Measurement of a multi-layered tear film phantom using optical coherence tomography and statistical decision theory

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Abstract: To extend our understanding of tear film dynamics for the management of dry eye disease, we propose a method to optically sense the tear film and estimate simultaneously the thicknesses of the lipid and aqueous layers. The proposed method, SDT-OCT, combines ultra-high axial resolution optical coherence tomography (OCT) and a robust estimator based on statistical decision theory (SDT) to achieve thickness measurements at the nanometer scale. Unlike conventional Fourier-domain OCT where peak detection of layers occurs in Fourier space, in SDT-OCT thickness is estimated using statistical decision theory directly on the raw spectra acquired with the OCT system. In this paper, we demonstrate in simulation that a customized OCT system tailored to ~1 μm axial point spread function (FWHM) in the corneal tissue, combined with the maximum-likelihood estimator, can estimate thicknesses of the nanometer-scale lipid and micron-scale aqueous layers of the tear film, simultaneously, with nanometer precision. This capability was validated in experiments using a physical phantom that consists of two layers of optical coatings that mimic the lipid and aqueous layers of the tear film.

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1. Introduction

Dry Eye Disease (DED) has been a serious public health issue, with symptoms including discomfort, visual disturbance, and irritation that may cause damage to the ocular surface [1]. However, the understanding of the mechanisms underlying DED is still at an early stage. According to Johnson and Murphy [2], it is a prerequisite that the normal tear film be better understood if we are to advance our ability to effectively manage DED. The tear film is the ocular surface fluid that contributes to keep the cornea healthy and functional, and as such it plays a critically important role in keeping normal visual function for the ocular optical system [3]. The normal tear film consists of three layers: the lipid layer, the aqueous layer, and the mucin layer [4]. The lipid layer is secreted by the meibomian gland and is about 20–150 nm thick; underneath the lipid lies the aqueous layer, which contributes the largest volume to the tear and is about 3–7 μm thick; the mucin layer is the interface between the aqueous layer and the cornea, which creates a rough interface between the cornea and the aqueous layer. The rough interface serves to attach tears to the corneal surface.[...]

2. Methodology

Since the invasive methods disturb the tear film in the measurement procedure, non-invasive methods have been sought. In 1989, Doane pioneered the development of a non-invasive interferometric method to measure the tear film [6]. He used the thickness-dependent fringe...
method based on the principle of thin-film white light interferometry, which is known for explaining the changing colors of a soap bubble as its thickness varies. Since then, different techniques have been deployed over two decades to quantify tear film thickness: interferometry based on wavelength-dependent fringe [7], confocal microscopy [8], and spectral domain optical coherence tomography (OCT) [9–12]. These methods lack in their ability to provide simultaneous measurements of both the lipid and aqueous layers, or they measure at a single point and are unable to spatially quantify the tear film dynamics.

In spectral domain OCT, the convention is to perform a fast Fourier transform followed by a peak detection technique to extract thickness information. The axial resolution of this method is fundamentally limited by the width of the axial point spread function (PSF), which is in the order of a micron in state-of-the-art systems, thus to date OCT has been used to measure the total thickness of the lipid and aqueous layers combined. To overcome this limitation, we approach the problem by combining the axial selectivity capability of OCT with statistical decision theory (SDT) [13]. In this approach, SDT is applied directly to each raw spectrum acquired by the OCT system to estimate the thickness configuration that has most likely generated a given spectrum. Thereafter, we refer to this fundamentally different approach as SDT-OCT to clearly distinguish it from conventional spectral domain OCT. The novelty of the approach is that it combines modeling with the hardware solution and importantly it enables thickness estimation down to nanometer scale with nanometer precision, as required for the lipid layer, a two orders of magnitude improvement from the conventional approach.

We first introduced the combination of statistical decision theory with OCT in 2005 for time-domain OCT in the context of a classification task [14,15]. Recently, we extended the framework to spectral domain OCT for a single layer thickness-estimation task [16,17]. We used the root mean square error (RMSE) of single layer thickness estimates as a figure of merit to quantify the impact of different system parameters. Specifically, we theoretically investigated the impact of the axial PSF as well as the integration time on the system performance. Results showed that to achieve nanometer precision with high imaging speed (i.e. integration time < 10 µs), one micron axial PSF (FWHM) was needed. We further demonstrated in simulation that the system was able to estimate thickness down to the nanometer scale. In the context of DED management and the investigation of the core mechanisms leading to DED, it is critical to expand on the prior framework to a two-layer estimation, to simultaneously quantify the thicknesses of the lipid and aqueous layers.

