The amplitude and the phase or: Measuring directional and random motion with optical coherence tomography
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CHAPTER 8

Outlook

Figure 8.1: (a) Scanning electron microscopy image of the dehydrated biofilm grown during the experiments reported in Chapter 4. (b) Zoomed-in view of the biofilm and the attached tracer particles. Images courtesy of K. El Tayeb El Obied, University of Twente.

In this thesis we have developed, validated, and applied a model based on the autocorrelation function of the OCT signal to measure the dynamics of a sample. Besides the limitations and advantages of the autocorrelation function discussed in those chapters, one additional drawback of this approach is the relatively long measurement times required. The minimum length of time that the OCT signal is to be acquired is determined by the upper limit of the time decay rates of the autocorrelation function. This, in turn, is determined by the slowest dynamic process in the sample. For a colloidal suspension, this is given by the Brownian motion of the particles. More precisely, for the samples measured in this thesis, this was in the order of 1.5 to 3 ms. However, in practice, the OCT signal is acquired longer to perform averaging and to increase the signal-to-noise ratio of the measurement (e.g., 200 ms in the experiments described in Chapter 3). For applications with time constraints, such as in-vivo measurements or for the biofilm application presented in Chapter 4, a shorter measurement time is preferable. To illustrate this, in Fig. 8.1 we show scanning electron microscopy images of the dehydrated biofilm grown during the experiments reported in Chapter 4. Figure 8.1(a) shows the microfluidic channel and the biofilm and Fig. 8.1(b) shows at higher magnification more details of the biofilm surface. The small spheres visible on the biofilm surface (diameter $\sim 0.2 \mu m$) are tracer particles that attached to the biofilm’s surface in the course of the experiment. Based on these images it becomes clear that, if one is solely interested in studying
biofilm growth, the interaction with the tracer particles is to be kept to a minimum. In this Outlook chapter we report on three possibilities to achieve this.

The first approach is straightforward and is to reduce the tracer concentration to minimize the number of tracers interacting with the biofilm. However, this would reduce the signal-to-noise ratio of the OCT measurement and therefore, assuming constant measurement time, increase the influence of noise in the autocorrelation function. In Fig. 8.2(a) we show how the amplitude of the OCT signal increases with increasing tracer concentration. The increase of noise due to a reduction in signal-to-noise ratio at the high frequencies of the power spectral density is shown in Fig. 8.2(b). A detailed treatment of the effect of noise on the OCT autocorrelation function can be found in Ref. [58].

The second approach is to reduce the total measurement time by reducing the number of time samples used to calculate the time lags of the autocorrelation function. A reduction in the amount of time that the tracers are present in the channel, will reduce their total interaction with the biofilm. At this point, we re-visit the definition of the autocorrelation function of Chapter 1 in its time discrete form:

$$g(m) = \sum_{n=0}^{N-m-1} s(n + m)s^*(n), m \in [0; N),$$

where $m$ is the discrete time lag, and $N$ is the total number of time lags. If we assume here for simplicity of the argument that $N = 4$, then we can write the individual

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1 The power spectral density is the Fourier transform of the autocorrelation function [16].

2 Note that we have only written here the expression for positive time lags, however, by symmetry of the autocorrelation function, $g(-m) = g(m)$, for all time lags $m$ [16].
Figure 8.3: Autocovariance function of the amplitude of the OCT signal for a flowing suspension of polystyrene spheres. (a) and (b) show data for two different flow velocities. The solid line shows the autocovariance calculated using 1000 time uniform samples and the dots show the autocovariance calculated using a Golomb ruler with 12 non-uniform time samples. Note that averaging was the same for both cases.

terms of the autocorrelation function as:

\[ g(0) = s(0)s^*(0) + s(1)s^*(1) + s(2)s^*(2) + s(3)s^*(3), \]
\[ g(1) = s(1)s^*(0) + s(2)s^*(1) + s(3)s^*(2), \]
\[ g(2) = s(2)s^*(0) + s(3)s^*(1), \]
\[ g(3) = s(3)s^*(0). \]

