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Oxyhemoglobin measurements using 1064 nm light

Laura Di Sieno, Alessandro Bossi, Francesco Sangalli, Alessandro Torricelli, Ilias Tachtsidis, Turgut Durduran, Antonio Pifferi, and Alberto Dalla Mora

***Abstract*—While standard optical oximetry systems make use of two/more wavelengths across the isosbestic point of oxy/deoxy-hemoglobin and between 650 and 900 nm, this work explores the possibility to use only light at 1064 nm wavelength to detect the absolute oxyhemoglobin concentration in tissues using time-domain diffuse optics. Furthermore, the possibility to exploit a 1064 nm wavelength coupled with wavelengths of classical approaches is also discussed. Our findings demonstrate a reasonable overlap of the new approaches as compared to the standard one, with confined discrepancies potentially linked to a not established agreement in the scientific community on the exact value of extinction coefficients of tissue constituents beyond 1000 nm, as well as to an increased penetration depth in the tissue at 1064 nm due to a lower scattering coefficient as compared to the visible range. These findings open the way to further studies in the field, also given the increasing advancements in lasers and detectors at 1064 nm.**

***Index Terms*—Time-domain diffuse optics, tissue oxygen content, in-vivo measurements of hemodynamics, time-correlated single-photon counting.**

I. INTRODUCTION

SINCE five decades, light is considered an attractive tool to non-invasively probe the human body down to a depth of few centimeters [1] for purposes encompassing oximetry, neurology and oncology [2]. Indeed, information about tissue composition and microscopic structure are encoded into the absorption (μ_a) and reduced scattering (μ_s') coefficient spectra, respectively.

Among different near-infrared spectroscopy (NIRS) measurement techniques, the adoption of a time-domain (TD) approach is recognized as the one with the highest informative content, since it permits to independently resolve μ_a and μ_s' even with a single measurement point and for its high depth selectivity related to the knowledge of the photons' time of flight [3].

The number of constituents (chromophores) that can be independently estimated with NIRS is linked to the number of wavelengths used to probe the tissue. Indeed, at each wavelength (λ) the absorption spectrum - $\mu_a(\lambda)$ - is the result of overlapping contributions by different chromophores [4] following the Lambert-Beer law. The independent retrieval of each chromophore concentration is possible by solving a system of equations through a matrix inversion, where the number of unknowns to be resolved (*i.e.*, chromophore concentrations) must at least match the number of wavelengths adopted. The standard approach in optical oximetry is to focus on O_2Hb and HHb only, assuming negligible (or constant and known) contribution from other chromophores like water and lipids. To retrieve the absolute concentration of both oxy- and deoxy-hemoglobin (O_2Hb and HHb), at least two wavelengths across the isosbestic point (*i.e.*, $\lambda \approx 800$ nm) [5] are needed, while the use of $\lambda < 650$ nm or $\lambda > 900$ nm are normally avoided because of a high absorption from blood and water, respectively.

Recently, the use of light at wavelengths beyond the water absorption peak at 970 nm (e.g., 1064 nm [6],[7],[8], where water exhibits a local absorption minimum) has been validated for diffuse correlation spectroscopy, a technique sensitive to the microvascular tissue blood flow, while the present work

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This work involved human subjects in its research. Approval of all ethical and experimental procedures and protocols was granted by the Ethical Committee of Politecnico di Milano under Application No. 22/2023, and performed in line with the Declaration of Helsinki.

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ICFO has equity ownership in the spin-off company HemoPhotonics S.L. and TD is inventor of relevant patents. ADM, AP and AT are co-founders of PIONIRS s.r.l., a spin-off company from Politecnico di Milano (Italy).

