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Path Length Resolved Dynamic Light Scattering Measurements with Suppressed Influence of Optical Properties Using Phase Modulated Low Coherence Interferometry

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1. Introduction

In optical Doppler measurements, the path length of the light is unknown. This complicates the noninvasive diagnosis of tissue with light. For example, in laser Doppler blood flowmetry, the coherent light delivered into the tissue interacts with static as well as moving scatterers, e.g. red blood cells and it records values averaged over different and basically unknown path lengths. One of the important limitations of this technique is the dependence of the perfusion signal on the optical properties of the tissue, i.e. absorption coefficient, scattering coefficient and anisotropy factor. These dependences result from the varying optical path length of detected photons; the longer the optical path length the greater is the probability for Doppler scattering events to occur, thus yielding an overestimation of the blood perfusion, compared to the short path length situation [1].

If red blood cells in vascular blood can be regarded as independent scatterers, the average number of collisions between photons and red blood cells which is used to determine the concentration of blood cells moving in the tissue is given by

$$\bar{m} = \Sigma_{sc}(rbc) * [RBC] * L \tag{1}$$

Where Σ_{sc} is the scattering cross section of RBCs, [RBC] is the number of moving RBCs in 1 mm^3 of tissue and L is the mean path length of the detected light. For a homogeneous tissue of fixed concentration and blood volume, the value of $\bar{m}$ is proportional to the average path length of the detected light. The average path lengths will be different for different tissue types due to the changes in tissue optical properties in terms of absorption and scattering and thus laser Doppler flowmetry provides only a relative measure of the perfusion level. Therefore, development of techniques for monitoring Doppler shifts with path length information would result in more-quantitative and more reliable tissue perfusion information.

To facilitate quantitative path length resolved dynamic light scattering measurements with suppressed influence of optical properties we have developed an improved method based

on phase modulated low coherence interferometry [2-3]. In this chapter, we aim at describing the state-of-art of this novel interferometric technique and we show that we can measure dynamic properties of particles, independent of the optical properties of the surrounding tissue matrices. Furthermore, we demonstrate the feasibility of phase modulated low coherence interferometry in measuring *in vivo* optical path lengths and path length resolved Doppler shifts.

2. Review of coherence domain path length resolved approaches in laser Doppler flowmetry

To obtain path length distributions with widths of a few millimeters, several successful approaches based on low coherence interferometric methods were reported. In low coherence interferometry, a user-positioned coherence gate selects the light that has traveled a known optical path length in the medium to interfere with reference light. Dougherty et al. presented a new approach based on coherence modulation of semiconductor lasers using the variable coherence properties of the semiconductor laser [4]. In this technique, they exploited variations in effective coherence length properties of certain types of laser diodes by regulating the input drive current to these devices. For a long coherence length, all photons interfere, while for a short coherence length only photons with almost the same path length will interfere. This will relatively suppress the deep photons, since the (few) deep photons will only interfere with the few deep photons but not with the (many) shallow photons. However, these methods still give no control over the optical path length traveled by the detected light. McKinney et al. [5] and Haberland et al. [6] used a wavelength modulated continuous wave source as a variable-coherence source for measuring path length distributions. The frequency of the modulation used was much faster than the integration time of the detection and the authors demonstrated that the speckle contrast ratio measured in that way was linked to the photons path-length distribution [5]. Haberland et al. [6] used such a wavelength modulated source to demonstrate that chirp optical coherence tomography (OCT) can be an alternative to short coherence tomography with the advantage of a simplified optical set-up. However they reduced their investigations to unscattered light. Later, Tualle et al. [7] reported the development of a low cost interferometric set-up to record the scattered light by the use of a wavelength modulated continuous wave source. The principle of this technique relies on the facts that the shape of the time-resolved signal corresponds to the path-length distribution of the scattered light inside the turbid medium and the path-length differences can be measured using an interferometer. They showed that the study of the speckle pattern fluctuations within the modulation period can provide much more information, and that this information can be used to completely reconstruct the scattered light path-length distribution, or equivalently to perform time-resolved measurements. However, the slow rate that they used for the wavelength modulation limited their experiments to static scattering media.

With a fiber-optic low coherence Michelson interferometer, Bizheva et al. demonstrated that particle dynamics of highly scattering media can be imaged and quantified in the single scattering regime with dynamic low coherence tomography (LCI) by examining the intensity fluctuations of the backscattered light and extracting information from the photocurrent power spectrum [8]. Later, they showed that dynamic LCI permits path-length-resolved measurements of particle dynamics in highly scattering media with the ability to separate singly scattered, multiply scattered, and diffusive light and the results

