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In vivo Time-Domain Diffuse Correlation Spectroscopy with a Superconducting Nanowire Single-Photon Detector

L. Colombo[a,*], P. Lanka[a], A. Brodu[b], N. Noordzij[b], M. Pagliazzi[c], V. Parfentyeva[c], T. Durduran[c,d], and A. Pifferi[a,e]

[a]Politecnico di Milano, Dipartimento di Fisica, 20133 Milano, Italy; [b]Single Quantum BV, 2629JD Delft, The Netherlands; [c]ICFO-Institut de Ciències Fotòniques, The Barcelona Institute of Science and Technology, 08860 Castelldefels, Barcelona, Spain; [d]Institució Catalana de Recerca i Estudis Avançats (ICREA), 08015 Barcelona, Spain; [e]Istituto di Fotonica e Nanotecnologie, Consiglio Nazionale delle Ricerche, 20133 Milano, Italy

*lorenzo.colombo@polimi.it

ABSTRACT

Diffuse correlations spectroscopy (DCS) is a non-invasive optical technique that, studying the speckle intensity fluctuations of light diffused through a biological tissue, measures its microvascular blood flow. Typically, a long coherence length continuous wave source is used, which limits the possibility to resolve the photon path lengths. Recently, time-domain (TD) DCS was proposed, where a pulsed yet coherent light source is used to resolve the speckle fluctuations at different time-of-flights. Due to the constraint of single-speckle detection and time-resolved acquisition, the technique has a limited throughput which limits depth sensitivity. Here, we demonstrate TD DCS with a superconducting nanowire single-photon detector (SNSPD). The SNSPD has a high quantum efficiency and temporal resolution, while maintaining a very low background and no after-pulsing. We report results on phantom and in vivo experiments, which show the potentiality of the proposed detection system for highly accurate TD DCS experiments.

Keywords: Diffuse correlation spectroscopy, Diffuse Optics, Time-resolved spectroscopy

1. INTRODUCTION

Diffuse correlation spectroscopy (DCS), also called Diffusing Wave Spectroscopy, is a well-established optical technique for the monitoring of particles motion, by studying the speckle intensity fluctuations of diffused light. In the case of biological tissues, its main application is the monitoring of microvascular blood flow (BF)[1]. Typically, a continuous wave long coherence length laser is used for probing the tissue. The continuous wave acquisition limits the depth discrimination since photon with any possible path length are collected. A recent method to overcome this problem is the use of pulsed yet coherent light sources, coupled with time-resolved detection, a technique called time-domain (TD) DCS[2,3]. The technique has the possibility to measure both the optical properties, from the distribution of time-of-flights (DTOF), and the BF, from the intensity auto-correlation function. Also, by exploiting the physical relationship between the photon time-of-flight and the mean depth penetration[4], it is possible to improve significantly the depth sensitivity[5,6].

The main challenges of TD-DCS are on the light source and detection sides. On the source side, an almost transform-limited pulse is necessary to maintain a high temporal coherence together with a sufficiently low temporal resolution (few hundreds of picoseconds). On the detector side, a high quantum efficiency, low noise, single-photon detector is desirable to obtain a good signal-to-noise ratio (SNR). In this work we propose a novel detection system, namely superconducting nanowire single-photon detector (SNSPD)[7], to improve the performances of TD-DCS. After discussing the main differences compared to classical semiconductor single-photon detectors, we report the performance of this novel detector on a tissue-mimicking phantom and in vivo experiments.

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2. EXPERIMENTS AND DISCUSSION

The experimental setup was similar to the one described in Ref. [3]. Briefly, the pulses from a Ti:Sapphire mode-locked laser, with a wavelength of 785 nm, were delivered to the sample using a graded index 100 μm core diameter fiber. The diffused light was recollected in reflectance geometry, at a source-detector separation $\rho = 1\ cm$, with a single-mode 5 μm core diameter fiber (780HP, Thorlabs, Germany). The detection fiber was connected to the SNSPD system (Eos CS, Single Quantum, The Netherlands). The photons time-of-flight and arrival times were acquired with a time-to-digital converter board (TimeTagger Ultra, Swabian Instruments, Germany) with a resolution of 10 ps. First, we measured the instrument response function (IRF) by facing the injection and detection fibers. Then, we measured a tissue-mimicking phantom prepared by diluting a lipid emulsion (Intralipid20, Braun B. Melsungen, Germany) in water (5:95 proportion in mass, respectively). Finally, we performed an *in vivo* measurement on the brachioradialis (forearm) muscle of an adult subject.

Figure 1(a) reports the measured IRF, with the DTOF of the liquid phantom and the *in vivo* experiment (all without background normalization). The IRF full-width at half-maximum (FWHM) was 165 ps, while the full-width at tenth-maximum (FWTM) was 300 ps. Figure 1(b) reports the ungated intensity auto-correlation functions (g_2) of both the experiments, with a 10 s acquisition time. As can be seen, both the IRF and the DTOF have up to 4 decades of dynamic range, without detector diffusion tails typical of semiconductor-based detectors. Also, the auto-correlation functions show a good SNR even at short lag times ($\tau \sim 10^{-6} s$), which typically is perturbed by after-pulsing effects.