It becomes clear now that, for all time lags \( m \leq N - 2 \), a single autocorrelation value \( g(m) \) is calculated as the sum of all possible realizations of the particular time lag \( m \). Here, with the aim of reducing the total measurement time, we propose to drop the redundancy in the calculation of the autocorrelation function by choosing a reduced subset of time sample in \([0;N]\). Continuing with the previous example for \( N = 4 \), we write all four terms of the autocorrelation function \( g \) by using only the time discrete samples with index \( \{0,1,3\} \):

\[ g(0) = s(0)s^*(0) + s(1)s^*(1) + s(3)s^*(3), \]
\[ g(1) = s(1)s^*(0), \]
\[ g(2) = s(3)s^*(1), \]
\[ g(3) = s(3)s^*(0), \]

such that the signal value at \( s(2) \) is not used. The time indices given by vector \( \{0,1,3\} \) is called a Golomb ruler [97]. Golomb rulers provide a scheme to sample the autocorrelation function uniformly, based on a non-uniform time sampling of the underlying signal. Golomb rulers have been applied previously to radar applications [98] and radio astronomy [99] and we have applied them here to calculate the OCT autocorrelation function based on a reduced number of time samples of the OCT signal. Figure 8.3 shows a plot of the OCT autocovariance data of a flowing suspension of polystyrene spheres for two different velocities calculated using 1000
Chapter 8. Outlook

Figure 8.4: (a) Lay-out of a parallel OCT chip with 8 sample channels based on Y-splitters (image and design by LioniX BV). (b) Microscope image of the parallel OCT chip fabricated on TriPleX technology with light coupled from a 635 nm laser. (c) Normalized OCT amplitude measured using the first four channels of the parallel OCT chip and a mirror as a sample.

(uniformly sampled) time samples of the OCT amplitude (solid line) and calculated using a Golomb ruler using 12 (non-uniformly sampled) time samples of the OCT amplitude. The data is taken from a data set acquired in the experiments reported in Chapter 3. As expected from the lack of redundancy (averaging) in the individual terms of the autocorrelation function the data calculated using the Golomb ruler is noisier but is, nonetheless, in good agreement with the data calculated using the uniform time samples.

The third approach is based on measuring multiple lateral sample points simultaneously and therefore reducing the total time required to measure a sample. Typically, OCT generates path-length resolved measurements in the propagation direction of the imaging beam. A swept-source OCT system, as described in this thesis, produces 544 path-length (or depth) measurements simultaneously at a rate of 50 kHz. However, the imaging area in the plane perpendicular to the propagation direction of the imaging beam is given by the diameter of the (Gaussian) imaging beam which is typically in the order of 10 to 20 μm. If a larger scan area is needed, then the imaging beam is typically scanned with a galvanometric mirror. This results in a sequential acquisition of the different sample points in the transverse direction. An alternative to this approach would be to have a plurality of OCT sample arms scanning different points of the sample simultaneously. Although a conventional fiber-based OCT system would be unsuitable due to space and cost constraints, integrated optics-based-OCT presents a promising alternative [101]. In Appendices A-C we report on three different approaches for an integrated-optics-based OCT interferometer, based on TriPleX, silicon, and silicon oxynitride technologies. The extension of these approaches to accommodate a plurality of sample arms in combination with dynamic sample parameter estimation is a promising topic for future research. As a proof-of-concept we show in Figs. 8.4(a-b) a parallel OCT chip

For the interested reader, the optimal Golomb ruler of length 12 and order 85 used for Fig. is: \{0,2,6,24,29,40,43,55,68,75,76,85\} and was taken from Ref. [100].
design based on integrated optics. The chip consists of 8 sample channels realized with Y-splitters. The signal of each sample channel is separated by introducing an increasing path-length delay between the individual sample channels. Figure 8.4(c) shows the response of the first 4 OCT sample arms to a mirror sample. The distance between the different signal peaks corresponds to the on-chip length difference of the individual waveguides.

**The amplitude and the phase: Developments beyond this thesis**

From an experimental point of view, the range of applications of the developed approach for the OCT autocorrelation function are not restricted to the few cases presented in this thesis. Recently, other research groups have applied the OCT autocorrelation to measure red-blood cell flux in capillary networks [102], to image *in-vivo* stroke injury [103], to measure Cilia driven flow [104], to correct for rotational distortion in catheter-based OCT [105], to measure viscosity in middle ear effusions [106], and to measure microfluidic volumetric flow [107].

From a theoretical point of view, the relatively simple model presented in Chapter 2 has been further developed to resolve the directional ambiguity in the determination of the transverse flow velocity [57], to achieve improved velocimetry using a Bayesian approach [108], to include the influence of noise [58], to include the influence of the imaging optics [109], and to include explicitly the theoretical relation between the longitudinal velocity gradient and the autocorrelation function [110].