were compared with the predictions of the dynamic light scattering (DLS) and diffusive wave spectroscopy (DWS) theories in the single scattered and diffusion regimes, respectively. They showed the dependence of detection of multiply scattered light on the geometry of the detection optics and on the anisotropy of the scattering [8]. Even though these studies modeled the single scattering and the diffusive regimes of light fluctuations, they did not model the transition between the two regimes. With a free beam Michelson interferometer, Wax et al. applied path-length resolved DLS spectroscopy and a theoretical model was developed to predict this transition regime across the full range of path lengths from single scattering through diffusive transport [9]. By comparing the trends in the measured power spectra for various-sized microspheres with a theoretical treatment that decomposes the total power spectrum by the number of scattering events, they correlated the detection of multiply scattered light with scattering anisotropy. We reported the development of fiber-optic Mach-Zehnder interferometer for path length resolved measurements with two spatially separated fibers for illumination and detection, as used in conventional laser Doppler perfusion monitors [10]. Low coherence interferometry with phase modulation of the reference beam has been adopted by Ishii et al. in single scattering spectroscopy to analyze the characteristics of extremely dense colloidal suspensions [11]. Doppler optical coherence tomography based on low-coherence single-mode fiber optic Michelson interferometry has been proposed for path length resolved measurements adopting on axis back reflection and confocal detection of singly scattered photons [12]. Here two embodiments were reported due to the possibility of performing interferometric measurements either in the time domain or in the Fourier domain. In time domain OCT the path length of the reference arm is varied in time. In frequency domain OCT the broadband interference is acquired with spectrally separated detectors either by encoding the optical frequency in time with a spectrally scanning source (Swept source OCT) or with a dispersive detector, like a grating and a linear detector array (Spectral Domain or Fourier Domain OCT) [13-14]. In these techniques, optical path length distributions can be obtained about photons which where Doppler shifted by the medium. The photons that has been scattered by static structures can also be made to contribute to the interferometric signal by modulating the phase in the reference path.

3. Phase modulated low coherence Mach-Zehnder interferometry

In our research, we have developed a new bio-optical technique for path length resolved laser Doppler perfusion monitoring, by combining the principles of coherence gated interferometry and laser Doppler blood flowmetry [2-3]. The method is based on a phase modulated fiber optic low coherence Mach-Zehnder interferometer, in which the limited temporal coherence acts as a band pass filter in selecting the photons that have traveled a specific path length. We use a fiber-optic Mach–Zehnder interferometer (Fig.1) with a superluminescent diode (λ_c=832nm, $\Delta\lambda_{FWHM}$ =17 nm, L_C =18 μm) as the light source. A single mode fiber-optic coupler with a splitting ratio of 90:10 is used to create a reference arm (10%) and a sample arm (90%). Single mode fibers (mode field diameter=5.3 mm, NA=0.14) are used for illumination, while multimode graded-index fibers (core diameter =100 mm, NA=0.29) are used for detection, providing a large detection window. The path length of the reference arm is varied by reflection of the light in a translatable retroreflector and the position of the retroreflector is adjusted to yield an optical path length equal to the optical

path length of a certain part of the photons in the sample arm. The reference beam is polarized using a linear polarizer and the phase is sinusoidally modulated at 6 kHz using an electro optic broadband phase modulator with a peak optical phase shift of 2.04 radians applied to the modulator. The AC photocurrent is measured with a 12 bit analogue to digital converter sampling at 40 kHz. The coherence length of the light source, and the intermodal dispersion in the detection fiber, define the path-length resolution of the measurement.

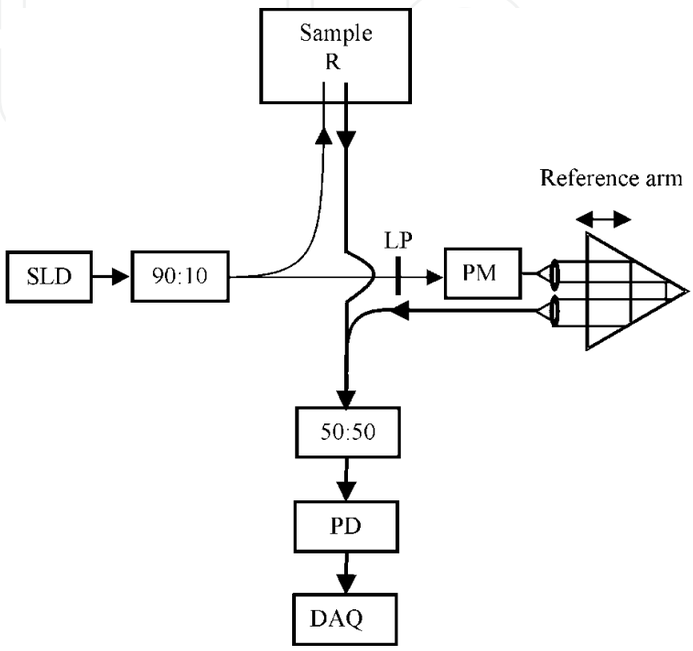

Fig. 1. Schematic of the fiber optic Mach–Zehnder interferometer. (Figure reprinted from Fig. 2 in Ref. [2] Copyright (2008) with permission from SPIE).

In phase modulated low coherence interferometry, for sufficiently small phase modulation angles, the power spectrum measured when the path length difference between the reference light and the scattered light is within the coherence length of light source, is a mixture of homodyne interference of light remitted by the sample, and heterodyne interference between sample light and unmodulated reference light, and a heterodyne spectral component around the phase modulation frequency resulting from the interference between sample light and modulated reference light. Path length resolved optical properties of the media are measured from the heterodyne peak appearing at the modulation frequency. This can be understood from the phasor description of the interfering fields, as shown in fig. 2. Here the reference wave and two Doppler shifted sample waves are represented by phasors R, S_1 and S_2, respectively. The angle ϕ is the peak phase deviation due to phase modulation in the reference light, which is depicted by a sinusoidal oscillation of the reference phasor between the extreme phasors R_1 and R_2 on either side of the average phasor R. For small values of ϕ, the oscillation of the reference phasor between R_1 and R_2 is equivalent to the summation of the average reference phasor R, and two phasors M_1 and M_2 of equal length that rotate in opposite directions with a constant angular speed equal to the phase modulation frequency ω_m. The initial phase of M_1 and M_2 should be chosen such that

