Microfluidic volumetric flow determination with Optical Coherence Tomography

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Abstract: We propose a methodology for OCT signal autocorrelation analyses to access volumetric flow rate, based on decorrelation time. We shows that this technique could distinguish flows with 3 µl/min resolution, only limited by system speed acquisition. We performed a B-Scan of gradient flow in a cross section of microchannel, generating an image of walls drag effect.

Key-Words*: microfluidics, optical coherence tomography, speckle analysis*

Introduction: Optical Coherence Tomography (OCT)[1] is a noninvasive, contactless imaging technique based on white-light interferometry that generates high resolution, cross-sectional images of scattering media. This images provide morphological information about internal structures of samples. The micrometer-resolution, aligned with its penetration depth places OCT in an unique spot among other imaging modalities[2-4].

Studies demand a morphological and functional characterization one of them is the Doppler OCT[5,6], which measures the frequency shift in scattered light of moving particles, but has low sensitivity to flows perpendicular to the imaging beam.

In OCT, even using a low coherence light sources, speckle arises as a consequence of the phase sensitivity to the cross correlation between the sample and reference optical fields[7], and in OCT, speckle is not limited only to the surface, the pattern that arises from inside the sample provides information about flows. The light travelling through the sample accumulate phase delays due to multiple scattering originating the speckle patterns. That pattern is dependent of individual scatterers causing the phase delays, then depending on such scatterers being static or moving. Different speckle analysis methods have been proposed to discern between the two scenarios using the speckle variance (SV) approach [8,9].

Our approaches the problem differently, using a hybrid method through a straightforward analysis of the autocorrelation decay, giving enough information to evaluate changes in observed flow, based on the autocorrelation method proposed by Wang and Wang[10] with a new estimator model, getting better results in both, fast and robust ways.

The speckles originating from moving scatterers are expected to have larger fluctuations of intensity over time than arising from static ones [11], these intensity fluctuations pattern are correlated for a shorter period of time when compared to the "static" one.

The proposed analysis consists in recording the intensity of speckle at a given fixed point in very short time intervals, such intensities are obtained from A-scans and the autocorrelation time is analyzed.

After N A-scans are acquired consecutively in time for a given sample point, no beam scanning or sample translation, a point p in a determinates depth is selected and all A-Scans acquired, enabling its temporal analysis. The normalized autocorrelation R can be written as:

$$R(p,\tau) = \frac{\sum_{t=1}^{N-\tau}\left(I_{p,t\Delta} - \mu\right)\left(I_{p,t\Delta+\tau\Delta} - \mu\right)}{\sum_{t=1}^{N}\left(I_{p,t\Delta} - \mu\right)^2}, \quad (1)$$

with $I_{p,t}$ being the intensity of the point p at given time t; τ is a lag interval, and Δ is 1 divided by our sampling rate. For each point, its temporal average μ is subtracted.

Calculating R for different lag intervals results in an array of the autocorrelation values that represent the speckle behavior in time. At zero lag the autocorrelation is expected to be total, R=1, as the time lag increases those values should drop to zero "decorrelates". The rate at which that decrease occurs is the parameter for this analysis, and can be used as a simple observation parameter, such as the time it takes for the autocorrelation to decay to a predefined value.

Experimental: A custom OCT system was, developed to achieve an adequate sampling rate. The light source used in the system is a frequency swept laser SL1325-P16 (Thorlabs, Newton, New Jersey, USA), with center wavelength of 1325 nm, tuning range of 120 nm and repetition rate of 16 kHz, with a built-in Mach-Zehnder Interferometer (MZI). A Michelson type interferometer with balanced detection, INT-MSI-1300 (Thorlabs), suitable for wavelengths from 1250 to 1350 nm, was utilized. The output was coupled to an acquisition board NI PCI 5122 (National Instruments, Austin, Texas, USA). The system setup is illustrated in Fig. 1.

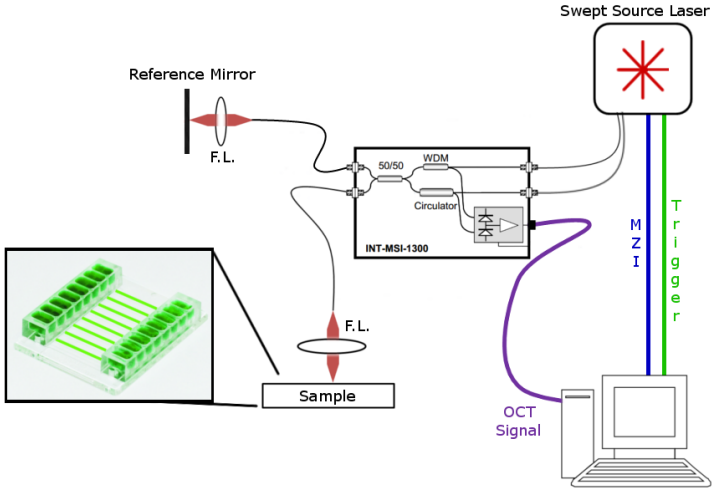

Fig. 1. OCT System setup illustration, with FL = Focusing Lens and WDM = Wavelength-division multiplexer. The inset shows the microfluidic device used in the tests.

