# Hybrid broadband NIRS/Diffuse correlation spectroscopy system for simultaneous monitoring of cerebral perfusion and cytochrome c oxidase

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**Abstract:** This article reports on the development and demonstration of a novel optical system combining broadband near-infrared spectroscopy and diffuse correlation spectroscopy to provide simultaneous acquisition of cerebral perfusion and cytochrome c oxidase.

**OCIS codes:** (170.3660) Light propagation in tissues; (170.3890) Medical optics instrumentation; (170.6510) Spectroscopy, tissue diagnostics

## 1. Introduction

Preterm infants born with very low birth weights are at a high risk of brain injury, in part because of limited cerebral autoregulation, which leaves the premature brain vulnerable to periods of low cerebral blood flow (CBF). There is, therefore, a need for a bedside neuromonitor that could alert the neonatal intensive care team to clinically significant reductions in CBF before injury occurs. Considering that injury is more likely if flow reductions are sufficient to impair cerebral energy metabolism, the goal of this work was to develop an optical system capable of continuously monitoring CBF and the oxidation state of cytochrome c oxidase (CCO) – a key marker of oxidative metabolism [1]. The system combined diffuse correlation spectroscopy (DCS) to measure CBF with broadband near-infrared spectroscopy (NIRS) to measure changes in the oxidation state of CCO. Experiments were conducted using an animal model of hypoxia-ischemia to demonstrate the system's ability to track dynamic changes in CBF and CCO.

## 2. Methods

A schematic of the hybrid DCS/broadband NIRS system is shown in figure 1a. Light from a NIRS broadband source (Ocean Optics Hl-2000-HP) was high-pass filtered at 500nm to minimize heat deposition before being sent towards a subject. Broadband light was detected by a spectrometer (P&P Optica, ON, Canada) coupled to a CCD camera (iDus, Andor Oxford Instruments). Broadband NIRS was implemented to ensure accurate measurements of CCO, which is an order of magnitude smaller in vivo than the hemoglobin signals measured by standard NIRS. Broadband NIRS allows measurements over a wide range of wavelengths, which is required to accurately measure oxCCO [2]. For the DCS acquisition, a continuous-wave 785nm laser (DL785-100s, CrystaLaser, Reno, NV) was used alongside a single photon counting module (SPCM-AQR4C, Excelitas, QC, Canada) and correlator board (Flex033LQ-1, Correlator.com, NJ, USA) to collect light at various delay times and compute an autocorrelation curve from which CBF was inferred. Operating broadband NIRS and DCS concurrently, however, will lead to inaccurate measurements of both CCO and CBF due to cross talk between the two systems, which operate within the same wavelength range (figure 1b) [3]. To mitigate this problem, a custom shutter-based multiplexing method was implemented [4]. In this design, the two systems were run simultaneously while cycling the shutters to capture data from each sequentially.

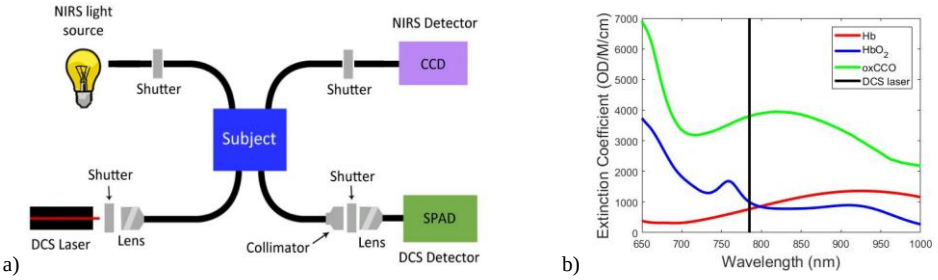


Figure1: a) Simplified system schematic of the mechanical shutter-based multiplexing method to combine broadband NIRS and DCS units; b) Extinction coefficients of deoxy-hemoglobin (Hb), oxy-hemoglobin ($HbO_2$), and the oxidation state of cytochrome c oxidase (oxCCO), with the DCS laser wavelength superimposed.

## 3. Results and Discussion

The ability of the hybrid broadband NIRS/DCS device to monitor dynamic changes in cerebral perfusion and metabolism was demonstrated in a piglet model of hypoxia-ischemia. In four subjects, different temporal perfusion and metabolic responses were measured during and immediately after hypoxia-ischemia (figure 2). During the insult, CCO fell by 3.0±0.8μM, with 59±12% of this drop occurring after CBF had reached its nadir. In contrast, hemoglobin changes generally reflected the flow response, including an overshoot in oxyhemoglobin (21±11%) that matched a hyperemic response immediately following the insult (31±8%).

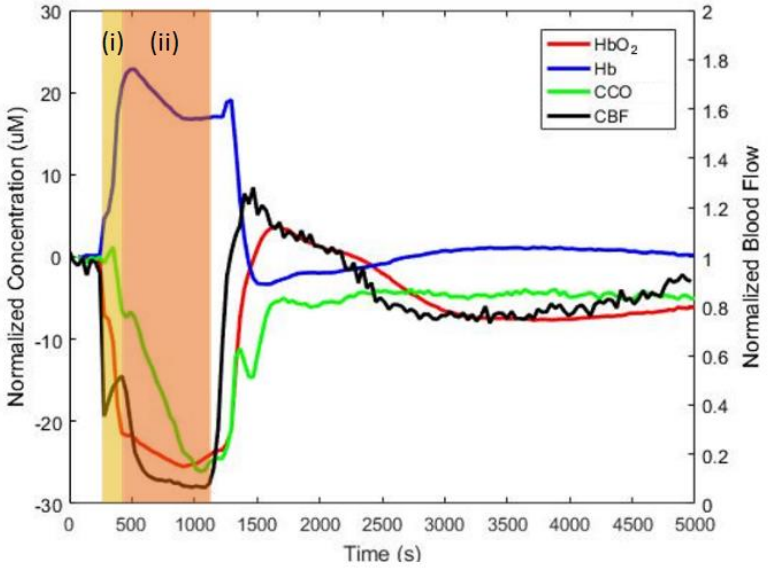


Figure 2: Simultaneous monitoring of changes in Hb, $HbO_2$, CCO, and CBF in an animal model of hypoxia-ischemia. Protocol was to first clamp both carotids (i), followed by reducing inhaled oxygen to 8% to cause hypoxia-ischemia (ii), insult recovery was achieved by removing clamps and returning oxygen content to baseline values.

The hybrid device successfully provided concurrent measures of CBF and CCO; however, there was a trade-off between the signal-to-noise ratio (SNR) and the temporal resolution. A 13s cycle – encompassing 10s for the DCS measure and 3s for the NIRS – provided accurate measures of CBF and CCO with the temporal resolution sufficient to capture the dynamic changes caused by hypoxia-ischemia. We believe that incorporating a software correlator to improve the temporal resolution of DCS [5], should enable the system to be operated at a resolution on the order of seconds.

## 4. Conclusion

This is the first report of a non-invasive monitor capable of tracking changes in CBF and CCO simultaneously, as demonstrated during hypoxia-ischemia. We believe this system could provide clinicians with greater insight into clinically significant hemodynamic events, enabling them to make adjustments to patient management to avoid brain injury.

## 5. References

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