The amplitude and the phase or: Measuring directional and random motion with optical coherence tomography
Weiss, Nicolás

Citation for published version (APA):
Weiss, N. M. (2016). The amplitude and the phase or: Measuring directional and random motion with optical coherence tomography

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
CHAPTER 1

General introduction

This general introduction discusses the technical background of this thesis and the interrelations between the chapters.

A note to the reader: this thesis should be regarded as a bundle of in peer-reviewed published and (yet) unpublished scientific material. In principle, every chapter in this thesis is self-contained and can be read independently from the rest.

A time-dependent complex-valued scalar signal \( s(t) \) in its most general form can be written as the product of an amplitude term \( A(t) \) and a phase term \( \phi(t) \) as:

\[
s(t) = A(t)e^{j\phi(t)},
\]

where \( t \) is time and \( j = \sqrt{-1} \) is the imaginary unit. Interferometric signals, such as the signal measured by optical coherence tomography (OCT) can be described by the above mentioned mathematical relationship. Typically, OCT uses a low-coherence light source and a Michelson interferometer to measure path-length resolved backscatter profiles of samples with micrometer resolution and up to a few millimeters long. A schematic of a basic OCT imaging geometry is shown in Fig. 1.1. Light from the low-coherence source is directed towards a reference mirror and a sample via a beam splitter. After reflection and scattering from the mirror and sample, respectively, light is recombined via beam splitter in a detector. The measured interferometric signal is then further processed by a computer.

Two realizations of OCT exist: time-domain OCT and Fourier-domain OCT. In time-domain OCT the low-coherence interferometric signal is detected with a single photo-diode and the path-length resolved information of the scattering sample is obtained by scanning the reference arm of the interferometer. In Fourier-domain OCT, as the name already indicates, the path-length information is encoded in the spectrum of the interferometric signal. The OCT signal is calculated by means of a Fourier-transform of the interferometric signal, such that, the conjugate variables become wave-number and optical path-length. Two implementations are widely used: spectral-domain OCT and swept-source OCT. In both cases, the reference arm mirror is static and the path-length resolution is achieved by either spectrally resolving the interferometric signal with a diffraction grating (spectral-domain) or by spectrally resolving the interferometric signal in time using a wavelength swept laser (swept-source). Fourier-domain OCT has a signal-to-noise ratio advantage when compared to time-domain OCT and has therefore experienced wider application. In this thesis we will use the term OCT loosely and will refer, unless stated otherwise, to the swept-source OCT configuration.

---

1 Electrical engineers, such as the author, use \( j \) to represent the imaginary unit, since \( i \) is usually reserved to denote current. It is left to the physicist readers to replace \( j \) by \( i \), wherever they see fit.
Chapter 1. General introduction

The OCT amplitude $A(t)$ is typically used to generate images of the sample. An example of an OCT image of the author’s thumb is shown in Fig. 1.2. Additionally, the amplitude and the phase of the OCT signal can be used to extract quantitative sample information. For example, the OCT amplitude has been used to measure static sample parameters such as layer thickness [4], refractive index [5], birefringence [6], scattering and absorption coefficients [7], and scattering anisotropy [8]. In the case of a dynamic sample, the fluctuations of $A(t)$ can be used to measure flow [9] and diffusion [10]. In the medical field, OCT has been applied, e.g., to measure blood flow in the retina [11] and to visualize tumors [12].

The phase of the OCT signal $\phi(t)$ of static samples can be used to measure layer thickness and refractive index with improved resolution when compared to using the OCT amplitude [13]. Most notably, in the case of dynamic samples, the OCT phase carries information about the Doppler shift which is directly proportional to the scatter velocity component in the propagation direction of the imaging beam [14, 15].

