Improved accuracy of quantitative birefringence imaging by polarization sensitive OCT with simple noise correction and its application to neuroimaging

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Abstract
Polarization-sensitive optical coherence tomography (PS-OCT) enables three-dimensional imaging of biological tissues based on the inherent contrast provided by scattering and polarization properties. In fibrous tissue such as the white matter of the brain, PS-OCT allows quantitative mapping of tissue birefringence. For the popular PS-OCT layout using a single circular input state, birefringence measurements are based on a straightforward evaluation of phase retardation data. However, the accuracy of these measurements strongly depends on the signal-to-noise ratio (SNR) and is prone to mapping artifacts when the SNR is low. Here we present a simple yet effective approach for improving the accuracy of PS-OCT phase retardation and birefringence measurements. By performing a noise bias correction of the detected OCT signal amplitudes, the impact of the noise floor on retardation measurements can be markedly reduced. We present simulation data to illustrate the influence of the noise bias correction on phase retardation measurements and support our analysis with real-world PS-OCT image data.

Keywords
biomedical imaging, birefringence, noise, optical coherence tomography, polarization

1 | INTRODUCTION

Polarization-sensitive optical coherence tomography (PS-OCT) is an optical imaging technique providing real-time, volumetric imaging with micrometer scale resolution [1, 2]. Other than standard OCT imaging, which generates images solely based on the intensity of backscattered light, OCT with polarization sensitivity enables the visualization and
Phase retardation is one of the most commonly used quantities in PS-OCT imaging and describes the axial walk-off \( \delta \) between the phase of the horizontal and the vertical polarization component. In uniformly birefringent tissue, this walk-off generally increases with depth and is linearly dependent on the material’s birefringence \( \Delta n \). In polarization-preserving tissue, \( \Delta n \) is nil and hence \( \delta \) is constant. In substances with strong local variations of the polarization state of the backscattered OCT signal, as is the case for depolarizing or strongly birefringent tissue, spatially varying retardation is observed. Hee et al. showed that, using their relatively simple polarization-sensitive interferometer layout, phase retardation can be calculated in a straightforward manner from the magnitudes of the OCT signals [3],

\[
\delta(\bar{x}) = \arctan\left[ \frac{A_2(\bar{x})}{A_1(\bar{x})} \right].
\] (2)

While \( \delta \) as computed per the above equation can take both positive and negative values, usually the magnitude of \( \delta \) is displayed in two- or three-dimensional PS-OCT phase retardation images. Then, owing to the output of the arctangent, \( \delta \) is confined to a range of \( 0^\circ \)–\( 90^\circ \).

Through the simplicity of the retardation calculation in Equation (2), which just relies on the signal magnitudes and not on their phases, PS-OCT imaging can be implemented quite easily using this approach. Arguably, this may also make this method more robust to noise than other PS-OCT techniques requiring more than one measurement and/or complex-valued OCT signal information to retrieve retardation. Still, noise impacts retardation measurements in this single-state approach as well and may produce false retardation readouts when the SNR is low. Next, we will have a look at the interrelation of the SNR and the observed PS-OCT signals.

The magnitudes \( A_{1,2} \) of the OCT signals detected in each of the two polarization channels can be described by the Rician probability density function (PDF) \( p_A \) [13, 14], which depends on the signal and noise amplitude as well as on the variance of the phasors describing the noise signal. The shapes of \( p_A \) for the signal magnitudes in the vertical and horizontal channel computed for different SNR settings are plotted in Figure 1A. Here, the theoretically expected retardation is \( 90^\circ \), meaning that channel 2 only detects noise (cf. Equation (2)). In other words, the PDFs of the signals observed in the dotted plots in Figure 1A always portray the (non-zero) noise characteristic. Conversely, the PDFs of channel 1 (solid
lines) present growing signal offsets from the origin as the SNR increases.