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considers the possibility to adopt 1064 nm light for NIRS. This approach can indeed bring several advantages, *i.e.*: *i*) a lower energy per photon, thus providing more photons per laser pulse and lessening the safety issue related to skin laser exposure; *ii*) a lower tissue scattering, thus potentially improving the penetration depth; *iii*) a broad availability of laser sources, also because of developments linked to their wide application for telecommunications; *iv*) a quasi-negligible extinction coefficient of HHb as compared to O_2Hb, thus both bringing to the possibility to sense the absolute tissue oxygenation level by adopting a single wavelength approach, removing ill-condition issues of the matrix to be inverted as compared to the traditional two/more wavelength approach [4], and providing a viable alternative in the choice of the $\lambda > 800$ nm in a more traditional two/more wavelength approach, with the potential to improve the condition number of the matrix to be inverted. On the other hand, these advantages are counterbalanced by: *i*) a missing agreement in the scientific community on exact values of hemoglobin species extinction coefficients beyond 1000 nm [9]; *ii*) a low hemoglobin absorption in general with respect to water and lipids that makes their contribution not negligible beyond 900 nm [10]; and *iii*) a limited availability of time-resolved (jitter of ≈ 100 ps) detectors with high diffuse optical responsivity [11], whose maximization requires the combination of a wide sensitive area and photon detection efficiency at this wavelength [12], thus limiting the maximum signal-to-noise ratio.

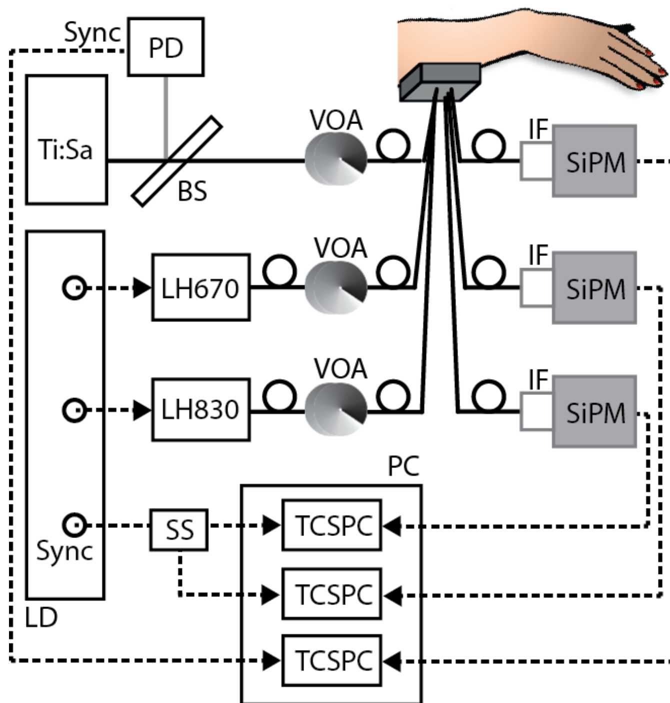

Fig. 1. Experimental setup.

In this context, the present work aims to provide a first preliminary evidence about the possibility to operate at $\lambda = 1064$ nm to estimate the absolute concentration of O_2Hb in vivo, independently of other chromophores. Further, its use in a dual wavelength approach is also discussed. Results are compared with those obtained using a standard system working at two/more wavelengths across the isosbestic point.

II. MEASUREMENTS PROTOCOL AND DATA ANALYSIS

To explore the possibility to use the 1064 nm wavelength to recover the absolute concentration of O_2Hb in tissues, we used the setup shown in Fig. 1, which hosts two different laser sources: a custom made tunable Titanium-Sapphire (Ti:Sa) laser with active mode-locking and acousto-optical modulation [13] providing pulses at $\lambda = 1064$ nm (repetition rate: 100 MHz) and a commercially available multichannel laser driver (LD, Sepia PLD 828 from Picoquant GmbH) connected to two pulsed diode source laser heads (LH670 and LH830, LDH-P-C-670M and LDH-PC-830M from Picoquant GmbH) at $\lambda = 670$ nm and $\lambda = 830$ nm, with repetition rate of 40 MHz. A timing reference signal (Sync) is derived from the optical beam of the Ti:Sa laser by taking a small fraction of the beam power through a beam splitter (BS), which is detected by a photodiode (PD). The timing reference for the diode laser is instead generated by the LD itself, and then split into two identical signals through an electrical signal splitter (SS). Each Sync signal is then connected to a PC-hosted Time-Correlated Single-Photon Counting Board (TCSPC, SPC-130 from Becker&Hickl GmbH, one per wavelength). Light exiting from the lasers is attenuated using variable optical attenuators (VOAs) and then injected into the sample through step index multimode silica optical fibers. The three collection fibers (one per wavelength) are 1-mm diameter core silica ones. Each collection fiber collects photons re-emitted from the tissue under investigation, which are then focused onto a single-photon detector (Silicon PhotoMultiplier -SiPM- module [14], one per wavelength) through a pair of 1 inch achromatic lenses with focal length of 30 mm. An interference filter (IF) was inserted in the collimated beam so as to record a single wavelength on each detector. When a photon is detected, an electrical pulse is generated by the SiPM and fed to the TCSPC board. The Instrument Response Function (IRF) was recorded and its full width at half maximum was computed to be around 180, 285 and 170 ps for 670, 830 and 164 nm wavelength respectively. The source-detector distance was set to 3 cm and fibers were arranged to probe the same volume of the sample. The in-vivo measurements were conducted on 4 healthy volunteers, after obtaining their written informed consent. The measurements got approved by the Ethical Committee of Politecnico di Milano and they were conducted in compliance with the Declaration of Helsinki. The task consisted of both arterial and venous occlusions induced with the sphygomanometer cuff inflation with the following timing: *i*) 60 s of baseline recording phase; *ii*) 180 s of arterial occlusion (cuff inflated well above the systolic pressure of the subject, i.e. 250 mmHg for all subjects); *iii*) 240 s of recovery phase; *iv*) 60 s of venous occlusion (cuff