their sum phasor M is perpendicular to R. The amplitude of M_1 and M_2 is $OM_1=OM_2=1/2.OR.\tan\phi/2$ to achieve the desired phase modulation angle. The sample waves S_1 and S_2 with Doppler shifts ω_{D1} and ω_{D2} interfere with both M_1 and M_2. Since only positive frequencies show up in the power spectrum interference peaks are expected at $\omega_m - \omega_{Di}$ and $\omega_m + \omega_{Di}$ $(i=1,2)$. This interference of sample light with reference light will be called 'heterodyne'. In practice from a turbid sample waves are obtained with a distribution of Doppler shifts, leading to a similar distribution of spectral components centered around ω_m. Hence the shape of the peak around ω_m corresponds to the Doppler shift distribution. The component of the reference light represented by the average phasor (OR) that still is at the original light source frequency will also interfere with the scattered light from the sample and thus, apart from the peak around the phase modulation frequency, a heterodyne component will also occur at low frequencies. Finally, the sample phasors S_1 and S_2, will mutually interfere to generate beats at frequency $\omega_{D1} - \omega_{D2}$, a component that we call 'homodyne'. Hence, the spectrum at low frequencies is a mixture of homodyne interference of light remitted by the sample, and heterodyne interference between sample light and unmodulated reference light, while the spectral component around the phase modulation frequency is the pure Doppler shift distribution. The power spectrum measured for widely different optical path lengths in the sample and the reference arm, contains the ordinary homodyne signal due to the mutual interference of scattered light over almost equal optical path lengths in the sample.

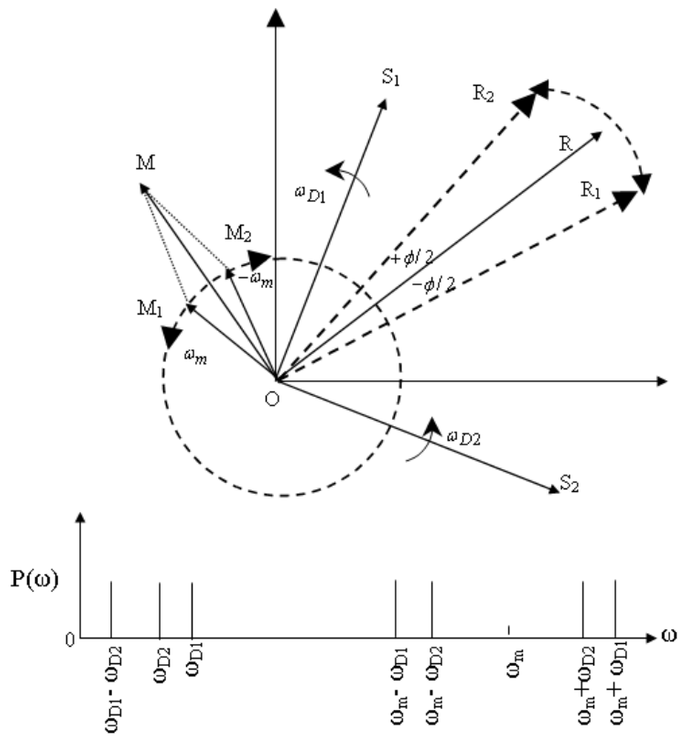

Fig. 2. Phasor diagram for the interfering fields (top) and the resulting power spectrum (bottom). (Figure reprinted from Fig. 1 in Ref. [2] Copyright (2008) with permission from SPIE).

The fundamental output quantity of a laser Doppler perfusion monitor is the first moment of the power spectrum $P(\omega)$ of the detector signal; in general, the ith moment is being defined as

$$M_i = \int_a^b P(\omega)\omega^i d\omega \tag{2}$$

Here a and b are device dependent low and high cut-off frequencies. With i=0, a quantity is obtained which is proportional to the concentration of moving red blood cells, while i=1 describes red blood cell flux, which is the product of concentration and the root mean square of the red cell velocity, at least for low blood concentrations [15]. In our instrument, for large phase modulation angles ($\Delta\phi$ =2.04 radians) the power spectra contain interference peaks at both the phase modulation frequency and higher harmonics (Fig.3). Optical path length distributions are obtained by adding the areas of all interference peaks (after subtraction of the background noise, and within a bandwidth of $\pm$ 2 kHz around all center frequencies) in the power spectrum [16]. The area of the Doppler broadened peak, excluding the statically scattered light contribution at the interference peaks, forms an estimation of the amount of Doppler shifted light at that specific optical path length. The average Doppler shift corresponding to the Doppler shifted light is calculated from the weighted first moments (M_1/M_0) of the heterodyne peak at the modulation frequency, after correction for the sample signal and for the reference arm noise (in a bandwidth of 50 Hz-2 kHz close to the phase modulation frequency and its higher harmonics, indicated by a and b in Eq.2)

$$M_i = \sum_{j=1}^{3} \int_{j\omega_m+a}^{j\omega_m+b} P(\omega)(\omega - j\omega_m)^i d\omega \tag{3}$$

