Diffusion-sensitive Fourier-domain optical coherence tomography

M. Hagen-Eggert[1], D. Hillmann[3], P. Koch[3], G.Hüttmann[2]

[1]Medical Laser Center Lübeck, Germany
[2]Institute of Biomedical Optics Lübeck, Germany
[3]Thorlabs GmbH Lübeck, Germany

ABSTRACT

Diffusion-sensitive optical coherence tomography (DS-OCT) is presented as a functional extension to OCT. Fluctuations of signal intensity and phase, which are caused by Brownian motion, are analysed by an autocorrelation function similar to dynamic light scattering measurements. Based on an ultra-fast Fourier-domain OCT, DS-OCT can determine quantitatively diffusion properties with high depth resolution, e.g. the hydrodynamic diameter of colloidal suspensions .
Performance of DS-OCT is demonstrated with polystyrene particle suspensions and compared to conventional DLS measurements. Applications for DS-OCT may be found in the measurement of particle size distributions of inhomogeneous samples or measurements of diffusion properties at boundary surfaces. Additionally, the method has the capability to become a useful benefit in clinical diagnostics, especially in ophthalmology, where the molecular compositions and pathological changes of anterior eye components could be detected.

Keywords: optical coherence tomography, dynamic light scattering, brownian motion, diffusion constant

1. INTRODUCTION

Optical coherence tomography is a coherent imaging modality which is sensitive to sub-micrometer movements of tissue structures. This is exploited by Doppler imaging,[1] OCT elastography,[2] magnetomotive contrast OCT,[3] and photothermal OCT.[4] But not only directional movements also Brownian motion in the sample can lead to fluctuations of the OCT amplitude and phase.
Interference of scattered light is also used by dynamic light scattering (DLS), which is quite a common technique for measuring diffusion properties of colloidal suspensions. The diffusion constant, the solvent viscosity or the hydrodynamic diameter are quantitatively determined for particles in the range of a few nanometers to a few micrometers. The technique is based on measuring the intensity fluctuations of scattered light caused by the Brownian motion from a suspension of particles. By autocorrelation analysis of the recorded fluctuations and by fitting the data to a statistical model diffusion properties of the colloid are determined. Simply speaking the faster the fluctuation-rate the smaller the diffusing particles or the lower the viscosity. The size range of particles which can be measured by a DLS system is limited for small diameters by the sample-rate of the detector and for large particles sizes by the measurement time.
For high scattering conditions or inhomogeneous samples the combination of low-coherence-interferometry (LCI) and DLS, which significantly reduces the sampling volume and enables spatially resolved measurements, was demonstrated.[5] By mechanically moving a reference reflector, which corresponds to a Time-domain OCT (TD-OCT) set-up, even depth-resolved data acquisition was demonstrated.[6]
Nowadays commercially available Fourier-domain OCT (FD-OCT) systems have reached A-Scans rates higher than 200 kHz[7,8] and are thus fast enough for a combination of DLS and FD-OCT, which would significantly improve the SNR compared to the combination with TD-OCT. We demonstrate that ultra-fast spectrometer-based OCT can be used for quantitative, depth-resolved measurements of particles sizes ranging from 20 nm to a few μm. Aggregation and segmentation can be followed with sub-second time resolution. With the possibility to make spatially-resolved measurements of the diffusion properties we now present a novel diffusion-sensitive contrast method (DS-OCT) which could be used as a functional imaging extension to OCT imaging.

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2. THEORY

2.1 Basic principle of dynamic light scattering

The measurement principle of dynamic light scattering is based on the Brownian motion of colloidal suspensions. If the sample is irradiated with a laser, interference of the light scattered by the diffusing particles results in a fluctuating intensity on the detector. Similar to OCT the implementation of a separate reference arm in the interferometric or heterodyne DLS system reduces detector noise (Fig. 1).