From the signal characteristics observed for each of the two polarization channels, it is clear that any retardation signals computed thereof will have SNR-dependent distributions too. For two independent Rice random variables $A_1$ and $A_2$, the PDF of the arctangent applied to the ratio random variable $A_2/A_1$ is plotted in Figure 1B for an expected retardation of 90° and the SNR scenarios shown in Figure 1A. As the SNR decreases, the peak of the PDF becomes less defined (i.e., the distribution broadens) and shifts toward 45°. To visualize the effect the SNR has for the entire domain of retardation values between 0° and 90°, the expected retardation signals simulated using Equation (2) with additive noise—a noise bias—on the two detection channels are shown in Figure 1C. In Figure 1D, the simulated retardation measurement data are plotted as a function of SNR. Low SNR clearly results in a reduction of the dynamic range of retardation measurements. The expected SNR-dependent retardation error is mapped in Figure 1E. While the noise bias only weakly affects retardation measurements at SNRs in excess of $-15$ dB, errors on the order of several tens of degrees may be observed for low SNR and expected retardation values beyond $\delta = 45°$. In order to avoid strong distortions of retardation image data, PS-OCT measurements are usually displayed with intensity thresholding such that pixels with SNRs below 5 dB [15], 6 dB [8], or even 10 dB [4] are masked.

To reduce the impact of the noise bias on PS-OCT retardation measurements, we here take a similar methodological approach as has been used to correct PS-OCT depolarization data [10]. For both polarization channels, we measure the two average noise signals $\Xi_{1,2}$ in a background region free from scattering structures and then subtract the respective noise biases from the OCT signal amplitudes prior to retardation calculation. The noise bias corrected retardation data is thus computed as:

$$\delta \left( \bar{x} \right) = \arctan \left[ \frac{A_2 \left( \bar{x} \right) - \Xi_2}{A_1 \left( \bar{x} \right) - \Xi_1} \right].$$

The retardation correction can also yield negative amplitudes, in particular for weak signals. However, since traditionally the magnitude of retardation data is displayed, $\delta$ will always be mapped to the 0°–90° range.
3 MATERIALS AND METHODS

3.1 Simulation of retardation and birefringence measurements with and without noise bias

B-scan images sized 100 (x) × 100 (z) pixels were simulated in Matlab (R2016a, MathWorks) for a uniformly birefringent sample. In each pixel, the noise-affected OCT signals of both detection channels were calculated using SNR and retardation as inputs. First, the expected retardation in a given pixel was computed for a birefringence of 5°/pixel while the retardation of the incident light at the top of the sample was set to 0°. This amount of birefringence per pixel enabled the observation of several retardation cycles from 0° to 90° and back while also providing an impression of the noise characteristic. Next, the relative signal strengths of the two channels were calculated using Equation (2) and scaled according to the relative signal strengths of both channels, and mean μ1 and μ2, respectively [13, 14]. For a given SNR and retardation δ, μ1 and μ2 were computed as:

\[ \mu_1 = \frac{\tan \delta}{\sqrt{1 + \tan^2 \delta}} \]  

and

\[ \mu_2 = \frac{1}{\sqrt{1 + \tan^2 \delta}}. \]  

As SNR used here refers to the ratio of pure signal (i.e. only signal without noise floor) and the standard deviation (SD) of the noise signal:

\[ \text{SNR} = \frac{\mu_1^2 + \mu_2^2}{2 \sigma^2}. \]  

we denote it as SNR similar to our recent work [16]. The complex signals in both channels were then computed as Beckmann random noise distributions, that is, binormally distributed complex signals with identical SD σ along both the real axis and the imaginary axis, offset by the relative signal strengths μ1,2. Finally, the magnitudes of these signals, A1,2, were calculated and noise afflicted retardation was calculated using Equation (2). In order to estimate the average noise level \( \Xi_{1,2} \), random noise was computed for 10 000 pixels with a Beckmann distribution having the same variance \( \sigma^2 \) as used for simulating the noise afflicted signals. Noise corrected retardation images were produced by applying Equation (3) to the noise bias subtracted signals, \( A_{1,2} - \Xi_{1,2} \).