To determine the parameters path length resolved, we measured the power spectra with the Mach-Zehnder low coherence setup. First, the background noise from the power spectrum around the modulation frequency (ω_m = 6 kHz) is subtracted. The calculated $M_0(0,b,\omega_m)$ of the broadened interference peak (until b=2 kHz from the phase modulation peak) is proportional to the total number of detected photons for that given (by the reference arm) path length. The full width at half maximum (FWHM) of the interference signal in a statically scattering medium has a value δ_s (δ_s = 50-60 Hz in our system) whereas in the case of dynamic media a Doppler broadened spectral peak around the phase modulation frequency is formed [2]. The area of the Doppler broadened peak, excluding the statically scattered light contribution at the interference peaks, forms an estimation of the amount of the Doppler shifted light at that specific optical path length. For a given optical path length, the fraction of Doppler shifted photons f_D is then given by $f_D = M_0(\delta_s,b,\omega_m)/ M_0(0,b,\omega_m)$. Here we regard the Doppler fraction f_D as a measure of the concentration of particles moving in the static matrix. The average speed of the moving particles is represented by the average Doppler shift of the Doppler shifted fraction of the detected light, which in terms of equation (1) is $<\omega_D> = M_1(\delta_s,b,\omega_m)/M_0(\delta_s,b,\omega_m)$ with the frequency ω_D in Hz.

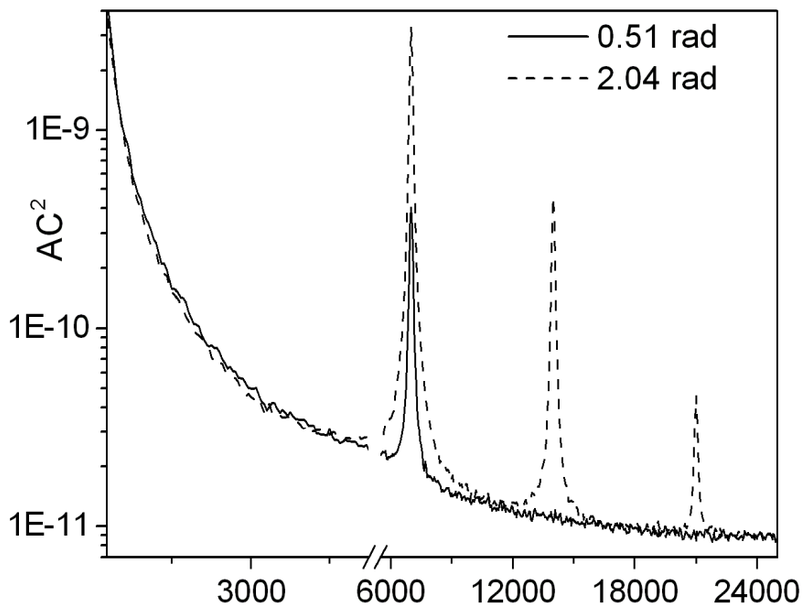

Fig. 3. Power spectra measured for water suspension of Polystyrene microspheres for two different peak optical phase shifts (0.51 and 2.04 radians), with the position of the retroreflector corresponding to an optical path length difference of 1.3 mm. (Figure reprinted from Fig. 1 in Ref. [16] Copyright (2008) with permission from Elsevier B.V.).

4. Path length resolved dynamic light scattering measurements with suppressed influence of optical absorption properties of surrounding tissue matrices

To study the effect of absorption on Doppler shift, measurements were performed on three samples with identical scattering properties but increasing absorption levels [2]. The media were an aqueous suspension of 25% of Intralipid 20% [17] and the same suspensions with absorption coefficients of 0.50 mm^{-1} and 0.85 mm^{-1}.

The estimations of path length distributions of photons in the aqueous Intralipid suspension (μ_a = 0.001 mm^{-1}) and for identical suspensions with different absorption levels (0.50 mm^{-1} and 0.85 mm^{-1}) are shown in fig.4. The estimation of the optical path length distribution is obtained for increasing absorption levels. The minimum path length is the same for all absorptions and is related to the fiber distance of 500 micrometer. At this path length all the distributions start to increase independent of the absorption. As the photons with longer path length have a greater probability to be absorbed in an increasingly absorbing medium, M_0 decreases with the absorption. Hence the path length distribution narrows and shows a decrease in the average intensity as the absorption coefficient increases. Lambert-Beer's law can describe the effect of absorption on the path length distribution. According to the law of Lambert–Beer, the light intensity I_0 in an absorbing medium decays exponentially as $I(L)= I_0$

