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Depth-resolved dynamics in turbid media via frequency-modulated scattering holography

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Abstract: Interferometric diffuse optics (iDO) enables non-invasive measurement of deep tissue blood flow without requiring photon-counting detectors. Due to hardware constraints, achieving both optical properties and depth-dependent dynamics within a single modality remains a challenge for iDO. We present a simple method based on frequency-modulated light scattering that overcomes this limitation. © 2025 The Author(s)

1. Introduction

In speckle-based blood flow (SBF) measurements, coherent laser illumination of biological tissue generates scattered photons that interfere, forming a random interference pattern known as speckle. To enhance sensitivity to deeper flow, the source and detector (SD) can be separated by a distance D, enabling specificity at a depth of approximately $D/2$. Common techniques such as speckle contrast optical spectroscopy (SCOS) [1], diffuse correlation spectroscopy (DCS) [2], and laser Doppler perfusion monitoring (LDPM) [3] infer flow rates by examining speckle contrast, intensity autocorrelation, or power spectral density, respectively. Nonetheless, their reliance on large SD separations causes photon throughput to diminish exponentially, resulting in low spatial resolution and necessitating the use of expensive, highly sensitive detectors that are also susceptible to ambient light. Time-of-flight (ToF)-dependent speckle contrast imaging can operate with smaller SD separation but requires sophisticated electronics and costly SPAD arrays [4].

Recent advances in interferometric diffuse optics (iDO) have demonstrated promising alternatives for SBF measurement. Leveraging heterodyne gain through the interference-based architectures, these techniques eliminate the need for single-photon counting detectors, relying instead on balanced detectors [5, 6] or conventional complementary metal–oxide–semiconductor (CMOS) cameras [7,8]. This approach considerably reduces cost and alleviates susceptibility to ambient light. Two major categories exist within iDO: single-speckle iDO and multiple-speckle iDO. Single-speckle iDO employs a single-mode fiber to collect a speckle, forming a Mach–Zehnder interferometer that, when combined with swept-source (interferometric near-infrared spectroscopy, iNIRS [5]) or dual-comb (dual-comb diffusing-wave spectroscopy, DC-DWS [6]) modalities, measures the photon distribution of time-of-flight (DTOF). These time-resolved measurements enable extraction of optical properties (absorption coefficient μ_a and reduced scattering coefficient μ_s') and depth-dependent dynamics without necessitating large SD separations, thereby increasing photon throughput and spatial resolution. Additionally, measuring optical properties allows for more accurate determination of blood flow index (BFi) and holds promise for metabolic measurements. Nevertheless, even when operating at the shot-noise limit, the signal-to-noise ratio (SNR) for single-speckle iDO remains lower than that achievable by single-photon counting detectors.

Multiple-speckle iDO addresses this limitation by harnessing numerous pixels to enhance photon throughput. For instance, interferometric diffusing-wave spectroscopy (iDWS) [7] collects multiple speckles through a multimode fiber and projects them onto a high-speed ($>$ 100 kHz) line camera, with each pixel functioning as an independent DWS channel. This parallelized approach provides high SNR while still using cost-effective CMOS cameras. Another example, interferometric speckle visibility spectroscopy (iSVS) [8], similarly utilizes multimode fiber collection but at a lower frame rate (100Hz). Although the frame rate is slower than typical scattered electric-field decorrelation times, the speckle visibility factor enables the determination of electric-field decorrelation. Both iDWS and iSVS, however, usually rely on large SD separations and thus provide limited spatial resolution while not measuring the DTOF as effectively as iNIRS or DC-DWS.

In principle, merging iNIRS-like approaches with camera-based detection could combine the advantages of time-resolved measurements and multi-speckle parallelization. However, the high detection bandwidth required poses a significant challenge. To address these constraints, we propose an alternate highly parallel strategy using a frequency-modulated light scattering interferometer [9], which can simultaneously acquire depth-dependent dynamics and optical properties with sufficient photon counting sensitivity.