In this paper we thus further extend the theory of SDT-OCT first established in [17] to enable the simultaneous estimation of the thicknesses of the lipid and aqueous layers. In Section 2, we present the development of the theoretical framework that takes into account different sources of statistical noise associated with the imaging chain. Specifically, we formulate a maximum-likelihood (ML) estimator as the observer to extract the dual thickness information. Section 3 details the OCT hardware instrumentation development as well as the experimental validation of SDT-OCT with a custom-developed physical phantom. Finally we discuss the results in Section 4 before concluding the paper.

2. Theoretical framework development

The theoretical framework presented in this paper addresses a dual estimation problem given one spectrum measurement per lateral position on the cornea. This section details the mathematical modeling of SDT-OCT and the principle of ML estimation for two layers.

2.1 Mathematical modeling of SDT-OCT for a two-layer tear film thickness estimation

The OCT system hardware tailored to this application is schematically shown in Fig. 1. The detector is a spectrometer, from which the output is a spectrum array. The broadband light source emits an electric field that can be regarded as a superposition of plane waves. The electric field for a plane wave with an angular frequency ω is denoted as \( E(\omega, t) \). It is split at
the beamsplitter and propagates to both reference and sample arms. The response \( m_r(\omega) \) associated with the electric field \( E_s(\omega,t) \) following its propagation through the reference arm can be written as

\[
m_r(\omega) = \frac{1}{2} r \cdot \exp \left( i2n_0 \frac{\omega}{c} l_r \right),
\]

where \( r \) is the reflectance of the mirror, \( n_0 \) is the refractive index of air, \( c \) is the velocity of light in vacuum, and \( l_r \) is the length of the reference arm. This term is set to be zero when a common path configuration is used.

Similarly, the response \( m_s(\omega) \) from the sample arm can be derived as

\[
m_s(\omega) = \frac{1}{2} \left( r_1 + r_2 (1 - r_1') \cdot \exp \left( i2n_1 \frac{\omega}{c} d_l \right) \cdot r_3 (1 - r_2') \cdot \exp \left( i2n_3 \frac{\omega}{c} d_a \right) \right) \cdot \exp \left( i2n_0 \frac{\omega}{c} l_s \right),
\]

where \( n_1, n_2, \) and \( n_3 \) denote the refractive indices of lipid, aqueous, and corneal epithelium, respectively; \( d_l \) and \( d_a \) are the thicknesses of the lipid and aqueous layers, respectively; \( l_s \) is the length of the sample arm; and \( r_1, r_2, \) and \( r_3 \) denote the reflectance of the air-lipid, lipid-aqueous, and aqueous-cornea interfaces, respectively. It is worth noting that the refractive indices and the reflectance have dependence on the optical frequency due to dispersion, and this dependence is accounted for in the model. Furthermore, due to the different thickness ranges of the lipid and aqueous layers and the fact that the double-pass reflections that occur in multilayered structures are estimated to be three orders of magnitude smaller than the single pass reflections, multiple reflections may be neglected in the model, which was also validated in simulation. Since there is no distinct interface between the aqueous and mucin layers, we consider them as one layer in this investigation. Due to the microplicae and glycocalyx on the corneal surface [4], the interface between the tear film and the cornea is rough as illustrated in Fig. 1. The reflectance at the rough interface between the aqueous and the cornea is given as [18]

\[
r_3 = \frac{n_2 - n_3}{n_2 + n_3} \cdot \exp \left( -2\sigma^2 n_2^2 \frac{\omega^2}{c^2} \right),
\]

where \( \sigma \) is the standard deviation of the surface height of the aqueous-cornea interface.

![Fig. 1. Schematic layout of spectral domain OCT in the context of the tear film imaging.](image-url)
line-scan camera with $M$ pixels, the output from the spectrometer is a discretized spectrum $N_x$, which is an array with $M$ elements. For the $x$th pixel along the line-scan camera, the reading $N_x(x,\Delta t)$ is proportional to the number of electrons accumulated in that pixel sensor during the integration time $\Delta t$. Given the laser intensity noise as well as the Poisson noise and dark noise of the detector, the randomness of $N_x(x,\Delta t)$ may be approximated by a normal distribution as

$$N_x(x,\Delta t) \sim \text{Normal}\left(\left\{\left\langle N_x|d_l,d_a\right\rangle (x,\Delta t)\right\}\right), K_{N_x|d_l,d_a}(x,\Delta t),$$