A custom software was developed in LabVIEW (National Instruments) programming environment, it communicates and controls the PCI 5122 acquisition board that. handles three inputs: the trigger for the laser source, the OCT signal and a Mach-Zehnder Interferometer (MZI) signal, used for calibration.

The OCT interferometric signals are processed in A-Scans only after all acquisitions are performed. There is no lateral scanning for the laser beam. In order to acquire data of different lateral locations, the sample was placed on a servo motor translator TDC001 (Thorlabs). For flow studies, a microfluidic device Vena8 Fluoro+ (Cellix, Dublin, Leinster, Ireland), with 8 microchannels, each with a width of 400 µm, height of 100 µm and length of 2.8 cm, was used. To control the microflow on the Vena8 Fluoro+, the syringe pump ExiGo (Cellix) was utilized, with flow rate capability ranging from 10 nL/min up to 20 mL/min. Whole milk (3% fat) was used as sample.

Results and Discussion: With the aid of the syringe pump, the milk was subjected to different volumetric flow rates on the microchannel, and sampled at the rate of 8 kHz. The microfluidic device was positioned so that the flow was perpendicular to the imaging beam. The autocorrelation values array for a single point at the center of the microchannel was calculated over 1024 consecutive acquisitions in time. Such a procedure was repeated five times, and the arrays averaged. The resulting averaged array is plotted as a function of time lag.

In this experiment, the milk was pumped at volumetric flow rates: 1, 2, 3, 4, 5, 7, 10 and 12 µl/min. The procedure adopted averaging five autocorrelation arrays for each sample. Once again, only the first data points were plotted and, to enhance visualization Fig. 2.

Complying with the expected outcome, the “decorrelation” does occur faster with higher flow rates. After long delays, all the curves overlap at values close to zero, as all the signals decorrelate. But the decrease occurs in a much steeper fashion for higher volumetric flows. It follows that the autocorrelation of speckle does bear relation with the velocity of the moving scatterers inside a sample.

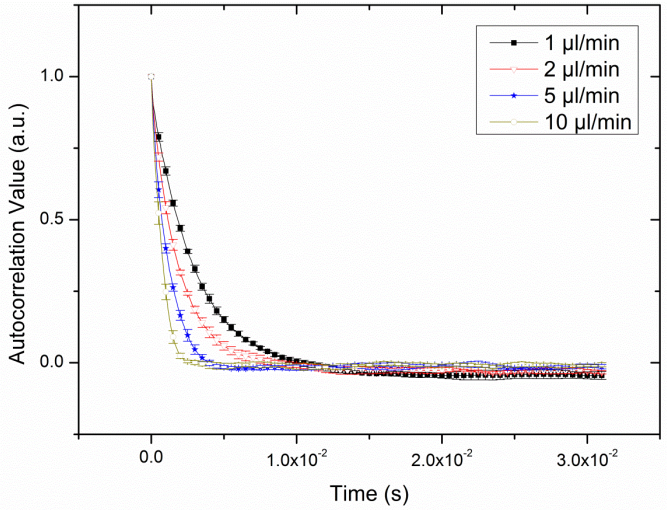

Fig. 2. Autocorrelation array for flows of 1 µl/min, 2 µl/min, 5 µl/min and 10 µl/min. Error bars are presented as +/- standard deviation.

We propose, therefore, a semiquantitative approach to differentiate the flow velocity, based on a simple analysis of the autocorrelation array, in order to be performed quickly. We established a "decorrelation time" as the time it takes for the autocorrelation values to drop below 1/*e*. One can, thereby, plot this decorrelation time as a function of volumetric flow, graph shown in Fig. 3, and observe its behavior.