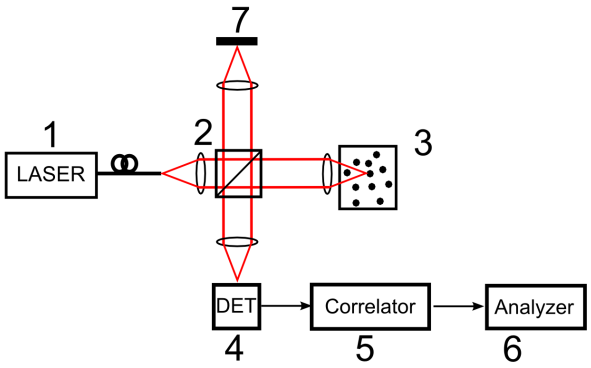


Figure 1: Schematic heterodyne DLS set-up with: Laser light source (1), focusing optics (2), a reference reflector (7), the sample suspension (3), the detector (4), a correlator (5) and a data analysing unit(6)

The autocorrelation of the recorded fluctuations carries information about the diffusion properties of the sample. For Brownian motion the autocorrelation $G(\tau)$ can be described by an exponential function:[9]

$$G(\tau) = A\left[1 + B\exp\left(-2\Gamma\tau\right)\right]. \tag{1}$$

Here τ is the delay time and A and B are two constants. The decay constant Γ is directly connected to the diffusion constant D and the scatter angle θ:

$$\Gamma = D\left[\frac{4\pi n}{\lambda_0}\sin(\frac{\theta}{2})\right]^2 \tag{2}$$

where λ_0/n is the wavelength of the irradiation in the solution. By the Stokes-Einstein equation the diffusion constant D can be related to the temperature T, the viscosity η and the hydrodynamic diameter d_h of the suspended colloids:

$$d_h = \frac{kT}{3\pi\eta D} \tag{3}$$

2.2 Diffusion-sensitive Fourier-domain OCT

For DLS measurements with a spectrometer based FD-OCT M-scans, i.e. a certain number of A-scans from the same point at a fixed A-scan rate, were measured. For each depth z the complex values of the M-scan (i.e. amplitude and phase) were autocorrelated. The depth-dependent correlation function $G(\tau, z)$ was then fitted to a single exponential function and D and d_h can be calculated according to eq. 2 and 3.

3. EXPERIMENTAL SET-UP

Figure 2 schematically shows the experimental setup for DS-OCT. It consists of a high-power SLD module ($\lambda_0 = 840$ nm, BLM-S-840-B-I-20, Superlum) with an output power of 20 mW, an ultra-fast spectrometer-based OCT (Hyperion, Thorlabs GmbH, Lübeck, Germany) and a fast PC for the data processing. The spectra of the interference of sample and reference irradiation were measured with 1024 pixel at 127 kHz. Typically 250,000 A-scans were collected over 2 s for determining the hydrodynamic particle diameter.
As measurement probe a fiber with a FC-PC connector, for which the polished fiber end worked as the reference mirror, or specially designed miniature interferometer[10] were used. For measurements of 2-dimensional images the sample was moved transversely with a linear translation stage (M-125.11, Physics Instruments).