Birefringence measurements were simulated by computing the average retardation signals of 100 axial scans and fitting the slope to the top 15 and 30 pixels beneath the sample surface, respectively. These window lengths were chosen in order to investigate the effect of available fit window length on the measured birefringence. The two different fit window lengths correspond to fitting a slope to half of a retardation ramp (i.e., \( -0°-45° \)) and a full retardation ramp (i.e., \( -0°-90° \)). Simulations were run for SNR’ ranging from 0 to 40 dB and for birefringence set to 3°/pixel. For each birefringence measurement, both traditional retardation data (Equation (2)) and noise bias corrected retardation data (Equation (3)) were evaluated and charted as a function of SNR’. To provide an easy comparison of the performance for the two approaches, the relative errors of the birefringence measurements were plotted as a function of SN’ as well.

3.2 Experimental PS-OCT setup and data processing

A high-resolution spectral-domain PS-OCT ophthalmoscope [17] was modified for imaging in a confocal scanning microscope configuration. In brief, the PS-OCT system used a multiplexed superluminescent diode (SLD) with a bandwidth of 100 nm centered at 840 nm as a light source. The light from the SLD was linearly polarized and fed into a polarization sensitive interferometer configuration [3]. The sample arm was equipped with two telescopes, one on either side of a pair of galvanometrically scanned mirrors [18], and a lens with a 6.2-mm focal length for imaging the sample. At the interferometer output, the interference signal was collected by a polarization-maintaining fiber and split by a polarizing beam splitter into its horizontal and vertical component, each of which was detected by a separate spectrometer including a transmission grating with 1200 lines/mm, an f-theta lens with 160 mm focal length and a 4096×2-pixel CMOS sensor (Basler Sprint). The spectral interferograms of both polarization channels were read out simultaneously with a resolution of 3072 pixels and a frequency of 83 kHz. PS-OCT datasets comprising 512 (x) × 400 (y) × 1536 (z) pixels per channel were acquired in just under 4 seconds. Processing steps featured standard spectral domain OCT computing [12] as well as the PS-OCT calculation described in section 2 above. En-face maps of reflectivity and retardation were computed by axially averaging the respective data. To compute birefringence maps, the sample surface was automatically segmented and a slab ranging from 11 pixels (21 μm) to 171 pixels (325 μm) underneath was extracted from the volumetric data.
The offset of 11 pixels was chosen to exclude potential artifacts caused by surface reflections, and the depth of 160 pixels enabled having both a sufficient number of pixels for each A-line to perform a linear fit and maintaining sufficient signal as the SNR degrades due to light attenuation at deeper depths. In this slab, the slope of a linear fit (Matlab function `polyfit`, first order) was computed for all axial retardation profiles and displayed as an

**FIGURE 2** Simulation of typical retardation patterns observed in birefringent samples for five SNR scenarios. A-E, Traditional retardation images with SNR's of A, 0 dB; B, 7 dB; C, 10 dB; D, 20 dB; and E, 30 dB. The left column shows simulated retardation B-scans consisting of 100 × 100 pixels. Depth profiles showing the individual retardation values are plotted in the middle column. The expected triangular profile of retardation vs. depth seen at high SNR in panel E turns into a more sinusoidally oscillating profile with reduced oscillation amplitude and increased noise when the SNR is low. The red line denotes the average at each depth position. The observed retardation histograms simulated for 10 000 pixels for an expected \( \delta = 0^\circ \) (e.g., at the sample surface) are shown in the right column. Mean and SD of the distributions are given in red font next to the individual histograms. F-J, Retardation images with noise bias correction. B-scans are shown alongside depth profiles (middle), and histograms for an expected retardation of \( \delta = 0^\circ \) (right). In particular for H-J, increased dynamics of the retardation data with the noise correction can be observed, and higher accuracy and precision are achieved in the histograms.
en-face map. A unitless representation of the birefringence data (i.e., wavelengths per depth unit) was used for the experimental measurements in order to enable a comparison between these birefringence data and measurements taken with other PS-OCT machines potentially operating at other wavelengths. Further, maps showing the absolute and relative difference between the birefringence measurements were generated, and the SNRs in the evaluation slab were calculated from the axially averaged reflectivity signals

\[ R = \frac{1}{N} \sum_{i=1}^{N} A^2_{x,i} + A^2_{z,i} \]  

and their SD \( \sigma_R \) as

\[ \text{SNR}_{\text{refl}} = 10 \log_{10} \left( \frac{\bar{R}}{\sigma_R} \right) \]

similar to Equation (6) and presented in an en-face map.

