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Design and Characterization of a Fast Multi-Channel Time-Domain NIRS and DCS Device for Clinical Applications

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Abstract: We present a device for combined Time-Domain NIRS and DCS measurements, featuring two detection channels and working at up to 50 Hz acquisition rates. Laboratory and *in-vivo* characterization shows its capability to make robust and reliable measurements.

1. Introduction

Time-Domain (TD) Near-Infrared Spectroscopy (NIRS) and Diffuse Correlation Spectroscopy (DCS) are non-invasive diffuse optics techniques that allow to assess absolute oxy- and deoxy-hemoglobin concentrations and blood flow, respectively [1]. By using both techniques simultaneously, it is possible to obtain a comprehensive real-time characterization of tissues such as brain and skeletal muscles, both at rest and during various tasks.

Whereas low sampling rates (around 1 Hz) are sufficient to monitor extended brain activations or physiological changes, TD NIRS and DCS acquisitions at higher frequencies (20 - 40 Hz) allow to detect hemodynamic oscillations and pulsatile components of signals. The blood flow pulsatility, in particular, offers a uniquely non-invasive way of estimating intra-cranial pressure [2].

In this work, we present a hybrid TD NIRS and DCS device capable of fast (up to 50 Hz) acquisition rates. The system features two separate detection channels for both TD NIRS and DCS, improving depth discrimination in layered tissues.

2. Materials and methods

2.1. Device description

Figure 1 shows a block scheme of the main components of the system.

The TD NIRS module is a state-of-the-art device (PIONIRS s.r.l., Milan, Italy), employing two laser sources at 685 nm and 830 nm. The output pulses are sent through two variable optical attenuators before being coupled into two graded-index optical fibers, bundled together to create a single injection spot. Diffuse light is collected by two separate bundles of graded-index optical fibers, and detected by two silicon photomultipliers. Two Time-Correlated Single-Photon Counting (TCSPC) boards allow reconstruction of photon Distribution of Time-Of-Flight (DTOF) histograms.

The DCS module uses a single highly coherent continuous-wave laser diode, emitting light at 784 nm. A 50:50 beam splitter is coupled to two step-index optical fibers, allowing light injection in two separate spots. The back-scattered light is collected by four step-index single-mode optical fibers, and detected by four single-photon avalanche diodes. A multi-channel time-tagging board allows storing of photon detection times for each channel, which are then processed by a software correlator to obtain the autocorrelation functions.

The whole device is housed inside a 47 cm × 41 cm × 17 cm case, and is operated by an external PC. An in-house software allows synchronized TD NIRS and DCS acquisitions and real-time data analysis and visualization through a user-friendly interface.

The injection and collection optical fibers are hosted in a custom-made 3D-printed optical probe. It makes use of 3.5 mm prisms to deflect light by 90° both in injection and detection, and its flexibility allows it to adhere easily to the skin for *in-vivo* measurements. As shown in Figure 1, it features two separate injection spots: one hosts a fiber bundle with the TD NIRS injection fibers and one DCS injection fiber, while the other hosts the other DCS injection fiber. Splitting the injected DCS power this way allows us to double the signal level while complying with safety limitations for *in-vivo* measurements. The short-distance detection channel is placed 15 mm away

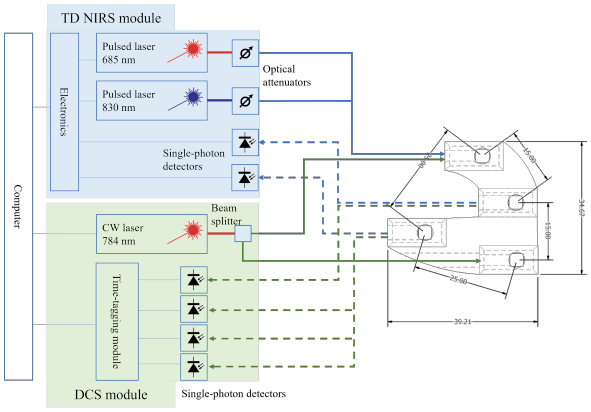


Fig. 1: Block scheme of the device and optical probe. Solid arrows indicate injection fibers, dashed arrows indicate collection fibers. Units are in mm.

from both injection spots and hosts a fiber bundle coupled to one TD NIRS detector and one DCS detector, while the long-distance channel (placed 25 mm away from both injections) is coupled to one TD NIRS detector and three DCS detectors. The probe incorporates a combination of a 0.8 OD neutral density filter and a black-printed transparent film to equalize the TD NIRS signal detected at the long and short channels.

2.2. *Characterization measurements*

To characterize the TD NIRS module, the MEDPHOT protocol [3] was adopted, comprising assays of linearity, accuracy, noise, stability and reproducibility. A kit of 32 solid resin phantoms with varying optical properties (absorption coefficient μ_a ranging from $\simeq 0$ to $\simeq 0.42\,\mathrm{cm}^{-1}$, reduced scattering coefficient μ_s' ranging from $\simeq 5\,\mathrm{cm}^{-1}$ to $\simeq 20\,\mathrm{cm}^{-1}$ at 690 nm) was employed for the measurements. The optical properties were retrieved using the solution of the diffusion equation for homogeneous semi-infinite media.