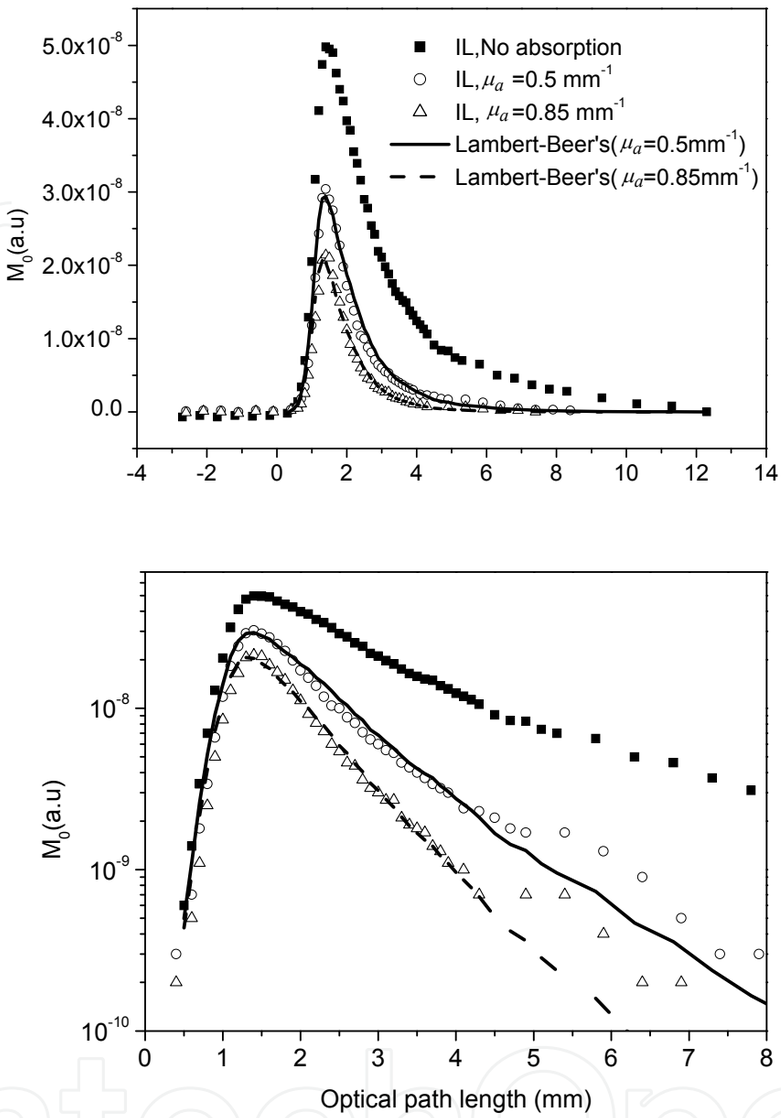

Fig. 4. Optical path length distributions estimated from the zero order moment of the phase modulation peak for an aqueous Intralipid suspension (μa = 0.001 mm^{-1}) and for identical suspensions with two different absorption coefficients (0.50 mm^{-1} and 0.85 mm^{-1}), but equal reduced scattering coefficient (linear and logarithmic scales). The lines result from the application of Lambert-Beer's law on the experimental dataset for zero absorption. (Figure reprinted from Fig. 4 in Ref. [2] Copyright (2008) with permission from SPIE).

exp(-L. μ_a/n) with *L* the optical path length, and μ_a and *n* the absorption coefficient and the refractive index of the medium. To validate that the results shown in figure 4 represent the true optical path length distributions, we verify whether the path length distribution of the

original Intralipid and the same suspensions with high absorption coefficients are mutually related by Lambert-Beer's law. The path length distributions of original Intralipid multiplied by the exponential decay function $exp(-L.\ \mu_a/n)$ and the experimental data are shown in figure 4 in linear and logarithmic scales. There is a good agreement between the experimental data and the calculated values (for n = 1.33, μ_a = 0.50 and 0.85 mm^{-1}) on the basis of Lambert-Beer's law up to an optical path length of 4.5 mm, which proves that path length distributions have been correctly measured.

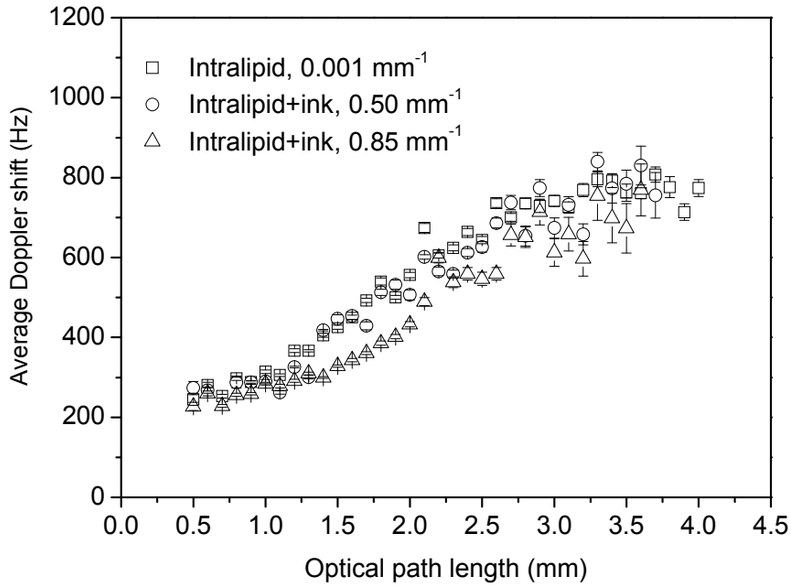

Fig. 5. The average Doppler shift extracted from the phase modulation peak, as a function of the optical path length for an aqueous Intralipid suspension with different absorption coefficients. (Figure reprinted from Fig. 5 in Ref. [2] Copyright (2008) with permission from SPIE).

The average Doppler shift, measured from the width of Doppler broadened phase modulation interference peaks is represented in fig.5 as a function of the optical path length. The average Doppler shift increases with the optical path length, which can be expected from the increase in the number of scattering events with the optical path length. For a given medium with a constant scattering coefficient but absorption coefficients μ_a = 0.001 and 0.50 mm^{-1} the Doppler broadening of path length resolved heterodyne spectra is shown to be independent of the absorption level, for a given optical path length. Therefore, our results indicate that for absorption levels realistic for tissue, our method enables Doppler measurements independent of the absorption level of the medium in which the moving particles are embedded.

