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High Signal-to-Noise Ratio and Depth Penetration in Time-Domain Functional Near-Infrared Spectroscopy Combining Large Area Detector and High Throughput Electronics

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Abstract: A time-domain functional near-infrared spectroscopy system with probe-hosted large-area detector capable of a throughput of 30 million of counts per second is presented and validated on phantoms and in vivo.

1. Introduction

Time-domain functional near-infrared spectroscopy (TD-fNIRS) relies on injection of short laser pulses in the scattering tissue under investigation and on collection of the shape of the optical pulse backscattered by the tissue at a given distance from the injection point by using time-correlated single-photon counting techniques (TCSPC) [1]. The operation in the time domain has several advantages like the possibility to disentangle absorption from scattering information with a single source-detector pair or the possibility to probe the tissue at different depths just processing photons detected at different delays with respect to the injection time. On the other hand, TD-fNIRS systems are typically complex and bulky, requiring the use of optical fibers to guide the light from the tissue under investigation to the detector. In this way, light collection is limited by the optical fiber core dimension and its numerical aperture. Additionally, state-of-the-art detectors and TCSPC systems typically feature a limited photon counting rate of few millions of counts per second (Mcps) due to a dead-time occurring after each photon detection, requiring a long measurement time to obtain a significant amount of late-arriving photons, i.e. photons having the chance to probe deeper regions of the tissue under investigation. Here we present a TD-fNIRS system based on: i) high average power (~50/30 mW at 670/830nm) pulsed laser sources (LDH-P-C-670M/830M, PicoQuant GmbH, Germany) operated at 40 MHz repetition rate; ii) probe-hosted (to maximize collection of light) 3 x 3 mm^2 SiPM (S13360-3050CS, Hamamatsu Photonics, Japan) combined with home-made electronics to optimize the single-photon timing resolution; iii) high-throughput (up to 160 Mcps with < 650 ps dead time) TCSPC electronics (MultiHarp 150, PicoQuant GmbH, Germany). The overall timing resolution of the system is < 300 ps full-width at half maximum and it is capable of reaching count-rates up to 40 MHz, only limited by the laser repetition rate. Due to the extreme photon counting rate, suitable pile-up distortion [2] correction strategies were implemented.

2. Results

The performances of the new system have been tested on phantoms at different count rates (1 Mcps, 15 Mcps and 30 Mcps) with a 3 cm source-detector separation using the 670 nm laser head. After having successfully tested the system performance in retrieving homogeneous optical properties (data not shown), we tested its sensitivity to localized absorption perturbation set at different depths inside a homogeneous background. For this purpose, a solid mechanically switchable phantom was used [3]. Inside the phantom, a rod featuring the same optical properties of the bulk phantom (at 670 nm, absorption coefficient $\mu_a \approx 0.1$ cm^{-1}, reduced scattering coefficient $\mu_s' \approx 10$ cm^{-1}) can move. The rod embeds a perturbation equivalent to a $\Delta\mu_a \approx 0.17$ cm^{-1} over a volume of 1 cm^3. The contrast (i.e. the relative change in the number of counts produced by the perturbation inside a 500 ps gate window starting at a delay of 720 ps with respect to the injection of the laser pulse inside the phantom) produced by the perturbation set at different depths is shown in Fig. 1 (left). As expected from theory, thanks to the proper correction of pile-up distortions in the distribution of time of flight of the detected photons [2], the contrast does not significantly change with the counting rate. On the contrary, contrast-to-noise ratio (i.e. the ratio between the absolute change in the number of counts used to compute the contrast and the fluctuation of the number of counts in the homogeneous case

in the same gating window) improves in the high-throughput case thanks to the increased number of detected photons. However, measurements performed at 30 Mcps appear to be less effective, probably due to the strong pile-up distortion that increases the weight of the fluctuations in the number of counts, since correction algorithms typically introduce scaling factors for the different bins of the histogram amplifying both signal and noise. Additionally, we tested the system in-vivo, checking both the capability to properly follow trends in oxy-/deoxy-hemoglobin (O_2Hb/HHb) during venous/arterial arm occlusions (data not shown) by placing the probe on the arm of healthy volunteers, as well as during finger tapping exercises by placing the probe on their head (around the C3 position according to the 10⁄20 EEG international system). In this latter case, the protocol was composed by 5 repeated blocks, each consisting of: 20 s of rest, 20 s of task, and 20 s of recovery, for 300 s of total measurement time. Both laser wavelengths were used, with a relative delay of 12 ns so that they are reconstructed together in the same histogram. The acquisition rate was 1 Hz at an overall count rate of 30 Mcps (i.e. 15 Mcps/wavelength) and the source-detector distance was 3 cm. To enable the comparison with a system close to the state-of-the-art, a second detector (SiPM module, active area: 1.3 x 1.3 mm^2 where light was coupled though a 1-mm-core optical fiber collecting the same backscattered light very close to the probe-hosted SiPM) was always acquiring in parallel, counting photons at a rate of about 1 Mcps. This protocol was approved by the Ethical Committee of Politecnico di Milano and conducted in agreement with the Declaration of Helsinki.