### 3.3 | Samples

To experimentally demonstrate the impact of noise bias correction, the retardation characteristics of two wave plates (Thorlabs, Linos) were investigated. The objective lens was removed and the sample beam was attenuated by a neutral density filter plus a variable neutral density filter wheel, which enabled systematic attenuation of the sample signal to perform retardation measurements at different SNRs. One wave plate and a mirror were inserted as a sample into the sample arm. During data acquisition, the sample beam was kept stationary (i.e. no beam scanning) and datasets were acquired with the mirror placed ~150 \( \mu \text{m} \) away from the zero delay. Histograms of retardation values from 10 000 A-scans were computed and the mean retardation of 100 A-scans were evaluated and plotted for different SNR settings.

The plastic cap of a marker pen (Edding 8020) was used as a static birefringent sample to be imaged with variable SNR. To attenuate the sample signal, again a variable neutral density filter wheel was inserted into the interferometer’s sample arm and PS-OCT datasets were acquired at optical densities ranging from 0 to 1.2. The distribution of the retardation signals measured at the sample surface was plotted in histograms for both traditional and noise-corrected data. Birefringence measured as the slope of a linear fit to the retardation data beneath the surface was evaluated.

As a representative biological sample, a formalin-fixed murine brain specimen was coronally sectioned using a scalpel and embedded in 5% agarose. The cut face was imaged in a region of interest spanning approximately 4 \( \text{mm} \times 4 \text{mm} \). The focus was set ~100 \( \mu \text{m} \) below the tissue surface. In addition to a PS-OCT dataset, a color photo was taken for orientation.

### 4 | RESULTS

#### 4.1 | Simulation of impact of noise bias correction on retardation and birefringence measurements

PS-OCT retardation images of birefringent materials exhibit a typical banded pattern. We simulated retardation images for five SNR scenarios, namely for SNRs of 0, 7, 10, 20, and 30 dB, as shown in the left column of Figure 2A-E. The banded pattern of retardation oscillating between 0° and 90° shows a strong dependence on SNR. The triangular profile of retardation A-scans seen at high SNR in Figure 2E is damped to a more sinusoidal contour with reduced oscillation amplitude and increased noise for low SNR. In the right column of the figure panels, the histograms of 10 000 simulated retardation pixels are shown for an expected \( \delta = 0° \) as would be the case at the sample surface when retardation offsets caused by the PS-OCT interferometer can be neglected [19]. Both peak and bandwidth of the histograms decrease as the SNR increases. Simulated retardation images with noise bias correction are shown for the same SNR’ presets in Figure 2F-J. Interestingly, the noise floor appears substantially broader for SNR = 0 dB, that is when the pure signal is equal to the SD of the noise intensity (see Figure 2F). However, once the signal exceeds the noise floor, increased dynamics of the noise bias corrected retardation data can be observed, and the histograms in Figure 2H-J clearly evince higher accuracy and precision than their noise-afflicted counterparts.

Birefringence measurements in uniform birefringent tissue are typically performed by fitting a linear function to the PS-OCT retardation profiles in the axial direction [20]. We assessed the slopes of such fits to simulated PS-OCT data consisting of 100 depth profiles for the same birefringence setting but with two different fit range lengths (15 pixels and 30 pixels) and SNR’ ranging from 0 to 40 dB. Figure 3 shows the results. While for low SNR’ settings, birefringence is massively underestimated regardless of any noise bias correction, more accurate results are achieved at high SNR’. Beyond an SNR’ of 5 dB, the noise-corrected signal appears to converge more rapidly. For the simulation with the longer fit spanning a retardation range from 0° to 90° shown in Figure 3B, an overshoot of the measured birefringence can be observed in excess of SNR’ of 10 dB once the noise bias has been corrected for. Note, however, that birefringence measurements based on noise-corrected retardation data tend to...
be more accurate (except for very low SNR'), which is further illustrated in the plots showing the relative errors at the bottom of Figure 3.

