

# A compact dual-channel system for time-domain NIR spectroscopy of muscle and brain

Rebecca Re<sup>1</sup>, Davide Contini<sup>1</sup>, Matteo Caffini<sup>1</sup>, Lorenzo Spinelli<sup>3</sup>, Rinaldo Cubeddu<sup>1,2,3,4</sup>, Alessandro Torricelli<sup>1,4</sup>

<sup>1</sup>Dipartimento di Fisica, Politecnico di Milano, Piazza Leonardo da Vinci 32, I-20133 Milan, Italy

<sup>2</sup>ULTRAS-INFM-CNR, National Laboratory for Ultrafast and Ultraintense Optical Science, Piazza Leonardo da Vinci 32, I-20133 Milan, Italy

<sup>3</sup>IFN-CNR, Istituto di Fotonica e Nanotecnologie – Sezione di Milano, Piazza Leonardo da Vinci 32, I-20133 Milan, Italy

<sup>4</sup>Research Unit IIT – Politecnico di Milano, Piazza Leonardo da Vinci 32, I-20133 Milan, Italy

rebecca.re@mail.polimi.it

## 1. Introduction

In 1977, Jobsis demonstrated that it was possible to employ near-infrared (NIR) light to perform noninvasively measure of blood and tissue oxygenation [1,2]. Initially, Near-Infrared Spectroscopy (NIRS) was utilized for clinical investigation of cerebral oxygenation and hemodynamic response to a wide range of stimuli in the human brain [3]. Later the interest was focused on the study of the oxidative metabolism in healthy and pathological subjects [4]. Today commercial NIRS instruments working in continuous-wave and frequency-domain are on the market, whereas time-domain NIRS systems are still in a laboratory stage. This approach is based on the use of picosecond pulsed lasers, sensitive photodetection devices and fast acquisition electronics. With this method is possible to discriminate the absorption and scattering coefficient, to quantify the hemodynamic parameters, and to get information about depth-dependent attenuation even for a measurement with a single source-detector distance [5]. For imaging studies were developed several multichannel time-resolved systems [6]. For other clinical applications, for which is important to monitor the pathophysiological changes, it's more suitable an instrument with a limited number of channels, e.g. to clinical monitoring of tissue oxygenation during muscle rehabilitation [7] and to monitoring patient during treatment. The use of a limited number of channels moreover reduces the size and the cost of the instrument. We present the development of a compact two wavelengths and two channels time-resolved NIRS system. The system is based on a novel approach consisting of space-multiplexing of the two wavelengths in order to exploit the full temporal dynamic range of the acquisition boards, thus increasing the signal to noise ratio and avoiding wavelengths cross-talk with respect to the typical approach based on time-multiplexing.

## 2. System description: materials and methods

Most of the Time-domain NIRS systems are typically based on time-correlated single-photon counting (TCSPC) to acquire the distribution of photon time-of-flights (DTOF) [8]. They make use of the principle of time-multiplexing of the wavelengths [6-9], according to which, the optical pulses at different wavelengths are delayed one respect to the other by optical fibers of proper length (see Figure 1). Then, a fiber optic coupler [9,10] or a fiber optic splitter [11,12] is used to time-multiplex the laser pulses at the two wavelengths, that is to allow recording of the DTOF within the same TCSPC sweep. With this configuration measurements can be performed simultaneously at the two wavelengths, but problems of crosstalk between the pulses can arise, which might hamper the overall performance of the system. A first source of crosstalk is the superposition in time of the DTOFs. To avoid pulse overlap, the delay between wavelengths must be less than the inverse of the laser repetition rate. Nonlinearity in the time-to-amplitude converter (TAC) might also reduce the available time-interval in the TCSPC apparatus. In case of large source detector distance and/or low absorption coefficient the DTOFs are rather broad and this would result in partial overlapping of DTOFs. Another source of crosstalk arises when the count rate is high and there are significant changes in the count rate of one of the wavelengths. In this case, to minimize the crosstalk it's necessary to keep low the count rate with an overall reduction of performances.

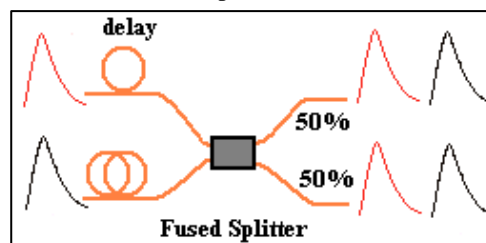


Fig. 1: Time-multiplexing of the wavelengths.

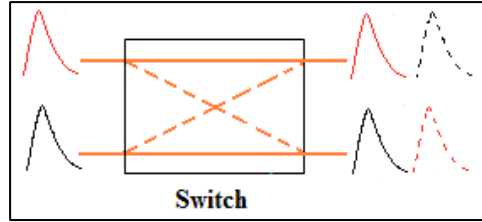


Fig. 2: Space-multiplexing of the wavelengths.