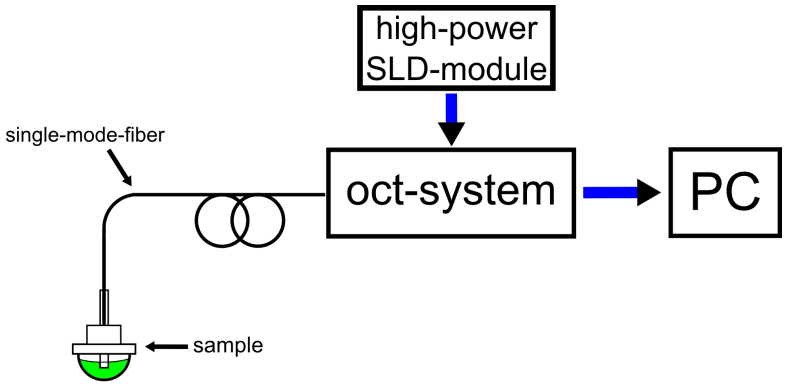


Figure 2: Schematic set-up for diffusion-sensitive oct

4. RESULTS

4.1 Comparison of DS-OCT with DLS

Diffusion-sensitive OCT (DS-OCT) was compared to a conventional DLS device (Malvern Zetasizer) by measuring suspensions of different sized polystyrene nanoparticles (20 nm, 100 nm, 200 nm and 1000 nm). The measuring time of DS-OCT was about two seconds, whereas the measuring time of the DLS device was in a range of minutes. DS-OCT could measure the hydrodynamic diameter with good precision in shorter time (figure 3).

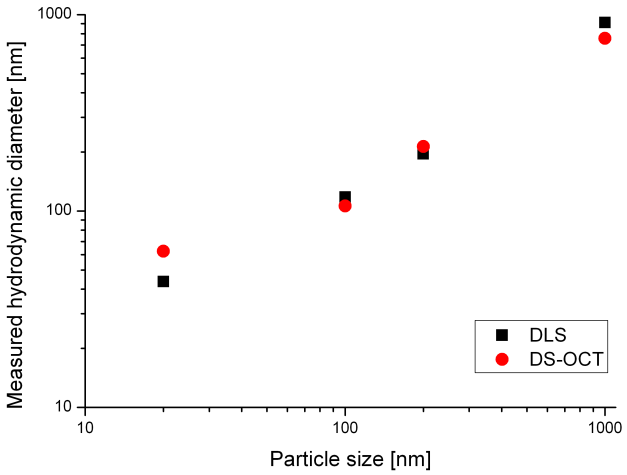
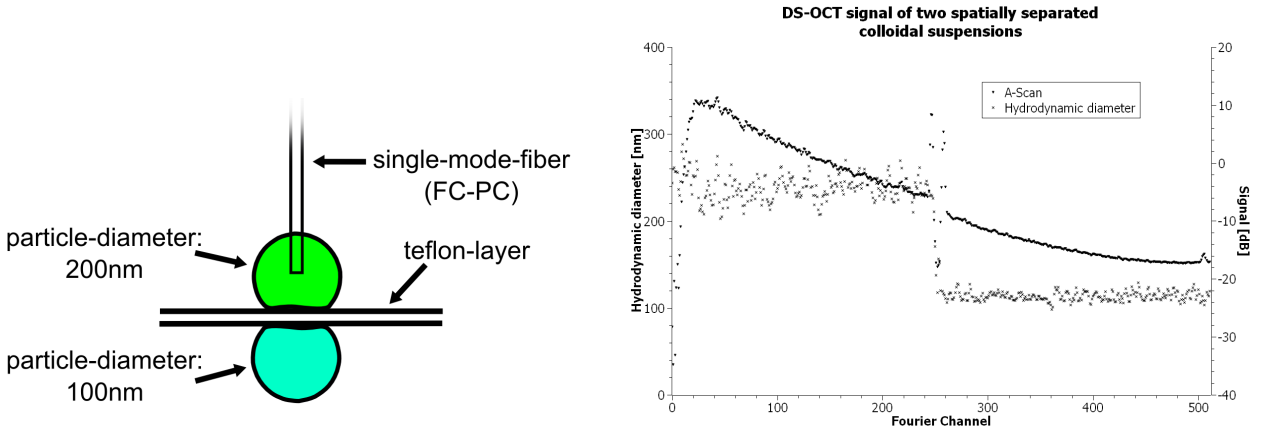


Figure 3: Comparison of DS-OCT with a commercial DLS device. Polystyrene particle suspensions with different sizes (20 nm, 100nm, 200nm and 1000 nm) were measured.