### 4.2 Wave plate measurements

PS-OCT retardation measurements were made for two wave plates retarding the sample beam by 90° and 38° (as verified by a commercial polarimeter), respectively. Figure 4 shows histograms of datasets comprising 10,000 repeated retardation measurements performed for different SNR settings. For an achromatic quarter wave plate with an expected retardation of 90°, the retardation data is focused around 45° for traditional computation (Figure 4A) and more uniformly distributed for noise-corrected PS-OCT data (Figure 4B) when the SNR is low. At higher SNR levels, the quarter wave plate measurements with noise bias correction are clustering towards higher retardation values. Albeit the measured values are also considerably lower than 90°, in particular when the SNR is low, the accuracy of mean retardation measurements is definitely improved by noise bias correction. Figure 4D-F shows corresponding retardation plots for the zero-order wave plate. In this setting, where the signal level is almost similarly high in both polarization channels, the histogram shapes again are changed by the noise correction (Figure 4D,E) whereas their means have very similar characteristics across the investigated SNR range. These results demonstrate that the noise bias correction has a stronger influence away from δ = 45°, that is when the signal levels $A_1$ and $A_2$ are rather dissimilar.

### 4.3 Birefringent plastic sample

PS-OCT reflectivity and retardation images of a plastic sample are presented in Figure 5. Reflectivity and retardation B-scans are shown for traditional and noise-corrected processing in Figure 5A. The left set of four panels features data from unattenuated imaging with a rather high SNR of 28 dB (SNR computed from the average signal intensity in the green box over the noise in the red box), whereas the right panels show similar B-scans with a signal attenuation of 22 dB dialed in using the neutral density filter wheel in the sample arm. Note the noise floor reduction in the respective reflectivity B-scans on the right hand side. In the retardation B-scans, noise bias correction yields an increased contrast of the banded pattern and at the same time visibly broadens the noise distribution in the background regions at the top and bottom of the images. Histograms of the retardation values
FIGURE 4 Retardation measurements of two wave plates in the sample arm. A-C, Achromatic zero-order quarter wave plate ($\delta = 90^\circ$). D-F, Zero-order wave plate designed as a quarter wave plate at 1300 nm wavelength providing a retardation of $\sim 38^\circ$ at 840 nm wavelength. A and D, Histograms of 10 000 repeated retardation measurements without noise bias correction. The color map encodes the different SNR levels. B and E, Histograms of 10 000 repeated retardation measurements with noise bias correction. Note that the noise floor becomes more uniformly distributed. While the histograms are rather centered around the expected value in the middle of the measurement range, the distributions of the quarter wave plate measurements are clustered more towards higher retardation values for the noise corrected data. Also note that the distributions of some measurements such as the one at an SNR of $\sim 4$ dB are slightly displaced from the expected value. We attribute such systematic distortions to minor sample beam displacements caused by manual adjustment of the filter wheel position. C, Average retardation for different SNR settings for $\delta = 90^\circ$. The noise-corrected data (blue) tends to be closer to the expected value. F, Average retardation for different SNR settings for $\delta = 38^\circ$. In the middle of the measurement range, no benefit of noise correction can be observed.
measured at the surface of the sample are displayed in Figure 5B for the images with SNRs of 28 and 6 dB, respectively. A broader distribution can be observed for the lower SNR which, after noise bias correction, features a more uniform floor. At the same time, the histograms of the noise-corrected retardation data are more skewed towards the expected value of $0^\circ$ in both SNR settings.

Birefringence was measured in the location indicated by the white line in Figure 5A for several acquisitions with different optical densities provided by the filter wheel. In Figure 5C, the measured birefringence is plotted as a function of optical density for both traditional and noise-corrected PS-OCT data. With decreasing SNR (i.e. with increasing optical density of the filter), the birefringence measurement is progressively underestimated for data from the traditional retardation computation. Stronger and more robust birefringence measurements are observed after noise bias correction, albeit the SNR dependent roll-off cannot be completely diminished.