(4)

which is experimentally validated in section 3.2.2. $\langle\langle N_x|d_l,d_a\rangle(x,\Delta t)\rangle$ represents the ensembles average of the output over all sources of noise, for a given lipid layer thickness $d_l$ and aqueous layer thickness $d_a$, and is given as [16]

$$\left\{\left\langle N_x|d_l,d_a\right\rangle (x,\Delta t)\right\} = \frac{R(x)}{e^{\Delta t}} \int_{\omega_0-\Delta\omega}^{\omega_0} S(\omega)\left[m_r(\omega) + m_s(\omega)\right]^2 d\omega + N_{\text{dark}},$$

(5)

where $S(\omega)$ is the power spectral density of the source, $N_{\text{dark}}$ is the average dark noise over the integration time, $\Delta\omega$ is the optical frequency bandwidth at the $x$th pixel, $e$ is the charge of an electron, and $R(x)$ is the pixel’s responsivity. As shown in [17], $K_{N_x|d_l,d_a}$ is a $M \times M$ covariance matrix, but only the diagonal elements of the matrix are non-zero. Thus $K_{N_x|d_l,d_a}$ can be simplified as an $M$ element array that denotes the variance of the readout at each pixel. Given the fact that the variance depends on the specific source and detector being used, we experimentally quantify $K_{N_x|d_l,d_a}$ as reported in Section 3.2.2.

2.2 Formulation of the maximum-likelihood estimator for the lipid and aqueous layers

The OCT system is a point-to-point imaging modality. During one measurement, a spectrum $N_x$ from one lateral point of the sample is acquired. Building on the basic SDT-OCT framework reported in [17], for a measured spectrum $N_x$, the likelihood of this spectrum being generated by different possible combinations of tear film thicknesses $d_l$ and $d_a$ is given as

$$P(N_x|d_l,d_a) = \frac{1}{(2\pi)^u \prod_{x} K_{s(x),\omega}(x,\Delta t)^{-\frac{1}{2}}} \times \exp\left[-\frac{1}{2} \sum_{x} \frac{\left\langle\left\{N_x|d_l,d_a\right\rangle (x,\Delta t)\right\} - \left\langle\left\{N_x|d_l,d_a\right\rangle (x,\Delta t)\right\rangle}{K_{s(x),\omega}(x,\Delta t)}\right]^2.$$

(6)

It is worth noting that in Eq. (6), $N_x$ is the raw spectrum and no spectrum rescaling is needed.

The ML estimator makes estimates by maximizing $P(N_x|d_l,d_a)$, which is equivalent to finding the minimum of the negative conditional log-likelihood. The estimates are then given as

$$\left(\hat{d}_l,\hat{d}_a\right) = \arg\min_{d_l,d_a} \left\{P(N_x|d_l,d_a)\right\}.$$

(7)

The ML estimator is next further detailed and applied in an experimental setting.

3. Experimental investigation

3.1 Development of a customized OCT system

We designed and built a custom spectral-domain OCT system operating in the spectral window of 600 to 1000 nm. Because of the lack of fiber directional couplers for the considered broadband spectral window, the system was built in free-space and is schematically shown in Fig. 2. The OCT system consists of a commercial supercontinuum...
source (WhiteLase Micro, Fianium Inc.), a custom bandpass filter, and a custom broadband astigmatism-corrected Czerny-Turner spectrometer [19]. Because no commercial filter met our requirement for this broad bandwidth, we developed an optical filter with two diffraction gratings (830 grooves/mm, Richardson Gratings™) to disperse and recombine the spectrum, two off-axis mirrors (45° off axis parabola mirror, EFL = 89.28mm, Edmund Optics Inc.), and a custom adjustable iris diaphragm to select the desired spectrum. By doing so, we eliminated the spectrum outside the operating window because it may deliver extra power to the eye and cause safety issues. After the filter, the beam is then split into the reference and a sample arms by a 50/50 non-polarizing cube beamsplitter (BS014, Thorlabs Inc.). In the sample arm, a galvanometer-based scanner (Dual axis, Cambridge Technologies Inc.) directs the beam to the sample, currently in telecentric geometry, and is focused on the sample using a broadband NIR achromatic doublet lens (EFL = 40 mm, Thorlabs Inc.). The beam size is 2 mm in diameter, yielding 20 µm FWHM lateral PSF. In the reference arm, an equivalent lens is used to compensate for the dispersion. The back reflection/scattering light beams from both arms are focused into a broadband astigmatism-corrected Czerny-Turner spectrometer [19]. The spectrometer interfaced to a line-scan camera of 8192 pixels (SPL8192-70km, Basler Inc.) provides 0.1 nm spectral resolution. In addition, the design is corrected for astigmatism over the 400 nm bandwidth. In this driving application for the measurement of tear film thickness, the reference arm is used to guide the positioning of the sample at the focus of the light beam and perpendicular to the beam, while for imaging we block the reference arm and use the air-tear interface as a new effective reference that helps minimizing the effects of environmental vibrations as established in common path interferometers. The measurements using a common path setup can be considered a special case of the OCT model that has been reported in Section 2.1, in which the response from the reference arm is considered to be zero.