4.2 Measurement of spatially separated suspensions

An experiment with two homogeneous suspensions of polystyrene particles of different diameters (100 nm and 200 nm), which were spatially separated by a PTFE membrane of 25 μm thickness, demonstrates a depth-resolved measurement of the particle diameters. Figure 4(a) shows the probe set-up. The results of this experiments are shown in figure 4(b). The A-scan which shows the amount of backscattering can not distinguish the different particles, because the difference in scattering is compensated by different particles concentration. The depth depended hydrodynamic diameter which was calculated from the signal fluctuations clearly differentiated the two particle species. The peaks in the A-Scan in the middle of the measurement range were caused by the surface of the PTFE-membrane.



(a) (b)

Figure 4: Probe for the measurement of spatially separated suspensions (a); The results of the measurement (b) show the A-scan and the hydrodynamic diameter (x-dotted plot) as a function of depth

DS-OCT was also able to monitor the separation of a mixture of different sized particle suspensions (polystyrene particles, diameters: 100 nm and 1000 nm) by sedimentation. Directly after mixing both particle species an average particle diameter, which was independent from the depth, is determined. At the surface (lower measurement depths), over time the calculated diameter decreases and eventually reaches 100 nm whereas the particle diameter at the bottom of the sample (higher measurement depths) increases above 500 nm (see figure 5 x-dotted plots). The larger particles sediment faster, so that the average particle size shows a strong gradient with depth.

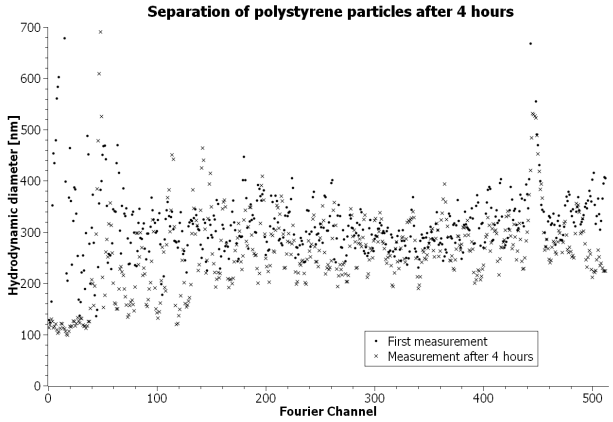
4.3 DS-OCT as a functional extension to OCT

To demonstrate the capability of DS-OCT as a functional imaging extension to OCT imaging the B-Scan of a common ivy leaf was acquired. The sample was moved transversely in steps of 20 μm between each data acquisition. Figure 6(a) pictures the averaged A-scans of each data acquisition combined to a B-scan.

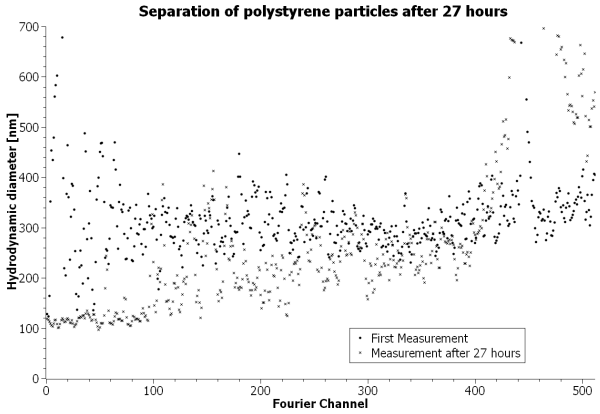
In figure 6(b) the depth-dependent decay-constant Γ (see eq. 1) which is proportional to the hydrodynamic diameter (diffusion constant) for each measurement location is shown. In comparison to the OCT B-scan one can detect the surface of the leaf and several structured layers at higher depths. Due to the unknown molecular composition and the cellular structure of the leaf it is not possible to calculate the an exact hydrodynamic diameter or other diffusion parameters from the measured data, but the spatial-dependent variation in the decay-constant gives a contrast which can be used as an imaging modality.