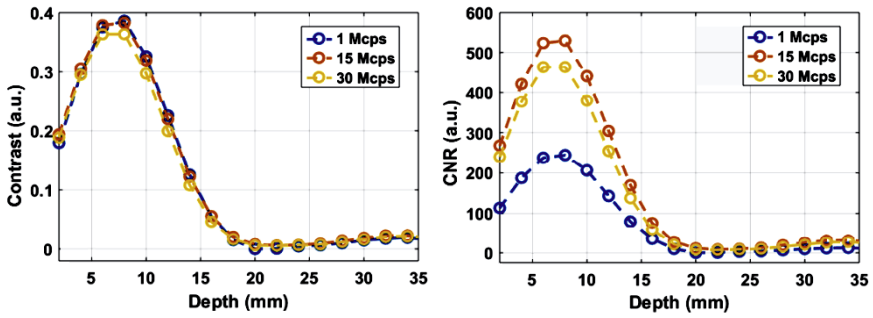

Fig. 1. Contrast (left) and contrast-to-noise ratio (right) of a 170% absorption perturbation at different depts.

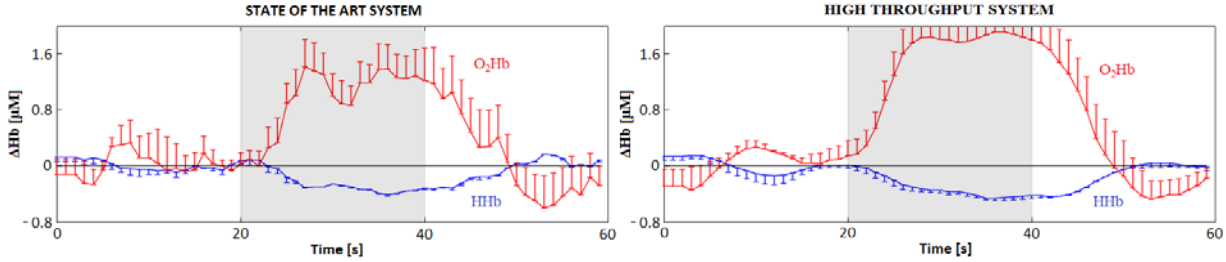

Fig. 2. Changes in brain hemoglobin (ΔHb) during finger tapping exercise monitored with the 2 systems.

Fig. 2 reports the variation of both HHb and O_2Hb obtained after folding average of the 5 repetitions on one of the subjects (moving average 3 s). Error bars represent the standard deviation among the 5 blocks. Both the state-of-the-art system (left) and the high throughput system (right) can properly detect the task-related increase in O_2Hb and the fainter decrease in HHb, which are the typical fingerprints of a brain activation. However, it is evident a significant improvement in signal-to-noise ratio with the high throughput system as compared to the acquisition performed in classical conditions. Additionally, in this case time-gated contrast analysis demonstrated higher depth penetration (data not shown). In conclusion, a new system able to operate at photon counting rates far beyond (> 1 order of magnitude) classical conditions for TD-fNIRS system has been designed and validated. The huge improvement in signal-to-noise ratio opens the way more robust, deeper and faster diffuse optical measurements.

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3. References

[1] T. Durduran et al., "Diffuse optics for tissue monitoring and tomography," Rep. Prog. Phys. **73,** 1-43 (2010).
[2] P. B. Coates, "The correction for photon 'pile-up' in the measurement of radiative lifetimes," J. Phys. E: Sci. Instrum. **1,** 878-43 (1968).
[3] A. Pifferi et al., "Mechanically switchable solid inhomogeneous phantom for performance tests in diffuse imaging and spectroscopy," J. Biomed. Opt. **20,** 1-10 (2015).