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inflated between the specific systolic and diastolic pressure of each subject); *v*) 60 s of recovery. During the overall 10 minutes of acquisitions for each subject, measurements were taken with an integration time of 0.5 s. The O_2Hb and HHb concentration was computed using the modified Lambert-Beer law. The extinction coefficient for the two chromophores at the three wavelengths of the system where taken from Ref. [15]. Not depending on the approach used, to retrieve the concentration of the O_2Hb and HHb, the μ_a due to the both hemoglobin species is needed. It was computed, together with the μ_s' values, fitting the experimental curves to the radiative transfer equation under the diffusion approximation [16],[17]. The finite response of the system was taken into account convolving the theoretical curve with the acquired IRF of the system. In all cases, the value of μ_a due to the O_2Hb and HHb where derived after the subtraction of both water and lipid contributions, supposing the overall composition to be 30% and 70% respectively [18]. Furthermore, when recovering both O_2Hb and HHb, a subject specific water fraction has been estimated using baseline acquisitions and supposed to be constant during the whole task. To do so, the three wavelengths have been simultaneously considered to solve the modified Lambert-Beer law.

III. Results and Discussion

Fig. 2 represents the variation of O_2Hb concentration with respect to baseline for all subjects (rows) recovered using the single wavelength approach (1064 nm) and compared with the standard NIRS approach (*i.e.*, solving the system using two "standard" wavelengths – 670 and 830 nm – thus recovering both O_2Hb and HHb). Baseline values computed in the first 15 s of the exercise are reported in Table I. For the first 30 s of the arterial occlusion, the O_2Hb concentration variation recovered using only 1064 nm or the standard NIRS system are overlapped. At larger times, the value recovered using the 1064 nm wavelength keeps decreasing, while the standard 2-wavelength system seems to reach a plateau. Moreover, as reported in Table I, the baseline value of O_2Hb concentration recovered using the pure 1064 nm is higher than what computed using the standard NIRS approach (except for subject 2). As soon as the arterial occlusion is removed, the agreement on the O_2Hb concentration recovered with both systems is restored. For what concerns the venous occlusion, the variation in O_2Hb concentration for the two cases is fairly comparable also in terms of slope (except for some discrepancy in subject 3, though the general shape and ripples are preserved).

Regarding the overestimation of both the O_2Hb baseline and variation when using the 1064 nm alone, the cause may be ascribed to several factors, such as: *i*) a non-correct value of the O_2Hb and HHb extinction coefficient at 1064 nm, which is not extensively reported in literature; *ii*) to the different penetration depths explored by photons (photons at 1064 nm are expected to experience a higher penetration depth, about 22% higher) [16], which may determine a different O_2Hb concentration, while HHb is less affected as veins are in general more superficial than arteries; *iii*) to the contribution of