To overcome these limitations, we have developed a novel approach based on space-multiplexing of the two wavelengths (see Figure 2). By means of an optical 2X2 switch, the two wavelengths are injected alternatively in the two channels. In order to exploit the full temporal and dynamic range of the acquisition boards, we acquire one wavelength in each detection line and in each temporal window. In this way measurements are performed with two independent but temporally parallel channels. Using this approach we obtain an increase of the signal-to-noise ratio avoiding wavelength cross-talk with respect to the typical approach based on time-multiplexing of the wavelengths. This method has only the disadvantage that the two wavelengths are not simultaneously measured in the same point. This problem is overcome by using an elevated switching rate ( $>20$  ms), so that hemodynamic changes during brain activation or muscle work can be followed with acquisition times less than 1 s. In figure 3 the complete scheme of our instrument is presented. As light sources are used a couple of pulsed diode lasers, operating at 690 nm and 829 nm, with 80 MHz repetition rate and 1 mW average power (PDL, Picoquant GmbH, Germany). During measurements on biological tissue it's necessary the use of variable attenuators to equalize the signal at the two wavelengths or during acquisition of the instrument response function (IRF) to avoid damage of the detectors. The laser heads are therefore connected to multimode graded index fibers (50/125  $\mu\text{m}$ ) by means of a custom-made coupler which combines a neutral density attenuator (NT43-770, Edmund Optics GmbH, Germany), with variable attenuation in the range 0-80 dB, and a standard FC fiber optics coupler. A stepper motor (440-436, RS Components, Italy) is used to automatically control the variable attenuator. Before going into the sample, light pulses, go through the optical 2X2 switch (LEONI Fiber Optics GmbH, Germany). After migration in the diffusive medium the remitted photons are collected by two custom-made fiber optic bundles (Loptek Glasfasertechnik GmbH, Germany), composed of plastic optical fibers with total dimension of 3 mm. Signals are attenuated, after the bundle, by a system similar to the one in the acquisition section and coupled to the cooled photomultiplier tubes (PMC-100, Becker&Hickl, Germany) with a proper optical system. The acquisition of time-resolved reflectance curves is accomplished by 2 parallel and identical boards (SPC130, Becker&Hickl, Germany) for time-correlated single photon counting (TCSPC), placed in a PCI-box (PCI-Cardbox 2F, IBP Instruments GmbH, Germany) interfaced with a laptop. Each board has two independent banks of memory, for speeding data transfer to PC memory. A protocol for standardization of diffuse optical instrument performances, developed within the framework of the European Thematic Network "Medphot" [13], was applied to determine linearity, accuracy, noise, stability and reproducibility of the NIRS-TR set-up.

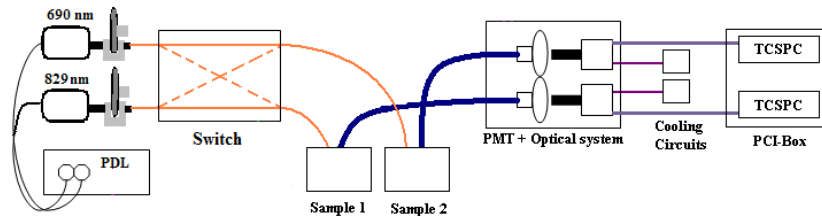


Fig. 3: Scheme of the complete system. On the left: source block (PDL, external laser driver). On the right: detection block (PMT: photomultiplier tubes, TCSPC: Time-Correlated Single Photon Counting boards).

### 3. In vivo experiments

We realized preliminary in vivo measurements to test the use of the system for tissue oximetry studies. We arranged simultaneously one source and one detector on each arm, at a relative distance of 2 cm. The protocol consisted in 60 s baseline, 60 s task (venous occlusion on the left forearm muscle) and 120 s recovery with an acquisition time of

0.5 s. We are interested in the changes of the hemodynamics parameters (oxygenated hemoglobin: O<sub>2</sub>Hb, deoxygenated hemoglobin: HHb, total hemoglobin: tHb = O<sub>2</sub>Hb+HHb, tissue saturation: SO<sub>2</sub> = O<sub>2</sub>Hb/tHb). As expected, during the whole experiments no significant changes occur in the right arm (not occluded), while a significant increase in HHb and in O<sub>2</sub>Hb hemoglobin is reported (figure 4). An increase of the tHb in the left arm occurs during all the venous occlusion: new oxygenated blood can enter in the occluded part through arteries, whereas the deoxygenated blood can't go out through the veins. SO<sub>2</sub> have a slight decreasing.