4.4 | Murine brain sample

In order to present the effect of noise bias correction for real-world image data, PS-OCT imaging was performed in a mouse brain specimen. The scanned region of interest is indicated by a violet square in Figure 6A. A
reflectivity en-face image generated by averaging the signals along the entire z-range is shown in Figure 6B. Anatomical structures including the corpus callosum, the caudoputamen, the lateral ventricle, and the bundle of the anterior commissure can be observed. Note that the reflectivity of the anterior commissure is rather weak because the fiber orientation is close to parallel to the OCT beam. Representative PS-OCT reflectivity B-scans before and after noise bias correction are shown in Figure 6C,D, respectively. Corresponding phase retardation B-scan images are shown in Figure 6E,F. Pixels with SNRs lower than 7.2 dB in the reflectivity scans were masked and displayed in gray to improve the visualization of the retardation ramps within the tissue. While prima vista, there are no striking dissimilarities to be observed between the retardation images, the birefringence maps computed thereof (Figure 6H,I) exhibit more pronounced differences. Most obviously, the

FIGURE 6  PS-OCT imaging of birefringence in a mouse brain specimen. A, Photo/sketch indicating the location of the OCT volume scan. B, Reflectivity projection image. The green line shows the location of the B-scans in panels C-F. C, Reflectivity B-scan image. D, Reflectivity B-scan with noise correction. E, Traditional retardation B-scan. F, Retardation B-scan with noise correction. In panels E and F, pixels with low SNR are masked and displayed in gray. G, En-face map showing the average SNR within the tissue slab used for birefringence evaluation. H, Birefringence image computed from the retardation data of a 160 pixels deep superficial slab. The asterisk indicates an area with unexpectedly decreased birefringence potentially caused by an imperfect flatness of the sectioned sample surface. The birefringence observed in the lateral ventricle is caused by the posterior wall of the VL. I, Birefringence image with noise correction. J, Absolute difference of the birefringence image data in I and H. K, Relative difference image revealing up to 50% higher birefringence estimated in I compared to H. Even in the corpus callosum, which provides a high SNR, birefringence is ~10% higher in I, that is after noise correction. ACO, anterior commissure; CC, corpus callosum; CP, caudoputamen; VL, lateral ventricle
contrast of the anterior commissure is improved after noise correction. An en-face map showing the average SNR within the tissue slab used for birefringence evaluation is shown in Figure 6G. Quantitative comparisons of the absolute and relative differences of the birefringence maps in Figure 6H,I are provided in Figure 6J,K, respectively. In absolute numbers, the difference appears largely homogenous, whereas the relative difference seen in Figure 6K reveals higher birefringence measured after noise bias correction, ranging from ~10% in strongly scattering structures, such as the corpus callosum to ~50% in other, more weakly scattering parts of the cerebrum.

To further visualize the dependence of birefringence measurements in the murine brain on noise floor correction and SNR, we used histograms of the birefringence en-face maps as shown in Figure 6H,I are presented in Figure 7A in red and blue color, respectively. The histogram of the noise-corrected birefringence map was used to divide the birefringence data into 10 evenly sized portions. Then, the distribution of the relative difference between corresponding pixels in the traditional and noise-corrected birefringence maps were plotted as a function of average SNR in the evaluation slab (see Figure 7C). Alongside the ordinate, the somewhat randomly distributed differences of A-scans devoid of structural signals are located. Birefringence differences measured in actual tissue can be observed as a cluster with a centroid in the positive region. For signals with a higher birefringence (indicated by lighter colors of the color map), the distribution appears more confined. We then used the histogram of the SNR map shown in Figure 7B to classify the pixels of the relative birefringence map according to the average signal strength within the evaluation slab. The distribution of the relative difference between the traditional and
noise-corrected birefringence maps is plotted as a function of birefringence measured after noise bias correction in Figure 7D. A characteristic distribution centered in the first quadrant can be observed in these scatter plots which, again, appears more confined for greater SNR (indicated by lighter colors of the color map) and stronger birefringence.