Fig. 2. Customized spectral domain OCT experimental setup.

3.2 Evaluation of system parameters

In this section, key system parameters, including the axial PSF and the statistical noise associated with the customized OCT, are evaluated.
3.2.1 Axial Point spread function (PSF)

The axial PSF was measured by using a flat mirror as the sample. The measured PSF width (FWHM) was calculated from the Fourier transform of the interference fringes, which was 1.30 µm in air and 0.93 µm in corneal epithelium (n = 1.401) [20]. To make sure there was no PSF degradation due to k-space interpolation and dispersion, the theoretical PSF was calculated from the Fourier transform of the envelope of the interference signal, which is shown as the solid line in Fig. 3. Results show a good agreement in the evaluation of the PSF and the achievement of < 1µm axial PSF needed for this application.

Fig. 3. Experimental and theoretical PSFs.

3.2.2 Characterization of system noise

Since the specific variance of the output depends on the source and detector being used, the variance associated with the customized spectral domain OCT was evaluated. To quantify the variance of $N_g$, we placed a variable neutral density filter (VNDF) before the input of the spectrometer. Because all the pixels in the line-scan camera use the same type of sensor, the noise was evaluated at one random pixel. Readings from that chosen pixel were recorded for a fixed light intensity level. Figure 4(a) shows the histogram of output readings, from which the mean and variance of the digital number (D.N.) were calculated. The red envelope in Fig. 4(a) shows a Gaussian curve with the calculated mean and variance, which validates that the output follows a normal distribution. The calculated mean and variance from Fig. 4(a) correspond to the data point in the red square shown in Fig. 4(b). Then as we adjusted the position of the VNDF, the intensity of the light reaching the line-scan camera monotonically increased. After quantifying the mean and the corresponding variance at different light intensity levels, the relation of the mean power spectrum value $K_{N_g}(x,\Delta t)$ and its variance $K_{N_g}(x,\Delta t)$ is shown in Fig. 4(b). The red curve in Fig. 4(b) is a second-order polynomial fitting, which gives the following relation

$$K_{N_g}(x,\Delta t) = C_1 \left\langle \left\langle N_g(x,\Delta t) \right\rangle \right\rangle + C_2 \left\langle \left\langle N_g^2(x,\Delta t) \right\rangle \right\rangle + C_3.$$  \hspace{1cm} (8)

From the fitting curve, the coefficients $C_1$, $C_2$, $C_3$ were evaluated to be 3.2 x $10^{-4}$, 0.33, and 25, which correspond to the laser intensity noise, the Poisson noise, and the dark noise, respectively.
3.3 Phantom preparation

To test the performance of the ML estimator in an experimental setup, we fabricated a physical phantom with known thicknesses that provide ground truth in the estimation task. Optical coating was chosen to make accurate deposition of a layered structure.

We deposited coatings using Ta2O5 and SiO2 on a BaK2 glass substrate, to mimic the lipid layer, the aqueous layer, and the corneal epithelium, respectively. The substrate was 3 mm thick (i.e., 4.6 mm in optical thickness) and the back surface of the substrate was grinded to be rough in order to, together with being a thick substrate, effectively eliminate any contribution from that surface. The refractive indices of these materials and the tear film components are listed in Table 1 [21,22]. Although the refractive indices are listed at 589 nm for comparison, the dispersion curves (the wavelength dependence of the refractive indices) of the materials were measured during manufacturing and those of the tear film components are known from the literature. The impact of the uncertainty in the refractive indices will be discussed in Section 4.