5. Path length resolved dynamic light scattering measurements with suppressed influence of scattering properties of surrounding tissue matrices

To study the effect of scattering of surrounding tissue matrices on Doppler shift, mixed static-dynamic scattering phantoms were prepared with aqueous suspensions of polystyrene microspheres of ∅4.7 μm and ∅0.20 μm respectively [19]. Three scattering phantoms with the same concentration of particles ∅0.20 μm (g=0.18, $\mu_{s'}$=0.55 mm^{-1}, μ_a=0.001 mm^{-1}) were prepared and two scattering levels of the static medium were realized (μs'=1.4, 0.8, 0.4 mm^{-1}). For estimating the flux of particles moving inside static matrices in absolute terms, we related the outcomes of our measurements to the optical and dynamical properties of the dynamic part of the medium. Here we focus on the concentration of moving particles, which may be retrieved from models which relate the measured Doppler fraction f_D to the contribution of the dynamic part of the medium to the total scattering coefficient of the entire medium. We will consider a simple exponential decay model and compare it with the gold standard provided by the Monte Carlo simulation technique. In the exponential decay model we assume that the fraction of *unshifted* light decays exponentially with the traveled optical path length l_{opt}. Consequently, the fraction of Doppler shifted photons will be given by $f_D=1-exp(-\mu_{s,dyn}\ell_{opt}/n)$, with $\mu_{s,dyn}$ the scattering coefficient of the ensemble of moving particles. Monte Carlo simulations were performed with the algorithm and software as described by De Mul [18]. The single mode fiber used in the experiment was modeled as a point source. Photon detection was performed in a ring with inner and outer radius of 0.25 and 0.35 mm (in agreement with the core diameter and position of the real detection fiber), concentric to the light beam for illumination. The simulated numerical apertures for illumination and detection were identical to the experimental values. The three mixed static-dynamic phantoms were exactly mimicked, with the scattering phase functions being calculated using Mie's theory. Photons which were scattered by the ∅0.20 μm particles were given a Doppler label. For each medium and each path length, 20000 photons were detected.

Figure 6 shows the fraction of Doppler shifted photons f_D as a function of the optical path length, for the three media. As expected, the measured Doppler fraction increases with the optical path length and the confounding influence of the surrounding static matrices is suppressed. Furthermore, fig. 6 shows the results of Monte Carlo simulations and for the exponential decay model $f_D=1-exp(-\mu_{s,dyn}\ell_{opt}/n)$. The models in general predict higher values of the Doppler fraction than the experimental values. Furthermore, the experimental and Monte Carlo results show biphasic behaviour, with a different trend for optical path lengths below and larger than 2 mm. For a given optical path length, f_D is independent of the influence of static matrices, in particular for optical path lengths larger than 2 mm. Furthermore f_D increases with optical path length with a trend that can be depicted by the simple exponential decay model. However, the theoretically predicted Doppler fractions are higher than the experimental values. Nevertheless, if in this model we define scattering coefficient $\mu_{s,dyn}$ as a fitting parameter, it appears that the exponential decay model properly fits the observations for ℓ_{opt}>2mm, with $\mu_{s,dyn}$=0.55 mm^{-1}. For ℓ_{opt}>2mm, the predicted Doppler fractions by Monte Carlo simulations are similar for the three media and are in good agreement with the experimental results. Figure 7 shows the average Doppler shift generated by the moving particles $\langle\omega_D\rangle=M_1(\delta_s,b,\omega_m)/M_0(\delta_s,b,\omega_m)$ as a function of optical path length. For optical path lengths larger than 2 mm, $\langle\omega_D\rangle$ increases linearly with optical path

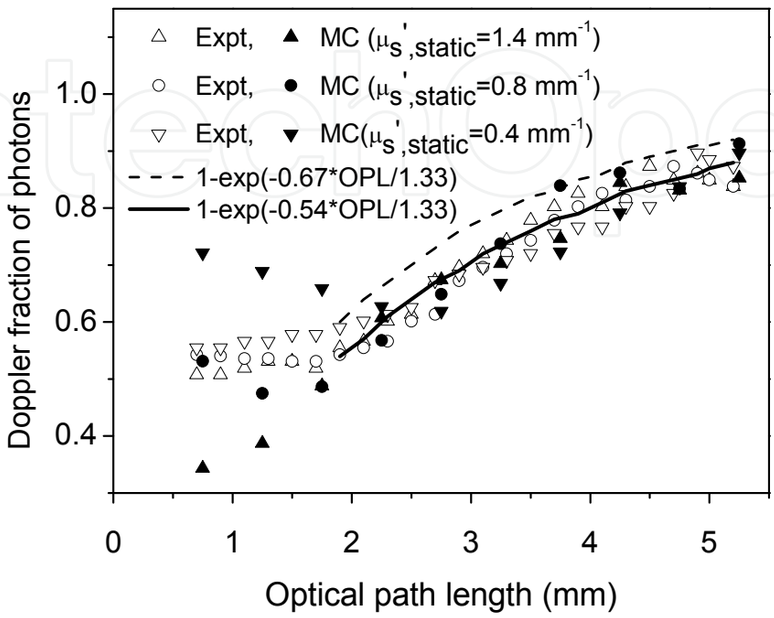

Fig. 6. The fraction of Doppler shifted photons as a function of optical path length, as a result of experiments (open markers), Monte Carlo simulations (filled markers), and experimental decay models, one with a theoretical decay rate (dashed line), and one with the best fit to the experimental results (thick line). (Figure reprinted from Fig. 2 in Ref. [19] Copyright (2010) with permission from OSA).

length as expected theoretically and experimentally [3]. However, $\langle\omega_D\rangle$ also shows a different behaviour for optical path lengths smaller than 2mm. The average Doppler shift decreases with increasing scattering of the static material.