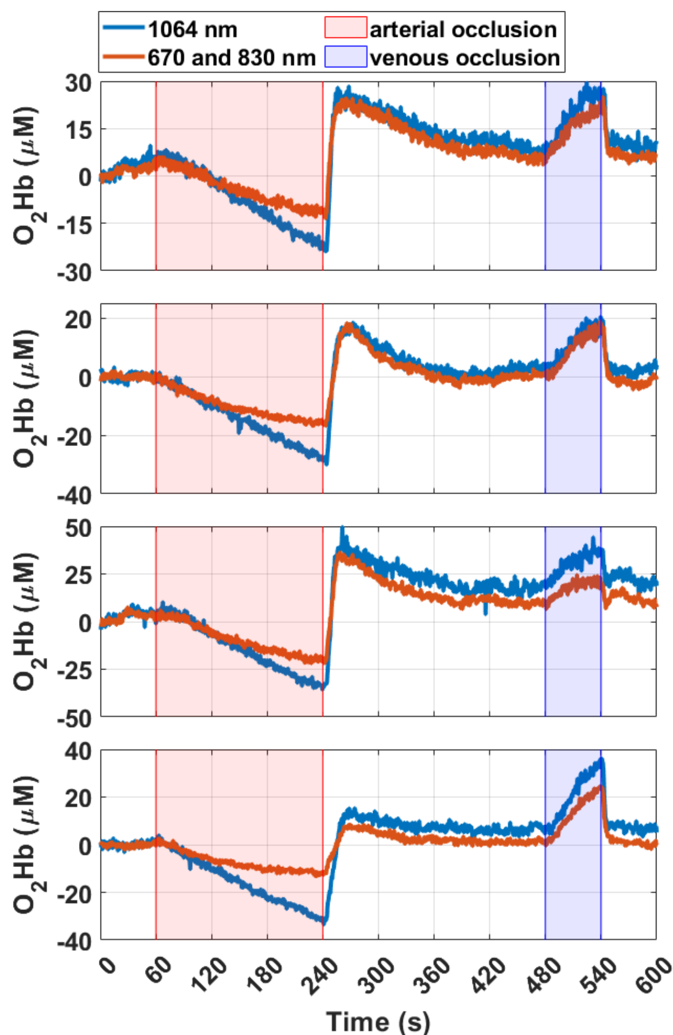

Fig. 2. Concentration of O_2Hb retrieved using the standard NIRS system (employing 670 and 830 nm, orange lines) and with the single wavelength approach (1064 nm, blue lines). Each graph represents a single volunteer.

additional absorbers (e.g. water, lipids).
So far, we investigated the capability of 1064 wavelength alone to detect O_2Hb variations. As a further insight we explored the usefulness of the same 1064 wavelength combined with another "standard" wavelength to detect both O_2Hb and HHb. Fig. 3 reports the variation of O_2Hb and HHb concentrations with respect to the average baseline value (reported in Table I).
Three cases are considered, namely: *i*) 670 and 830 nm (*i.e.*, the standard NIRS approach); *ii*) 670 and 1064 nm (*i.e.*, a combination where the former wavelength mostly probes HHb, while the latter is almost insensitive to HHb); *iii*) 670, 830 and 1064 nm with the idea to improve the robustness of the retrieval of O_2Hb and HHb, adding a third equation.

For the O_2Hb variation (Fig. 3 left), it is clear that the use of 1064 nm always determines an increase in the reported changes. In-fact, while using the two-wavelength (*i.e.*, 670 and 1064 nm) configuration, the O_2Hb reaches higher variation with respect to the standard NIRS system (*i.e.*, 670 and 830 nm), on the other hand, if the 1064 nm is added to 670 and 830 nm, the recovered