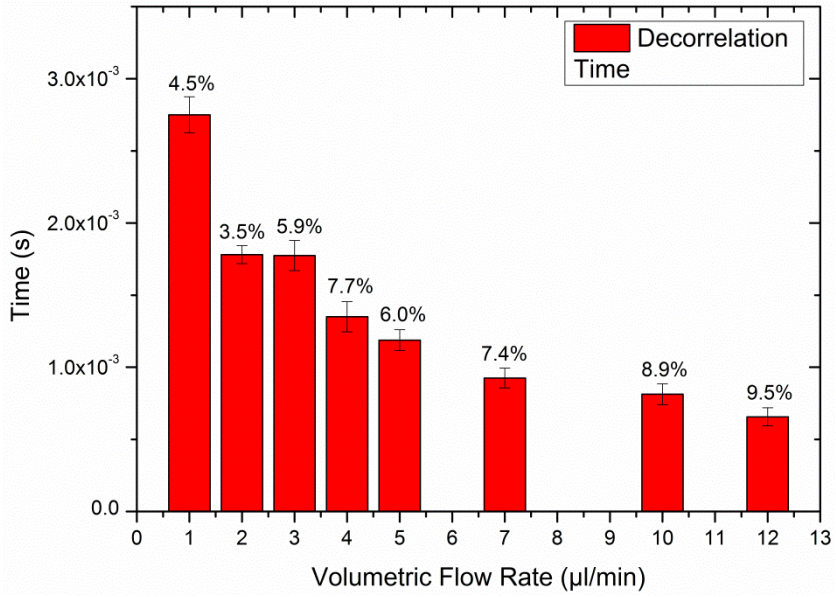

Fig. 3. Decorrelation time calculated for different flow rates. Note the trend of decrease with increasing volumetric flow. Error bars are presented as +/- standard deviation. Above each bar the Coefficient of Variation (in %) is reported.

In addition to those tests, to further demonstrate the applicability of the method, the microchannel was placed on an automated translator and laterally displaced, with five series of acquisitions taken for each lateral location. After completed the sampling at a given point, the sample was laterally translated 25 µm, and new acquisitions were made. The flow of milk was kept constant at 5 µl/min, that is showed in Fig. 4.

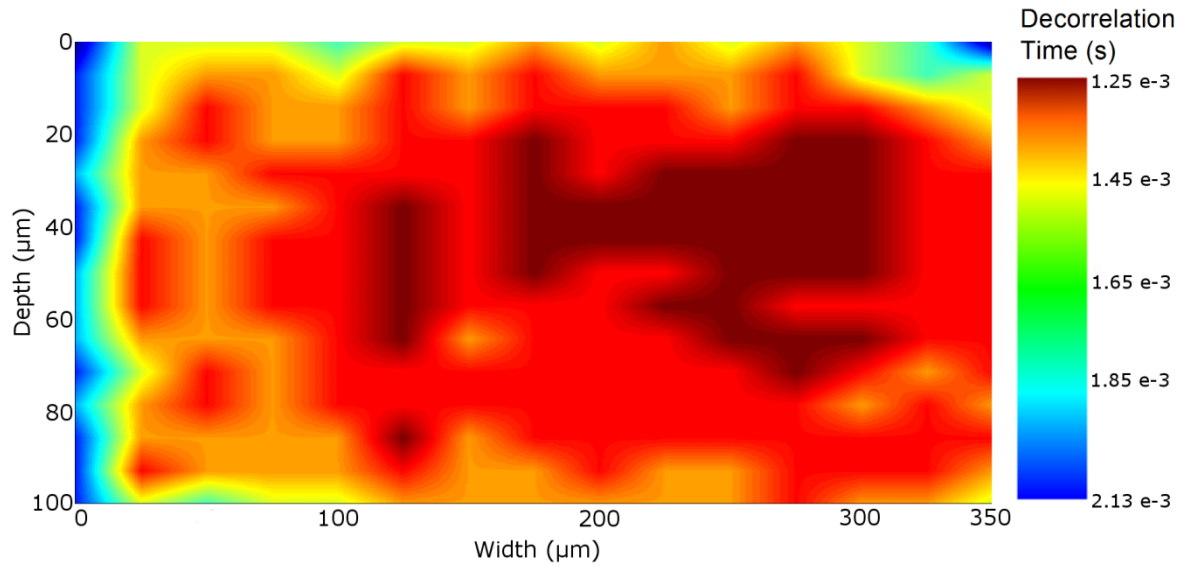

Fig. 4. Decorrelation time calculated for several points inside the microchannel while milk is pumped at 5 µl/min. It functions as a B-Scan of flow gradient inside the microchannel.

Conclusion: We demonstrated that through a parameter of observation in the autocorrelation array of increasing lags it was possible to discern the different volumetric flows inside a microchannel. The results were consistent, and, with the setup used, differences as low as 3 µl/min were perceived with statistical significance. Even the different flow rates inside the microchannel could be distinguished, through the use of our approach, which provides the ability to perform B-Scans of flow velocities

With all of that, the approach was demonstrated to have good results for the expected behavior, and is a viable tool to be applied with OCT, requiring no modification of system setup nor prior sample preparation.

References and Acknowledgements:

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