5. SUMMARY

Spectrometer-based Fourier-domain OCT is now fast enough to resolve the intensity and phase fluctuations which are caused by the diffusion of nanoparticles. DS-OCT provides a new functional extension to OCT which measures quantitatively the diffusion properties of nanostructures, like the hydrodynamic diameter of colloidal suspensions or the viscosity of the solvent.



(a)



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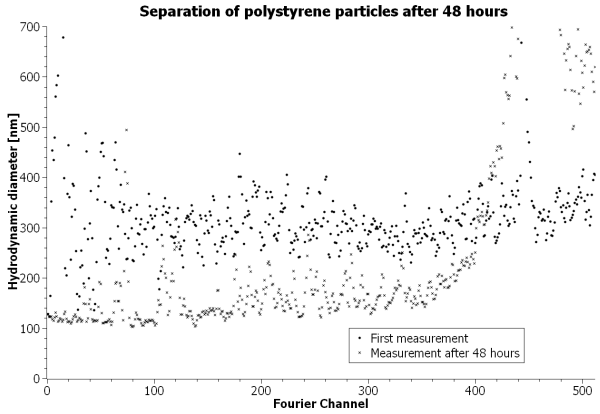
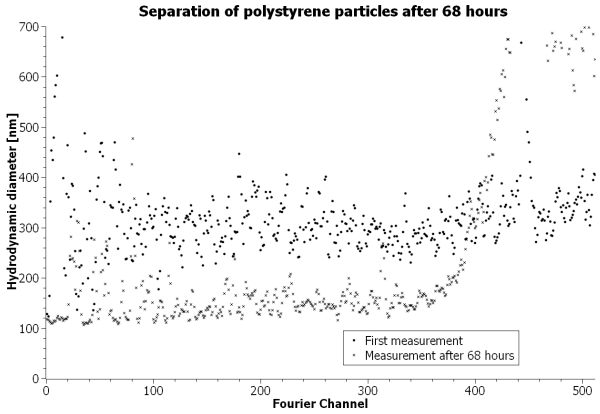
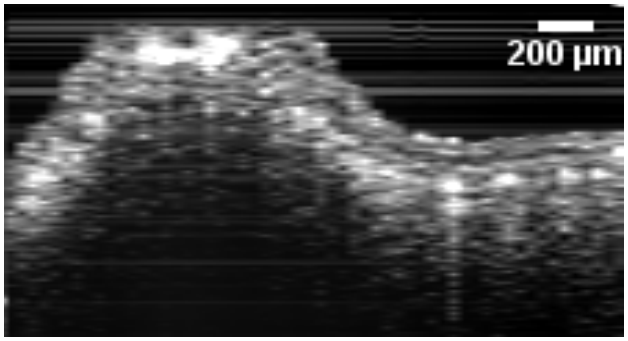


(c)

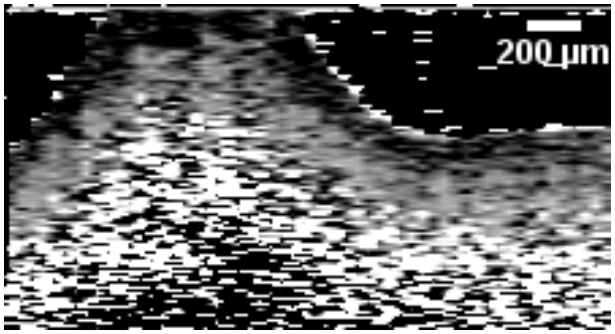


(d)

Figure 5: Measurement of the separation of two suspensions after 4 (a), 27 (b), 48 (c), 68(d) hours



(a)



(b)

Figure 6: B-Scan (a) and diffusion-sensitive B-Scan (b) of an ivy leaf (size: 224x120)

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