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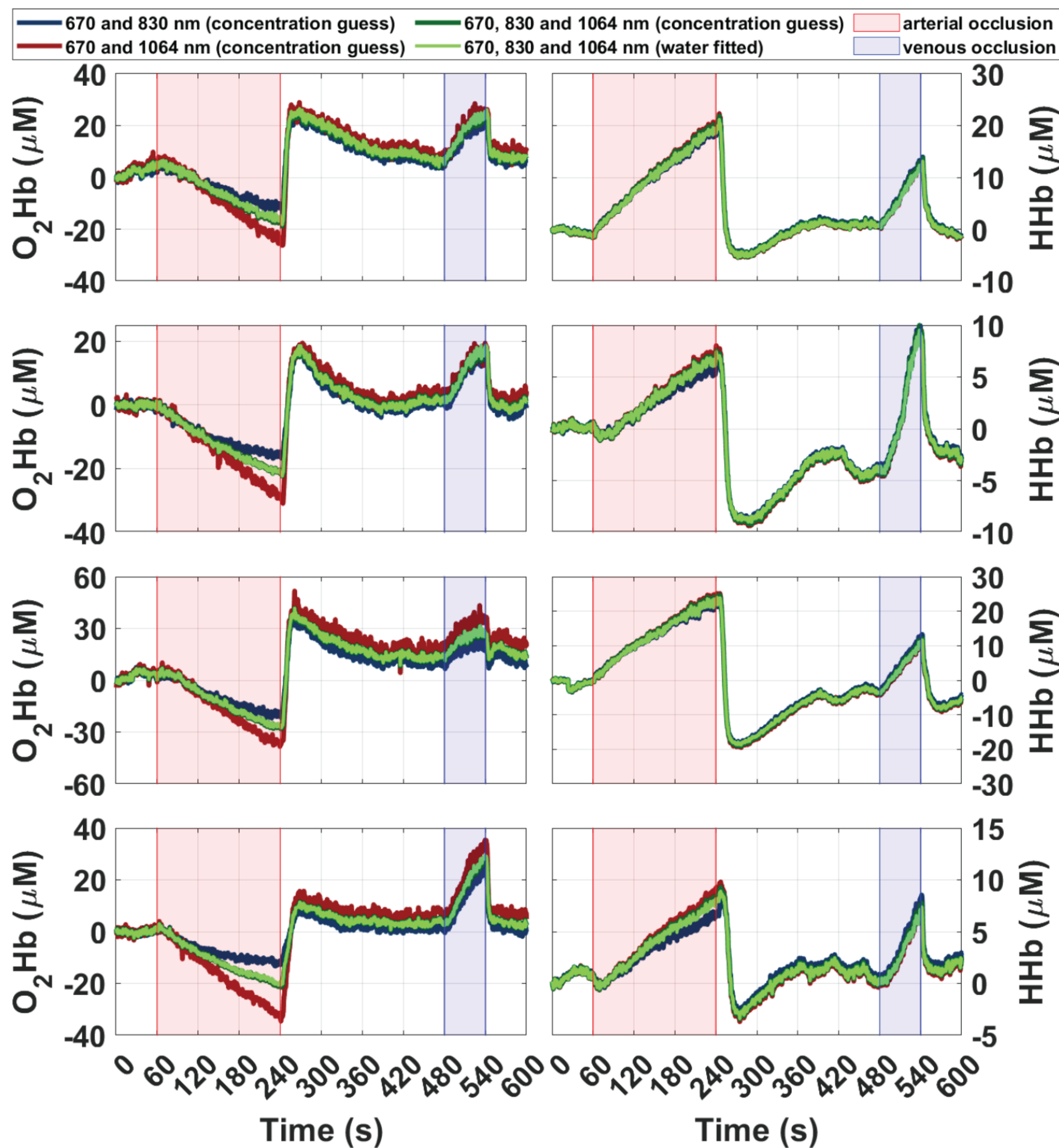

Fig. 3. Concentration of O_2Hb (left) and HHb (right) retrieved using the standard NIRS system (employing 670 and 830 nm, blue lines), 670 and 1064 nm (red lines) and 670, 830 and 1064 nm (dark green lines) for all volunteers (rows). Light green curves indicates the attempt to fit the subject specific water content.

concentration is in between the other two cases. Moreover, if the subject specific water content is extrapolated from the data (using the case with 3 wavelengths available), we see no significant differences in the retrieved concentration changes of O_2Hb as compared to the 30% water and 70% lipid assumption. For what concerns the HHb change (Fig. 3 right), no major variations are observed, as expected, notwithstanding the method use to estimate the water content.