2. Methods

The setup as seen in Fig. 1 (a) consists of a Mach-Zehnder interferometer which uses a frequency-modulated external cavity diode laser (ECDL, New Focus Velocity 6300) and a CMOS camera (Photron Fastcam SA3) to capture photons scattered by the turbid media. The laser has 5mW output power and is modulated by a ramp waveform with 20 GHz optical bandwidth. The camera is operated at 100k fps with 16*256 pixels. By substantially reducing the modulation frequency ($1/T = 200\,Hz$), the resultant beat frequency for signals with a few-nanosecond ToF difference (τ = 2ns) is reduced to the kilohertz range (f_{beat} = 16kHz), enabling detection by the camera. Consequently, each pixel records the temporal interferogram between the scattered photons and the reference beam, and in the frequency domain, the Doppler spectrum is separated according to ToF. This generates a Doppler-broadened DTOF that encodes both optical and dynamic properties (Fig. 1 (b)). Moreover, applying different bandpass filters in the frequency domain permits ToF-dependent speckle contrast measurement, thus enhancing specificity for deeper flow (Fig. 1 (e)(f)). This integrated approach therefore holds the potential to improve depth-specific sensitivity, SNR, and cost-effectiveness in blood flow imaging and related applications.

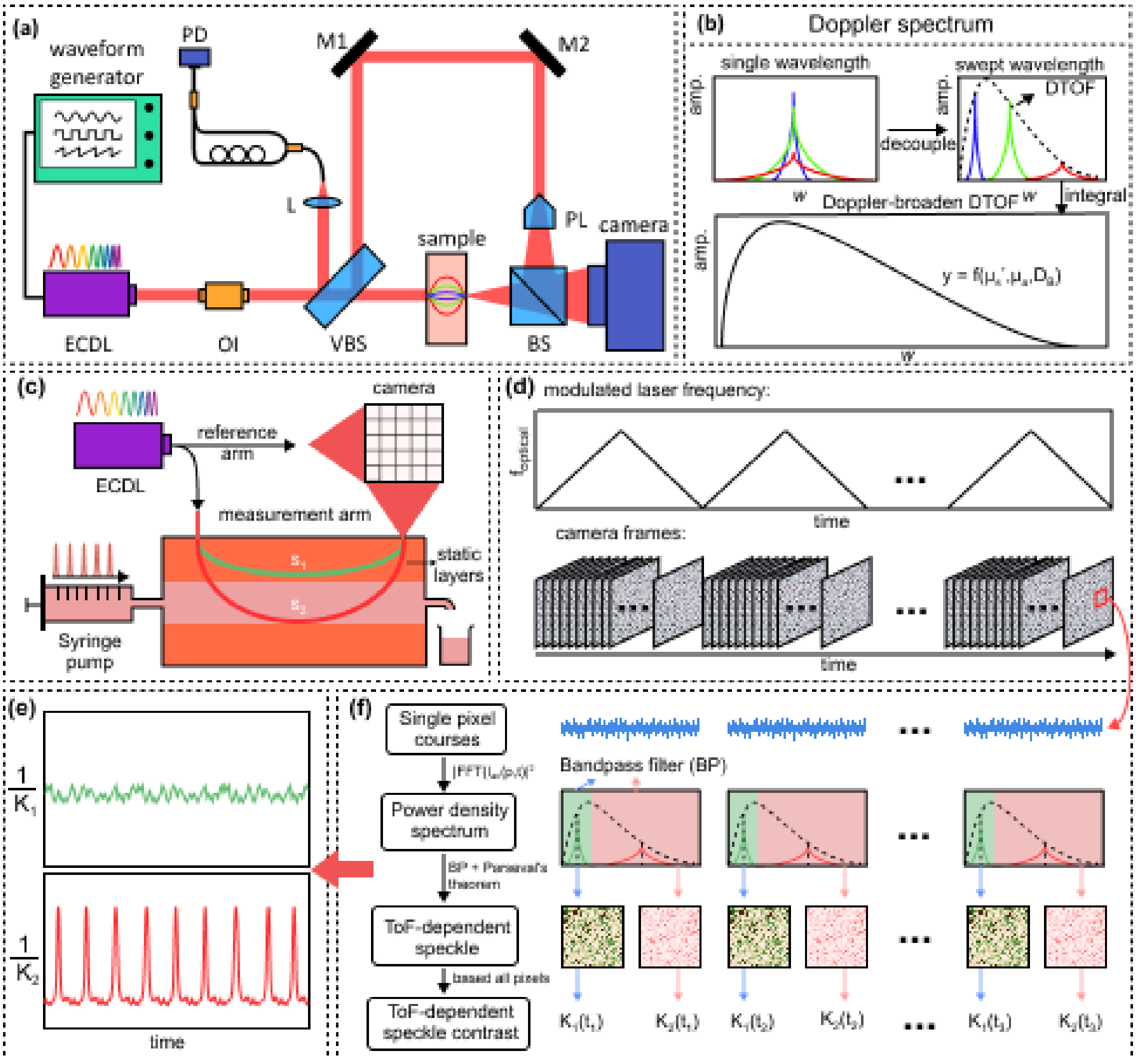

Fig. 1. Schematic diagram elaborating on the concept of frequency-modulated holography. (a) Two frequency-modulated interferometers work as reference and measurement respectively. ECDL–external cavity diode laser, OI–optical isolator, VBS–variable beam splitter, M1, M2–mirror, L–lens, PL–Powell lens, BS–beam splitter, SFC–single-mode