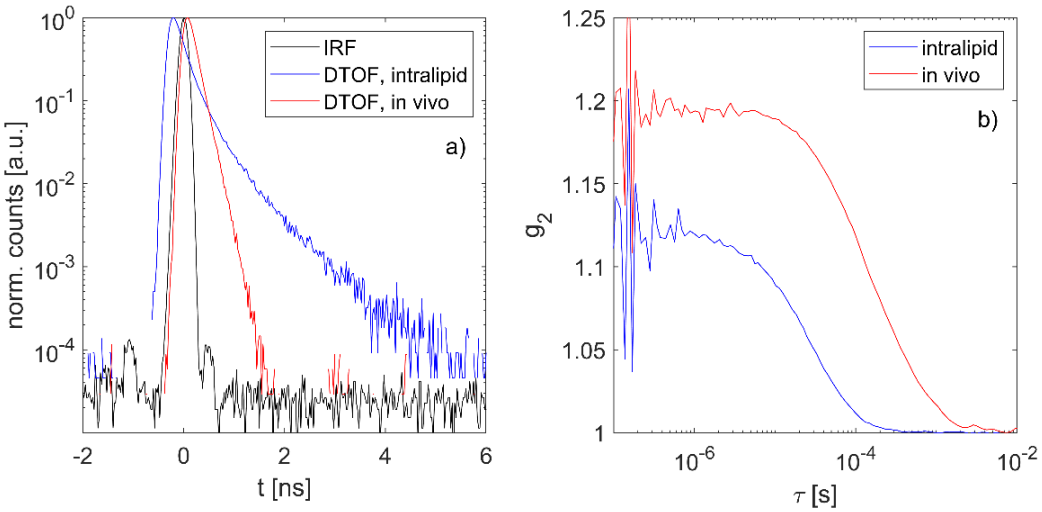

Figure 1: a) Measured Instrument response function (IRF, black line), and distribution of time-of-flights (DTOF) for the liquid phantom (blue line) and the in vivo experiment (red line), with 1 s acquisition time b) Measured ungated intensity auto-correlation functions (g2) for the two experiments (liquid phantom and in vivo), with 10 s acquisition time.

After the initial characterization, we performed two cuff occlusion experiments (on the same subject), by inflating a tornquinet placed above the optical probe to a pressure of 250 mmHg for an arterial occlusion, and 100 mmHg for a venuous occlusion. The intensity auto-correlation functions were acquired continuosly with 1 s sampling time. The average count rate was 400 kcps.

Figure 2 reports the relative BF index (rBFI), normalized by divition to the initial part of each experiment for the liquid phantom [Fig. 2 (a)], and the arterial and venous occlusions [Fig. 2 (b) and (c), respecively]. The vertical dashed lines enclose the time window were the torniqued was inflated. As shown in Fig. 2, the rBFI in the phantom experiment has a good long-term stability, with a coefficient of variation of 4.5%. Also, in vivo experiments showed the expected temporal trends, and sufficient SNR for sampling rates up to 1 s.

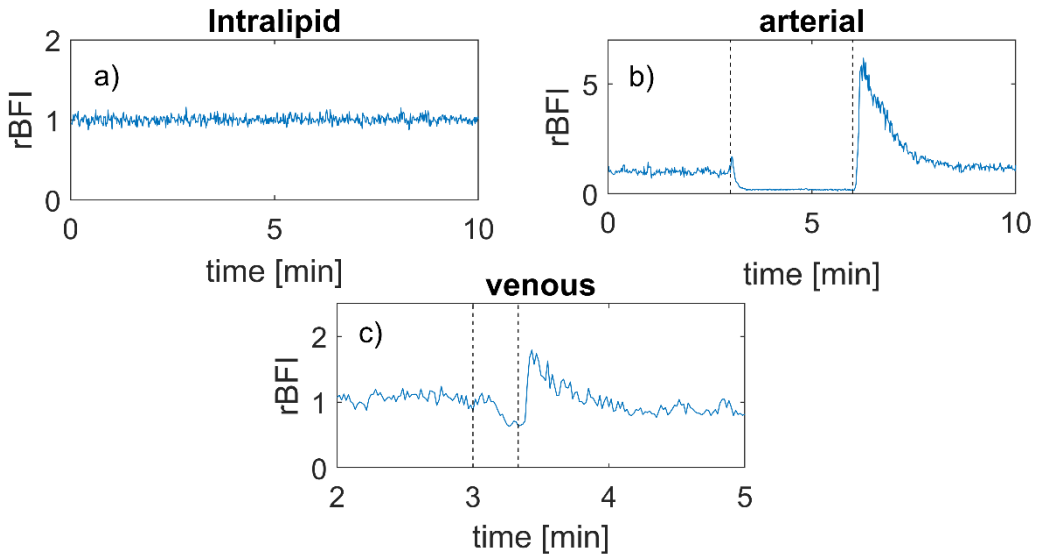

Figure 2: Relative BF index (rBFI) time traces for the intralipid (a), the arterial occlusion (b), and the venous occlusion (c) experiments. The arterial occlusion had a duration of 3 minutes and the venous of 20 seconds. For all three measurement, the rBFI was normalized using the first three minutes of experiment.

To conclude, we have reported a novel detection chain for TD-DCS, and we have discussed its key advantages with respect to previous system. In the future, we will explore multi-channel measurements to increase throughput and thus the depth sensitivity.

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