The overall dependence on the static matrix optical properties on the Doppler shift is small, as depicted in figure 7. In the case of a higher scattering coefficient (μ_s'=1.4mm^{-1}), for optical path lengths between 2.5 and 3.5 mm, the Doppler broadening is lower in comparison with those obtained for the lower scattering levels. We may express the overall dependence of the measured concentration, represented by f_D, and the particle velocity, represented by M_1/M_0, by their average value. This yields average Doppler fractions $\langle f_D\rangle$ of 0.692, 0.685 and 0.694, and average Doppler shifts $\langle M_1/M_0\rangle$, of 447.7, 447.9 and 442.2 Hz, for μ_s'=0.4, 0.8 and 1.4 mm^{-1}, respectively. Measurements at a single optical path length may be more suitable in practice. For single path lengths, figures 6 and 7 feature maximum variations of 10% for both f_D and M_1/M_0. These results clearly illustrate that the average Doppler shift measured with the low coherence interferometer, averaged over all optical path lengths, is much less sensitive to the influence of the scattering properties of the static medium.

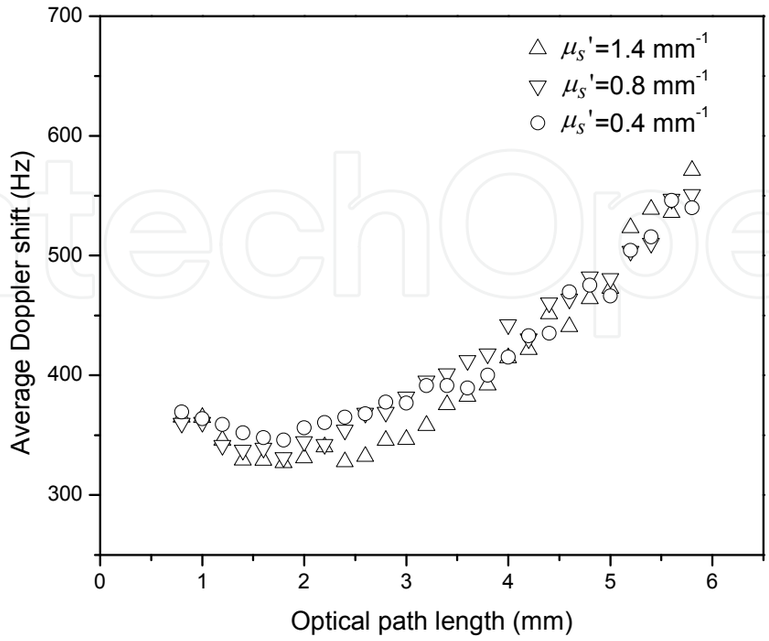

Fig. 7. The weighted Doppler shift measured as a function of optical path length in the medium. (Figure reprinted from Fig. 3 in Ref. [20] Copyright (2010) with permission from OSA).

6. Path length resolved optical Doppler perfusion monitoring

To assess the feasibility of the technique for path length resolved optical Doppler perfusion monitoring, measurements were performed on the skin of the dorsal side of the right forearm of a healthy human volunteer (Skin type- Type II) in the sitting position [20]. A probe holder (PH 08) was attached to the skin with a double-sided adhesive tape. The subject rested approximately 10 minutes prior to the measurements. Skin sites were avoided with visible large superficial blood vessels, hair and pigment variations.

The intensity of Doppler shifted and nonshifted photons measured in skin as a function of optical path length are shown in Fig. 8. The fraction of Doppler shifted photons and nonshifted photons averaged over the entire optical path length measured from the respective areas of the optical path lengths are 22 and 78%, respectively. As shown in Fig. 8, the weighted first moment M_1/M_0 of the Doppler shifted light, which represents the average Doppler shift, increased with the optical path length due to the greater probability of interaction of photons with moving scatterers for large optical path lengths. Further *in vivo* studies were performed to measure the variations in perfusion to external stimuli, inter-and intra-individual variations in optical path lengths and path length resolved Doppler shifts, and to compare these results with the perfusion signal measured with a conventional LDPM [21].