5 DISCUSSION

This work features two important aspects for PS-OCT imaging. First, we introduce a simple yet effective scheme for removing the noise bias and thereby improving the quality of phase retardation images as well as of quantitative birefringence measurements. Second, we more generally illustrate how retardation and birefringence measurements are impacted by noise, which may have implications for biomedical applications.

Our simulations (Figures 1-3) and experimental data (Figures 4-7) show congruent results in demonstrating the dependence of retardation measurements on SNR and the impact of noise bias correction on retardation and birefringence data. In particular for weak signals, birefringence readouts are underestimated. Noise bias correction helps to reduce this artifact, although it cannot completely remove it either (see Figure 3). An alternative approach for correcting phase retardation measurements is the use of a maximum a-posteriori (MAP) estimator [7, 9, 21] which employs the characteristics of the (known) probability density functions to estimate the true signals. MAP estimators have been demonstrated to work very well on Jones matrix OCT data [7, 9, 21] and would likely also improve image quality and fidelity of retardation and birefringence measurements based on the single input PS-OCT used here. MAP estimator based image correction, however, is computationally expensive. The more straightforward, low-tech approach presented here, which essentially corresponds to a simple background subtraction for both polarization channels in z-space, can be easily implemented in any data processing pipeline and may thus be rapidly performed in real-time.

Retardation measurements are usually fairly exact when the SNR is high. For instance, measurements performed with a single retarder and a reflector as a sample typically show exceptional accuracy and precision [4, 12, 22, 23]. In such high SNR settings, noise bias correction may still improve accuracy and precision of a retardation measurement, as demonstrated in Figures 2 and 4. For high SNR, retardation measurements are also well represented by the mean value (i.e. the expected value) of the then narrow distributions while for low SNRs broad and often asymmetric distributions are observed which could be more specifically characterized using proper skewness metrics. When the SNR is low, retardation measurements may be subject to strong distortions (cf. Figure 4) and thus affect reproducibility of PS-OCT data acquired with dissimilar SNR. The SNR and thus also quantitative PS-OCT data can be improved by averaging signals from repeat acquisitions [6, 8], though at the cost of measurement time. Still, retardation data from weak signals have to be interpreted with care as to not confuse SNR-related artifacts with (additional) birefringence or even depolarization.

The slope of retardation increase over depth has been used to measure tissue birefringence using PS-OCT. [5, 20, 24] Given that the uniformly birefringent tissue (or other material) is both thick enough and birefringent enough, a linear fit may be performed over up to a quarter of a retardation cycle ranging from 0° to 90°. However, the goodness of this fit and thus of the birefringence measurement not only depends upon the retardation noise and the number of pixels but may also be influenced by the SNR and the range within the retardation cycle that is available for the fit. For instance, the dissimilar shapes of the birefringence measurements such as the overshoot seen in Figure 3B but not in Figure 3A, which only differ by the length of the retardation ramp used for fitting, are also a result of the nonlinearity of retardation mapping in the presence of noise—even when accounting for the average noise level.

Last but not least, the results presented here may be relevant for both qualitative and quantitative PS-OCT imaging in biomedicine. In neuroimaging applications, as presented in the murine brain in this article, birefringence can serve as tissue property for generating image contrast [25-27] that may be improved by noise bias correction. The method could also be valuable in ophthalmology where PS-OCT has been used to assess the integrity of the retinal nerve fiber layer in healthy and diseased eyes [1, 2], and also for quantitative investigations of other structures, such as cartilage, muscles or cardiac tissue, as well as for non-medical applications in materials science.

6 CONCLUSION

Retardation and birefringence measurements by PS-OCT with a single circular input state are impacted by inherent noise. In this work, we applied a noise bias correction to both polarization channels prior to computing phase retardation in order to improve the accuracy of PS-OCT data. We simulated the effect of noise correction and demonstrated its performance in experimental PS-OCT data. Retardation and
birefringence measurements seemed to particularly benefit from this additional, computationally inexpensive processing step when the SNR was low, namely on the order of ~5–15 dB. Our results suggest that noise bias correction may be a worthwhile addition to current PS-OCT processing pipelines in a variety of biomedical applications.

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CONFLICTS OF INTEREST
The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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