_{fb}(k) \cdot \mathbf{U} \quad (7-2)$$

Only the first-row vector of $\mathbf{V}$ and $\mathbf{P}$ becomes relevant, and the Eq.(7-2) could be rewritten as:

$$[V_{11} \ V_{12}] = [P_{11} \ P_{12}] \cdot \mathbf{J}_{fb}^T(k) \cdot \mathbf{J}_{sam}(k) \cdot \mathbf{J}_{fb}(k) \cdot \mathbf{U} \quad (7-3)$$

Taking $[V_{11} \ V_{12}]$ as the transpose of virtual Jones vector $\mathbf{v}'$, $[P_{11} \ P_{12}]$ as the transpose of $\mathbf{p}'$, after the transpose on Eq.(7-3), we can get similar transmission matrix as we obtain in the mirror state constraint.

$$\mathbf{v}' = \mathbf{U}^T \cdot \mathbf{J}_{fb}(k) \cdot \mathbf{J}_{sam}(k) \cdot \mathbf{J}_{fb}^T(k) \cdot \mathbf{p}' \quad (7-4)$$

Comparing Eq.(7-4) and Eq.(6-1), it is easy to conclude that mirror state constraint also exists if we combine the first-row component as the elements of the new vector. Of note, the prerequisite of the existence of mirror state constraint is the unitarity of the system. This requirement mandates $\mathbf{U}^T$ unitary matrix.

In conclusion, for SD-OCT, generating two polarization state inputs might be a viable method to compromise one spectrometer which occupies a large amount of the cost of SD-OCT. While the matrix formed by the input Jones vector should be unitary. Otherwise, digital calibration methods are required to make it unitary. Once the system is unitary, reconstruction of local birefringence map with single spectrometer will become possible with the derived mirror state constraint.

Birefringence imaging with machine learning

Machine learning has become an emerging technology due to the expansion of computation power[114], [115]. Machine learning, especially deep learning has been established as a reliable method for pattern recognition, prediction, and optimization, etc[116]. In biomedical imaging, machine learning has outperformed the clinicians in the diagnosis[115]–[118]. And imaging enhancement has been demonstrated with deep learning. One audacious idea will be training the neural network with current existed PS-OCT data. We set the intensity image as the independent variables(features) while setting the birefringence map as the labeled dependent variables. Of note, this idea is just in the infancy stage, and much more validation should be done in the future. The promising part of this project is the ample labeled dataset. And the most compelling part is that we can achieve the goal of PS-OCT development, obtaining polarization contrast without more system complexity.

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Patent

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