The difference in refractive index between Ta2O5 and SiO2 was slightly higher than between the lipid and the aqueous layers, yet it was a best match among choices of materials that mimic the lipid and aqueous layers, and it is representative. The coating of SiO2 on top of BaK2 is a good match in refractive index difference to that of the aqueous layer on the corneal layer. Conservative uncertainties of the two layer thicknesses were within 2% of the thicknesses set by the manufacturing process. The thicknesses were measured at the coating facility with a Perkin Elmer Lambda 1050 thickness measurement unit. Ground truth was provided to be 67.3 ± 1.3 nm and 1015.6 ± 20.3 nm, for the lipid layer and the aqueous layer phantoms, respectively.

| Material               | Refractive index (@589nm) |
|------------------------|---------------------------|
| Lipid                  | 1.4820 ± 0.0004 [21]      |
| Aqueous                | 1.3371 ± 0.0015 [22]      |
| Corneal epithelium     | 1.401 ± 0.005 [20]        |
| Ta2O5                  | 2.11211 ± 0.00005         |
| SiO2                   | 1.46964 ± 0.00005         |
| BaK2                   | 1.53989 ± 0.00005         |

3.4 Validation at a single point

For the experimental application of the SDT-OCT approach, we first conducted measurements at a single point on the phantom. The phantom was accurately positioned in the sample arm using an optical length that matched between the reference and sample arms. The
reference arm was then blocked for the rest of the experiment, while using the air-phantom interface as reference to minimize the effects of environmental vibrations. The exposure time was set to be the limit imposed by the line-camera of 20 µs. The measured spectrum (an array with 8192 elements) was captured at the center of the phantom and used as the input to the ML estimator. Figure 5 shows the simultaneous estimation of thicknesses for both layers using the ML estimator. In Fig. 5(a), the false color represents the negative conditional log-likelihood that one measured spectrum is generated by different possible lipid and aqueous layer thicknesses. Figure 5(b) is the top view of the conditional-log likelihood shown in Fig. 5(a), where the horizontal axis and the vertical axis represent sets of lipid layer thickness and aqueous layer thickness, respectively. The dual estimates are determined by the coordinates associated with the minimum value. Figures 5(c) and 5(d) show the profile of the log-likelihood of the two lines passing across the minimum in Fig. 5(b). The estimates were found to be 67 nm and 1.015 µm for the lipid and aqueous layers, respectively. Considering Fig. 6, the blue curve shows one instance of the recorded spectrum from the phantom, while the red curve in that figure is the predicted mean spectrum by plugging the estimates shown in Fig. 5 into the mathematical model associated with the estimator.

Fig. 5. (a) Conditional log-likelihood that one measured spectrum is generated by different lipid and aqueous thicknesses; (b) Top view of the conditional log-likelihood in (a); (c) Conditional log-likelihood along the black line in (b) and the lipid layer thickness estimate; (d) Conditional log-likelihood along the red line in (b) and the aqueous layer thickness estimate.
To quantify the repeatability and robustness of the estimator, we repeated the measurements 2000 times at the center point of the phantom. The measured thicknesses were found to be $66.8 \pm 0.8$ nm and $1012.3 \pm 3.7$ nm, respectively, which is within the uncertainty boundaries given by the ground truth. Results show that the ML estimator is robust and achieves nanometer precision, as was predicted in [16,17] for the single layer sample and now extended to two layers. It is noteworthy that the lipid layer thickness estimates are more precise compared to those of the aqueous layer. The reason for this difference is that the refractive index change in the lipid layer phantom is larger compared to that of the aqueous layer phantom. The greater the refractive index change, the stronger is the layer interface, yielding more precise measurement of the thickness estimation task.

3.5 Thickness maps measurement

After validating the ML estimator at a single point, we applied telecentric scanning on the phantom to get the associated 2D thickness maps. Data were acquired in a 3 mm by 3 mm area with 300 by 300 sampling points (see Fig. 7). To make maximum use of the 20 µm lateral PSF of the system, the data points were acquired with 10 µm sampling step. Figure 7(a) shows the structure of the phantom. The measured thickness maps are shown in Fig. 7(b) and 7(c). The mean thicknesses of the measurements across the imaged area are 67.7 nm and 1006.0 nm for the lipid layer and aqueous layer, respectively, which are consistent with the values set by the manufacturing process. To test the repeatability of the measurements on different locations of the phantom, we repeated the measurements of thickness maps five times. The standard deviation distribution of the measurements are shown in Fig. 7(d) and 7(e), which shows that the repeatability of the ML estimator is invariant as we scan over the sample.