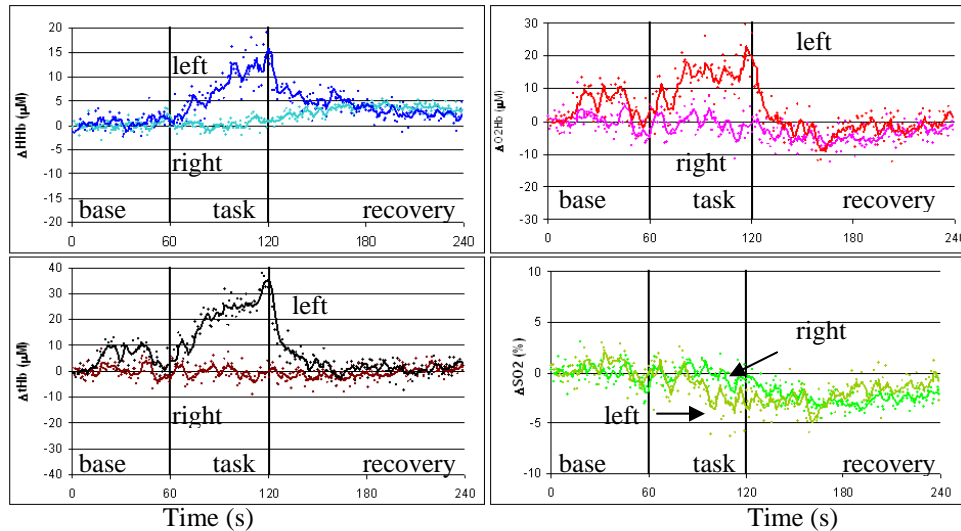


Fig. 4: Hemodynamic changes in the left (occluded) and right (not occluded) arm during venous occlusion.

#### 4. Conclusion

We have designed, developed, and characterized a compact dual-wavelength dual-channel system for time-resolved diffuse NIR spectroscopy. We have tested our instrument during preliminary in vivo measurements. Our perspective is to use it to monitoring the oxygenation of muscle and brain in ill patients.

#### References

- [1] F.F. Jobsis, "Non invasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters", *Science* 198:1264 (1977).
- [2] E.M.C. Hillman, "Optical brain imaging in vivo: techniques and applications from animal to men", *J. Biom. Opt.* 12(5):1402 (2007).
- [3] H. Obrig, A. Villringer, "Beyond the visible: imaging the human brain with light", *J. Cereb. Blood Flow Metab.* 23:1 (2003).
- [4] T. Hamaoka, K. K. McCully, V. Quaresima, K. Yamamoto, B. Chance, Near-infrared spectroscopy/imaging for monitoring muscle oxygenation and oxidative metabolism in healthy and diseased humans, *Journal of Biomedical Optics* 12(6), 062105 (2007)
- [5] Y. Hoshi, "Functional near infra-red spectroscopy: current status and future prospects", *J. Biom. Opt.* 12(6) 2106 (2007).
- [6] M. Wolf, M. Ferrari, V. Quaresima, "Progress of near infra-red spectroscopy and topography for brain and muscle clinical application", *J. Biom. Opt.* 12(6):2104 (2007).
- [7] A. Torricelli, D. Contini, L. Spinelli, R. Cubeddu, F. Molteni, S. Ferrante, A. Pedrocchi, and G. Ferrigno, "Monitoring muscle metabolic indexes by time-domain near infrared spectroscopy during knee flex-extension induced by functional electrical stimulation", in *Diffuse Optical Imaging of Tissue*, B. W. Pogue, R. Cubeddu, Editors, Proc. SPIE Vol. 6629, 66291L (5 pages) (Jul. 20, 2007).
- [8] W. Becker, *Advanced time-correlated single-photon counting*, Berlin, Germany: Springer Verlag, 2005.
- [9] H. Wabnitz, M. Moeller, A. Liebert, A. Walter, R. Erdmann, O. Raitza, C. Drenckhan, J.P. Dreier, H. Obrig, J. Steinbrink, and R. MacDonald, "A time-domain NIR brain imager applied in functional simulation experiments", *Photon Migration and Diffuse Light Imaging II*, Proceedings of SPIE Volume: 5859 Editor(s): K. Licha, R. Cubeddu (2005).
- [10] Y. Ueda, T. Yamanaka, D. Yamashita, T. Suzuki, E. Ohmae, M. Oda, and Y. Yamashita, "Reflectance diffuse optical tomography: its application to human brain mapping," *Jap. J. Appl. Phys.* 44, L1203-L1206 (2005).
- [11] D. Contini, A. Torricelli, A. Pifferi, L. Spinelli, F. Paglia, and R. Cubeddu, "Multi-channel time-resolved system for functional near infrared spectroscopy", *Optics Express*, Vol. 14, No 12:5418 (2006).
- [12] M. Kacprzak, A. Liebert, and R. Maniewski, "Time-resolved optical imager for assessment of cerebral oxygenation," *Journal of Biomedical Optics*, Vol. 12, No. 3, 2007, 034019.
- [13] A. Pifferi, A. Torricelli, A. Bassi, P. Taroni, R. Cubeddu, H. Wabnitz, D. Grosenick, M. Möller, R. Macdonald, J. Swartling, T. Svensson, S. Andersson-Engels, R. L. P. van Veen, H. J. C. M. Sterenborg, J. M. Tualle, H. L. Nghiem, E. Tinetti, S. Avriillier, M. Whelan, and H. Stamm, "Performance assessment of photon migration instruments: the Medphot protocol," *Applied Optics* 1112 (2005).