The emphasis of this thesis lies in exploiting the information carried by the time-dependent OCT amplitude and phase to measure the directional and random motion of a sample. One way of quantifying the rate of change of the signal $s(t)$ is by calculating its autocorrelation function [16]:

$$g(\tau) = \int_{-\infty}^{\infty} s(t + \tau) s^*(t) \, dt,$$

where $\tau$ is the time-lag of the autocorrelation function and * denotes the complex-conjugate operation. The autocorrelation function quantifies the resemblance of a signal with a time shifted copy from itself. Basically, each value of the autocorrelation function is calculated as a summation over $t$ of products of the signal $s(t)$ with a time-shifted version of itself $s(t + \tau)$. For non-periodic signals, the autocorrelation function $g(\tau)$ will decrease in amplitude for increasing values of $\tau$ [17]. An example
Figure 1.2: Two-dimensional image of the OCT amplitude of data from the author’s thumb where the fingerprint ridges, the dermis, and the epidermis can be clearly seen.

of the variations of the OCT amplitude and its autocovariance function is shown in Fig. 1.3 for a suspension of flowing polystyrene spheres. Figure 1.3(b) shows a faster decay rate for the black signal when compared to the red signal. The autocorrelation function for the red signal at a particular time point is larger than the autocorrelation function for the black signal. In this particular case, the measured amplitude fluctuations originate from the sample dynamics (flow and diffusion) inside the OCT imaging volume and measurement noise. The relation between the decay rate of the autocorrelation function and the sample dynamics will be treated later in this thesis.

Scope of this thesis

In this thesis we report on the development, validation, and application of a model based on the OCT autocorrelation function to extract information about the dynamic parameters of a sample from the time fluctuations of the OCT amplitude and phase. The work presented in this thesis, first, extends the understanding of dynamic fluctuations on the OCT amplitude and phase; and second, it opens up new opportunities and applications of OCT for the study of a range of rheological properties in complex dynamic geometries.

Outline of this thesis

The outline of the thesis is as follows: in Chapter 2 we report on a model for the measurement of flow and diffusion based on the OCT autocorrelation function. The model is validated with a simple flow system and shows that both the longitudinal and the transverse flow velocity components can be accurately measured at micrometer scale and in a single measurement. In Chapter 3 the results of the previous chapter are extended for the simultaneous measurement of flow and diffusion. We

2The difference between the autocovariance and the autocorrelation here is the subtraction of the mean of the signal $\int_{-\infty}^{\infty} (s(t + \tau) - \mu)(s^*(t) - \mu^*)\,dt$, with $\mu$ the mean.
Figure 1.3: (a) Normalized OCT amplitude for a suspension of polystyrene spheres flowing at two different velocities; and (b) the corresponding autocovariance functions.

also report on the limitations of the model with respect to the accuracy and precision of the individually estimated dynamical parameters. Most interestingly, we show experimentally that the decay of the Gaussian transverse flow term in the OCT autocorrelation function depends only on the beam radius at the focus and not on the local Gaussian beam radius. Based on the understanding gathered in the previous two chapters, we present three applications. First, in Chapter 4 we apply the OCT autocorrelation analysis to the measurement of biofilm growth and local flow velocities in a microfluidic channel. Second, in Chapter 5 we report on a method to correct for non-uniform lateral scanning of a sample in OCT. We show that based solely on the information carried by the phase of the OCT signal, the non-uniform trajectory of a sample can be reconstructed. We also demonstrate centimeters-long hand-held OCT imaging of the skin of the forearm. And third, in Chapter 6 we report on a method to measure the height profile of non-scattering soft (biological) samples in liquid environments using a combination of optical tweezers and OCT. We achieve this by using the phase of the OCT signal to measure the sub-micrometer displacements of an optically trapped sphere. Finally, in Chapter 7 we present the conclusions and in Chapter 8 we discuss possible future research directions.

In the Appendices of this thesis a collection of material is presented that deviates somewhat from the contents presented in the previous chapters. In Appendices A-C we present three approaches to achieve a broader spectrum of applications of OCT by reducing the form factor and cost of OCT systems based on integrated optics. We designed, fabricated, and characterized an integrated-optics-based swept-source optical coherence tomography system in TriPleX, silicon, and silicon oxynitride technologies. An external 1300 nm swept source is coupled to the chip, which contains waveguide structures for interferometric path-length ranging. In all three technologies, we demonstrate cross-sectional OCT imaging of a multilayered tissue phantom.

3The results presented in the Appendices were obtained using the swept-source OCT system build by the author that was used in all the other chapters of this thesis.