The acquisition time for each A-scan was 26 µs (i.e. integration time and readout time combined), which is the limit of the line period of the camera, yielding 2.34 seconds for acquiring the thickness maps shown in Fig. 7(b) and 7(c). In the case of the tear film thickness estimation, less dense samplings in order to operate at higher speed will be investigated. Provided the tradeoff between imaging speed and the lateral sampling step, as an example, 27 thickness maps per second can be acquired when sampling a 3 mm by 3 mm area with a 80 µm sampling step, yielding video rate recording of the tear film dynamics.
4. Discussion

4.1 Impact of uncertainties of refractive indices

In the SDT-OCT framework developed and validated with a physical phantom, we accounted for all sources of noise in the imaging chain. It is worth noting that in OCT, the refractive index and the physical thickness are coupled by a product that is the optical path length (OPL). Thus in estimating thickness from OCT measurements, we also need to account for the uncertainties in index of refraction of the materials. For a given uncertainty of $\Delta n$ in the refractive index, the uncertainty to the thickness estimation is given as

$$\Delta d = \frac{OPL}{n^2} \Delta n.$$  (9)

Equation (9) is used to evaluate the impact of the refractive index uncertainties. For the lipid layer of the phantom, the OPL is on the order of 100 nm and the refractive index uncertainty is 0.00005 as provided at manufacturing, yielding an uncertainty in thickness estimation due to refractive index in the order of 0.001 nm. For the aqueous layer of the phantom, which has an OPL in the order of microns and a refractive index uncertainty of 0.00005, the uncertainty in thickness estimation due to refractive index is in the order of 0.01 nm. However, as shown in Table 1, the uncertainties of the tear film refractive indices are greater than those of the materials used in the phantom. The impacts on the thickness estimation, due to the uncertainties of refractive index of tear film components, are evaluated to be in the order of 0.01 nm and 1 nm for the lipid layer and aqueous layer, respectively. This investigation shows that the uncertainty in thickness estimation due to refractive index is within the precision of the system.

4.2 Performance across the tear film thickness range

In the context of tear film thickness estimation, the thickness of the lipid layer ranges from 20 nm to 150 nm, while the thickness of the aqueous layer is in the order of microns. To investigate the performance of the ML estimator across these thickness ranges, we adopted a
simulation approach, in which we set the ground truth of the lipid and aqueous layer thicknesses. In the simulation, we also took into account the roughness interface between the aqueous layer and the corneal surface, which was studied to be 129 nm in terms of the standard deviation of the surface height [18]. For a given ground truth of tear film thicknesses, the mean and the variance of the output spectra from the OCT system were simulated using Eq. (5) and Eq. (8), respectively. The mean and the variance of the spectra were then input to a Gaussian random number generator, which represented the normal distribution in Eq. (4), to generate one instance of the simulated spectra. The simulated spectrum was then input to the ML estimator, from which the outputs were thickness estimates. For each given ground truth, 2000 simulated spectra were generated to evaluate the RMSE of the estimates. The ground truths of the thicknesses were then varied to investigate the performance of the ML estimator across the tear film thickness range. Results are shown in Fig. 8, which show that the ML is an unbiased estimator with precision < 5 nm for the lipid layer and < 20 nm for the aqueous layer.

4.3 Processing speed

The bottleneck of the current work is the post processing time. At this time, all the post processing is done with MATLAB®, and it takes about 10 hours to calculate the thickness maps shown in Fig. 7(b) and 7(c). The intensive computational task is to calculate the conditional log-likelihood distribution. Although we leveraged the parallel computing toolbox, the CPU computing is fundamentally limited by the number of cores available. In future work, we plan to leverage the GPU framework we recently implemented in our lab to significantly speed up the post processing time and allow for real time visualization of thickness maps [23].

Fig. 8. Estimation accuracy and precision for different thickness of (a) the lipid layer and (b) the aqueous layers.

5. Conclusion and future work

In this study, we demonstrated an SDT-OCT instrument that combines a custom 1 µm axial PSF (FWHM) spectral domain OCT setup with statistical decision theory, to enable simultaneously estimation of dual layer thicknesses to nanometer scale. To establish a ground truth for the purpose of validation, we built a double-layer phantom to mimic the layer structure of the tear film. We then imaged this phantom at both a single point and across a 3mm by 3mm area. Results show that the ML estimator is a robust estimator that achieves nanometer scale measurements with nanometer precision. In future studies, we will translate the SDT-OCT technique presented in this paper to a clinical setting for human subjects research. We are currently investigating some practical issues for human subjects imaging, such as the effect and control of involuntary eye motion, as well as the ability to scan...
perpendicular to the cornea to compensate for the curvature of the cornea that will be especially leveraged as we scan larger areas of the cornea, up to a 9 mm x 9 mm surface.

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