Looking now at the baseline concentrations (see Table I) for unconventional NIRS approaches (*i.e.*, “670, 1064 nm” as well as “670, 830, 1064 nm”), it is possible to notice a good agreement with the standard NIRS approach (*i.e.*, “670,

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TABLE I

AVERAGE BASELINE VALUE OF O_2HB AND HHB CONCENTRATION COMPUTED FOR THE DIFFERENT COMBINATIONS OF WAVELENGTHS USED IN THE EXPERIMENTS (IN BRACKETS ARE REPORTED VALUES COMPUTED FITTING THE WATER CONTENT).

Subject	***O_2Hb* baseline concentration [μM]**				***HHb* baseline concentration [μM]**			
	1064 nm	670, 830 nm	670, 1064 nm	670, 830, 1064 nm	1064 nm	670, 830 nm	670, 1064 nm	670, 830, 1064 nm
1	95.1	91.2	91.3	91.2 (72.6)	NA	33.4	33.4	33.4 (34.2)
2	84.8	89.9	80.9	86.0 (73.0)	NA	34.7	35.6	35.3 (35.3)
3	105.8	94.8	100.8	97.4 (75.5)	NA	45.4	44.7	44.9 (45.8)
4	89.7	71.6	86.8	78.1 (51.0)	NA	27.8	26.2	26.7 (28.9)

830 nm"). However, when estimating the subject specific water fraction, the retrieved O_2Hb values are lower for all the subjects, while consistency is preserved for HHb. This may be due to the unrealistic retrieved value of water fraction (in the order of 120-130%), most probably resulted in particular from neglecting other absorbers playing a role at 1064 nm, such as lipids and collagen, as well as again to the different penetration in the tissue at 1064 nm.

IV. CONCLUSIONS AND FUTURE PERSPECTIVES

To the best of our knowledge, in this manuscript we present for the first time the use of the 1064 nm wavelength for in-vivo time-domain NIRS measurements related to hemodynamics. We firstly demonstrated that the use of a wavelength longer than 900 nm (in our case 1064 nm) can enable the retrieval of O_2Hb even using a single wavelength. The results obtained show that the quantification of O_2Hb changes in concentration is feasible even using only 1064 nm despite some discrepancies with respect to the value recovered with a standard NIRS system (*e.g.*, based on 670 and 830) are observed. Also for what concerns the absolute value of O_2Hb concentration, an overestimation of the baseline value is reported when using the single wavelength approach.

Secondly, we tested the possibility to use the 1064 nm as a second (or even third) wavelength used in the retrieval of both O_2Hb and HHb. Also in this case, discrepancies in temporal changes with respect to the standard NIRS system are reported. All these discrepancies, found when using the long wavelength, could be partially ascribed to several reasons such as *i*) the difficulties to find reliable extinction coefficient for O_2Hb and HHb; *ii*) a different penetration depths explored by photons; *iii*) the contribution of additional absorbers (e.g. water, lipids). However, these may also be due to an increased depth of investigation within the tissue because of the inverse dependence on wavelength of the reduced scattering coefficient, thus opening the way to new approaches in the field of NIRS. Moreover, possible different behaviors in the O_2Hb concentration can be due to the choice of a simple homogeneous model for the fitting procedure yet realistic for a massive response as for arterial and venous occlusion. In future, theoretical works to better understand the effect of the long wavelength (in this paper, 1064 nm) are foreseen as well as measurements to gather precise extinction coefficient for both O_2Hb and HHb over a large wavelength range.

REFERENCES

[1] H. Ayaz et al., "Optical imaging and spectroscopy for the study of the human brain: status report," *Neurophotonics*, vol. 9, no. S24001, Aug. 2022, doi: 10.1117/1.NPh.9.S2.S24001.

[2] A. Torricelli et al., "Time domain functional nirs imaging for human brain mapping," *NeuroImage*, vol. 85, pp. 28–50, Jun. 2013, doi: 10.1016/j.neuroimage.2013.05.106

[3] T. Durduran, R. Choe, W. B. Baker, and A. G. Yodh, "Diffuse optics for tissue monitoring and tomography," *Rep. Prog. Phys.*, vol. 73, no. 7, Jul. 2010, Art. no. 076701, doi: 10.1088/0034-4885/73/7/076701.

[4] J. D. Veesa and H. Dehghani, "Functional near infrared spectroscopy using spatially resolved data to account for tissue scattering: A numerical study and arm-cuff experiment," *J. Biophotonics*, vol. 12, no. 10, Jun. 2019, Art. no. e201900064, doi: 10.1002/jbio.201900064.