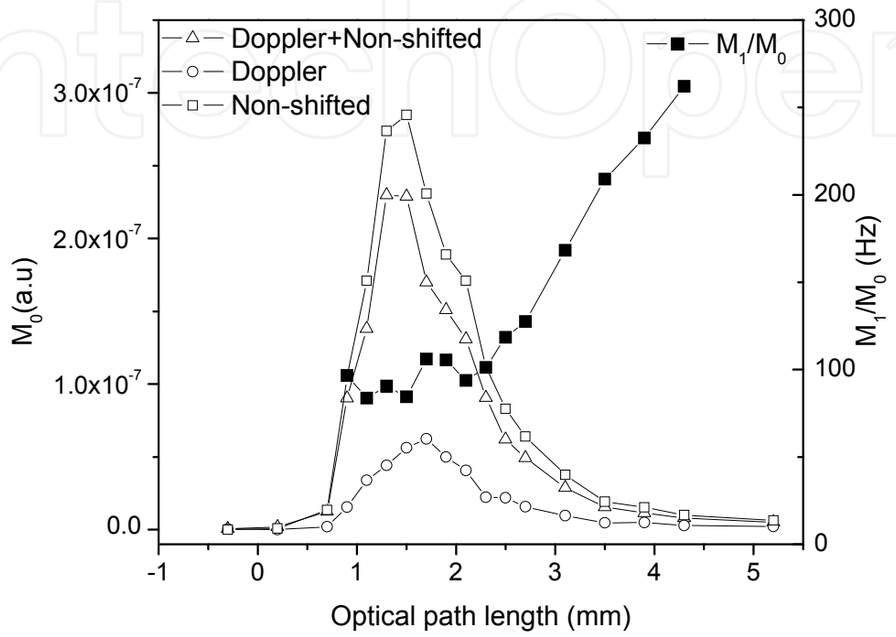

Fig. 8. Intensity of Doppler-shifted, nonshifted photons and the average Doppler shift as a function of optical path length measured in skin (Figure reprinted from Fig. 1 in Ref. [8] Copyright (2008) with permission from SPIE).

Here we have presented optical path length distributions and path length resolved Doppler shifts of multiply scattered light, extracted from the spectral peak that was generated by phase modulation of the reference arm in a low coherence Mach Zehnder interferometer. As such, these data can also be obtained without modulation, but then we only can obtain information about photons which where Doppler shifted by the medium. Hence, phase modulation will enable us to measure path length distributions of static, and mixed static and dynamic media. A second advantage of using phase modulation is that the information can be shifted to higher frequencies, where often the noise level is lower and its spectrum is more flat than for low frequencies [2]. The path length resolved perfusion measurements presented here may overcome the inherent limitation of conventional LDPM that restrict its clinical usefulness, where the perfusion signal depends on an unknown photon path length. This will enable to correctly interpret or counter-act the inter-and intra-individual variations in the LDF readings introduced by the variance in tissue optical properties. This approach enables to discriminate between

the Doppler-shifted photons resulting from interaction with the moving red blood cells and the non-shifted light scattered only by the surrounding static tissue matrices [20]. Another important feature of this approach is the tunable depth resolved perfusion information that can be achieved. By changing the optical path length in the reference arm, the photons migrated deeper into the tissue can be made to interfere with the reference light and thus enable to discriminate between the perfusion signal from superficial and deeper layers of tissue. Determination of superficial burn depth may be an important application of our technique [19]. However, further developments and fundamental research are required in developing this into a tool that is suitable for use in a clinical environment, with acceptable measurement times and suitable patient interfaces.

7. Conclusions

To summarize, we have developed a new bio-optical method "Path length resolved optical Doppler perfusion monitoring," to determine path length distributions of multiple scattered light in static and dynamic turbid media using phase modulated coherence gated interferometry. We have shown that path length-resolved dynamic light scattering can measure the dynamic properties of a medium independent of its optical absorption properties, at least when absorption levels are applied in the range found for biological tissues. Furthermore, we showed that our method enables optical Doppler or dynamic light scattering measurements of dynamic media embedded in a static medium, with suppressed dependence of the effect of the scattering coefficient of the static matrix in which the moving particles are embedded. Also, we have presented the first path length resolved Doppler measurements of multiply scattered light from human skin. The results presented here show that this approach has potential applications in discriminating between statically and dynamically scattered light in the perfusion signal. In general, path length resolved dynamic light scattering, of which the basic technique is presented in this work, may overcome the influence of photon path lengths on the measured perfusion signal in laser Doppler techniques and makes it possible to perform depth resolved perfusion measurements with suppression of the confounding influence of optical properties in the tissue matrix.

8. References

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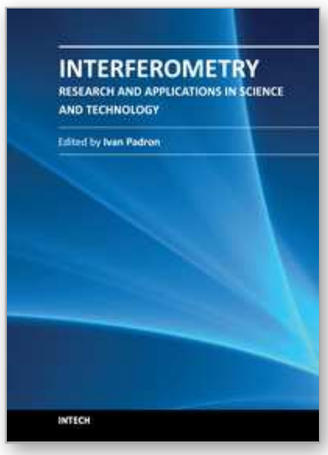

Interferometry - Research and Applications in Science and Technology

Edited by Dr Ivan Padron

ISBN 978-953-51-0403-2
Hard cover, 462 pages
Publisher InTech
Published online 21, March, 2012
Published in print edition March, 2012

This book provides the most recent studies on interferometry and its applications in science and technology. It is an outline of theoretical and experimental aspects of interferometry and their applications. The book is divided in two sections. The first one is an overview of different interferometry techniques and their general applications, while the second section is devoted to more specific interferometry applications comprising from interferometry for magnetic fusion plasmas to interferometry in wireless networks. The book is an excellent reference of current interferometry applications in science and technology. It offers the opportunity to increase our knowledge about interferometry and encourage researchers in development of new applications.

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