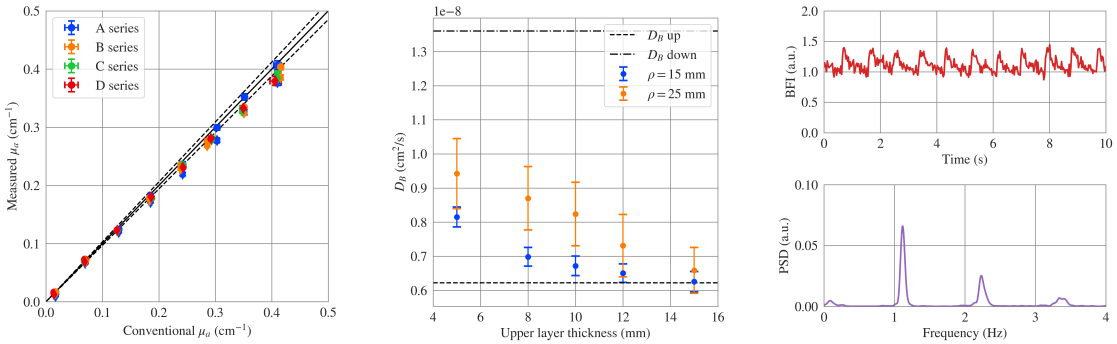
The DCS module was characterized through measurements on calibrated liquid phantoms, using lipofundin as the scattering element, black India ink as the absorbing element, and varying glycerol concentrations to control the viscosity [4]. Bilayer phantoms with different viscosities in the upper and lower compartments were measured to investigate the depth-resolving capabilities of the device. The solution of the correlation diffusion equation for homogeneous semi-infinite media was used to retrieve the Brownian diffusion coefficient D_B.

Additionally, an *in-vivo* measurement on one volunteer (male, 25 years old) was carried out to test the ability of the system to monitor the pulsatile component of blood flow in a clinical setting. During the measurement, the subject lay in a semi-reclined position, and the probe was placed on the forehead above the eyebrow. The probe used for this measurement had a single source-detector separation of 15 mm, and blood flow was monitored for 2 minutes with a sampling frequency of 33 Hz. The solution of the correlation diffusion equation for homogeneous semi-infinite media was used to analyze the data, and the blood flow index (BFI) was calculated assuming effective Brownian motion. The power spectral density (PSD) of the BFI signal was computed using Welch's method, with Hamming windows of 20 s and 50% overlap.

3. Results and discussion

Figure 2a shows the linearity and accuracy at 830 nm for both source-detector separations (similar results were obtained at 685 nm). The "conventional" values were obtained with a similar TD NIRS device by the same manufacturer. The general alignment of the data points shows good linearity, and the fact that they are disposed along the 1:1 line and generally fall within the $\pm 3\%$ error bars indicates good accuracy as well. The noise assay showed that at least 70,000 photon counts are needed in a DTOF to retrieve μ_a with a coefficient of variation CV $< 3\%$. During the 14-h stability measurement, the optical properties retrieved at the short source-detector separation took about 1 h to reach stationarity, while the long source-detector channel only needed 15 min. After warm-up, the optical parameters at both wavelengths and both channels exhibited a CV of about 1%. Good reproducibility was obtained for both μ_a and μ_s' at both inter-fiber distances, with the optical parameters measured each day being equal within one standard deviation and the inter-day CV being lower than 3%.

Results of the DCS characterization on the bilayer phantom are shown in Figure 2b. Since the data was analyzed assuming a homogeneous medium, the resulting D_B lies between that of the two layers. More specifically, as the upper layer thickness increases, the measured D_B gets closer and closer to that of the superficial layer, as expected. This effect is stronger at the short source-detector separation, since photons collected closer to the source haven't



(a) (b) (c)

Fig. 2: Results of the characterization measurements. Panel (a): MEDPHOT absorption linearity at 830 nm. Circles represent the values measured for an inter-fiber distance $\rho = 15$ mm, diamonds are for $\rho = 25$ mm. The colors represent the four MEDPHOT scattering series, error bars represent the standard deviation over 10 repetitions, and the 1:1 (solid) and $\pm 3\%$ lines (dashed) are also shown. Panel (b): Brownian diffusion coefficient of the bilayer phantom as a function of the upper layer thickness. Error bars represent standard deviations over 30 repetitions, black lines represent the value of D_B in the upper and lower layers. Panel (c): time trace of the BFI signal (top) and corresponding PSD (bottom) during the *in-vivo* measurement.

reached as deep into the sample. As such, especially for lower thicknesses, the D_B measured at $\rho = 25$ mm is closer to that of the bottom layer.

The results of the *in-vivo* validation are shown in Figure 2c, whose top panel shows the BFI signal over the first 10 seconds of measurements. The relatively low amplitude of the pulsatile waveform is due to the limited penetration of light inside the adult human skull. Nevertheless, the peak in the PSD at the cardiac frequency is visible in the bottom plot, together with its higher-order harmonics. These results show the ability of the DCS module to detect fast blood flow oscillations.

4. Conclusions

We have presented a new hybrid TD NIRS and DCS device and characterized it through established protocols. Measurements on calibrated phantoms showed good linearity and accuracy for the TD NIRS module, demonstrating its ability to detect variations of hemodynamic parameters without distortions, as well as to accurately retrieve their absolute values. As for the DCS module, the presence of two detection channels working at different source-detector separations allows some depth discrimination even when using a simple homogeneous model for data analysis. Better results could be obtained by adopting more refined models, which however are not part of the characterization protocols adopted.

In-vivo measurements demonstrated the capability of the device to make robust measurements, making it suitable for clinical applications. Indeed, on top of traditional functional state evaluation, the high temporal resolution of the device enables reliable detection of pulsatile signals and fast muscle activations during exercise protocols such as cycling.

5. Acknowledgments

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