[5] F. Scholkmann et al., "A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology," *NeuroImage*, vol. 85, pp. 6–27, Jan 2014, doi: 10.1016/j.neuroimage.2013.05.004.

[6] S. A. Carp et al., "Diffuse correlation spectroscopy measurements of blood flow using 1064 nm light," *J. Biomed. Opt.*, vol. 25, no. 9, Sep. 2020, Art. no. 097003, doi: 10.1117/1.JBO.25.9.097003

[7] M. B. Robinson, et al. "Portable, high speed blood flow measurements enabled by long wavelength, interferometric diffuse correlation spectroscopy (LW-iDCS)," *Sci. Rep.*, vol. 13, no. 1, May 2023, Art. no. 8803, doi: 10.1038/s41598-023-36074-8

[8] C.-S. Poon et al., "First-in-clinical application of a time-gated diffuse correlation spectroscopy system at 1064 nm using superconducting nanowire single photon detectors in a neuro intensive care unit," *Biomed. Opt. Express*, vol. 13, no. 3, pp. 1344–1356, Mar. 2022, doi: 10.1364/BOE.448135

[9] N. Bosschaart, G. J. Edelman, M. C. G. Aalders, T. G. van Leeuwen, and D. J. Faber, "A literature review and novel theoretical approach on the optical properties of whole blood," *Lasers Med. Sci.*, vol. 29, no. 2, pp. 453–479, Oct. 2013, doi: 10.1007/s10103-013-1446-7.

[10] M. B. Applegate, R. E. Istfan, S. Spink, A. Tank, and D. Roblyer, "Recent advances in high speed diffuse optical imaging in biomedicine," *APL Photonics*, vol. 5, Apr. 2020, Art. no. 040802, doi: 10.1063/1.5139647.

[11] H. Wabnitz et al., "Performance assessment of time-domain optical brain imagers, part 1: basic instrumental performance protocol," *J. Biomed. Opt.*, vol. 19, no. 8, Aug. 2014, Art. no. 086010, doi: 10.1117/1.JBO.19.8.086010.

[12] R. H. Hadfield, "Single-photon detectors for optical quantum information applications," *Nat. Photonics*, vol. 3, no. 12, pp. 696–705, Dec. 2009, doi: 10.1038/nphoton.2009.230.

[13] A. Bossi et al., "Time domain diffuse raman spectroscopy using single pixel detection," *Biomed. Opt. Express*, vol. 14, no. 11, pp. 5749–5763 Oct. 2023, doi: 10.1364/BOE.502022.

[14] E. Martinenghi et al., "Time-resolved single-photon detection module based on silicon photomultiplier: A novel building block for time-correlated measurement systems," *Rev. Sci. Instrum.*, vol. 87, no. 7, Jul. 2016, doi: 10.1063/1.4954968.

[15] A. Garcia-Uribe et al., "Dual-modality photoacoustic and ultrasound imaging system for noninvasive sentinel lymph node detection in patients with breast cancer," *Sci. Rep.*, vol. 5, Oct. 2015, Art. no. 15748, doi: 10.1038/srep15748.

[16] D. Contini, F. Martelli, and G. Zaccanti, "Photon migration through a turbid slab described by a model based on diffusion approximation i theory," *Appl. Opt.*, vol. 36, no. 19, pp. 4587-4599, Jul. 1997, doi: 10.1364/AO.36.004587.

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[17] W. H. Press, S. A. Teukolsky, W. T. Vetterling, and B. P. Flannery, *Numerical recipes in c*. Cambridge, UK: Cambridge University Press, 1988.

[18] A. Torricelli, A. Pifferi, P. Taroni, E. Giambattistelli, and R. Cubeddu, "In vivo optical characterization of human tissues from 610 to 1010 nm by time-resolved reflectance spectroscopy," *Phys. Med. Biol.*, vol. 46, no. 8, pp. 2227-2237, Aug. 2001, doi: 10.1088/0031-9155/46/8/313.

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His research interests mainly include development of innovative time-resolved diffuse optics techniques and instrumentation for biomedical applications.

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