fiber coupler, PD–photodetector. (b) Frequency-modulated source decouples the path-length dependent Doppler spectrum according to their times-of-flight (beat frequency w). (c) Specific experiment measuring a three-layer phantom in reflectance geometry. (d) The optical frequency is modulated in ramp waveform with 200 Hz and a 100k FPS camera acquires a series of frames. (e) The depth-dependent speckle contrast is calculated to obtain the deep flow.(f) The data processing flow of the depth-dependent speckle contrast.

3. Results

We will present the results from Intralipid phantoms in transmission geometry, using 19.8 ml of pure water mixed with 0.6 to 2 ml of 20% Intralipid emulsion. The measured μ_s' and μ_a were compared to previously reported values [10], as shown in Fig. 2(a) and 2(b). Additionally, a three-layer phantom was measured in reflectance geometry. Two bandpass filters were applied to calculate speckle contrast for photons with different time-of-flights (Fig. 1(f)). Since the first layer was static, the speckle contrast remained constant with small noise-induced fluctuations, while photons from deeper layers exhibited a pulsatile waveform modulated by the pump (Fig. 2(e) (f)).

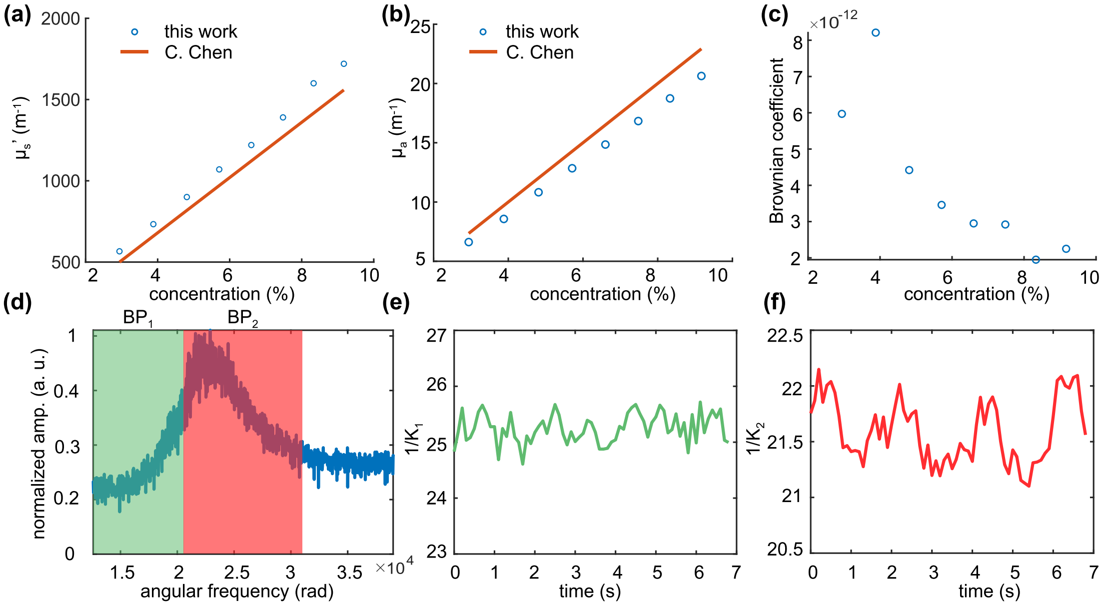

Fig. 2. experiment results. The broadened DTOF curve fitting gives (a) reduced scattering coefficient (μ_s'), (b) absorption coefficient (μ_a), and (c) Brownian coefficient. (d) The broadened DTOF curve is measured in the reflectance geometry (first layer thickness 4 mm). (e) The 1/K from the shallow layer remains constant. (f) The 1/K from the deep layer fluctuates due to the pump modulation.

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