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Originally published at:
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Abstract

Our group measures tissue oxygenation and the cortical hemodynamic response to sensory stimuli applying continuous wave near-infrared imaging (NIRI). To improve the method's quality and applicability and to explore new fields in clinical practice and research, we developed a miniaturized wireless NIRI system. It was validated by measuring muscle oxygenation in a blood-flow occlusion experiment and brain activity in adults.
Wireless miniaturized in-vivo near infrared imaging

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Abstract: Our group measures tissue oxygenation and the cortical hemodynamic response to sensory stimuli applying continuous wave near-infrared imaging (NIRI). To improve the method's quality and applicability and to explore new fields in clinical practice and research, we developed a miniaturized wireless NIRI system. It was validated by measuring muscle oxygenation in a blood-flow occlusion experiment and brain activity in adults.

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OCIS codes: (170.0110) Imaging Systems, (170.1470) Blood or tissue constituent monitoring, (170.2655) Functional monitoring and imaging

References and links


1. Introduction

In 2005 a novel highly accurate but cost effective continuous wave multichannel near infrared spectrophotometry and imaging (NIRI) system was introduced by Haensse et al. [1], which uses near-infrared light to quantify changes of oxyhemoglobin (O2Hb) and deoxyhemoglobin (HHb) concentration in tissue and is applied for non-invasive brain activity measurement in...
neonates i.e. to quantify the hemodynamic response of the cortex to visual, tactile or auditory stimuli. For such studies it is critical to perform the measurement as comfortable for the subject as possible to minimize distress. Current NIRI systems use cables (electrical or optical) to connect the sensor attached to the body of the subject to the acquisition electronics. These cables are disturbing and cause motion artifacts by dislocating the sensor. Additionally, the need for cables and the size and weight of current NIRI devices complicate the handling in demanding environments such as intensive care units (ICU) where one has to work under sterile conditions.

Furthermore, in situations where the NIRI monitoring of freely moving subjects such as athletes during exercise (to assess muscle oxygenation), subjects in social interaction or animals (to study brain activity) is required, the application of cable connections is not possible. Additionally, an easily transportable NIRI device opens new fields of application such as e.g. in emergency medicine. For these reasons, we developed a wireless and miniaturized NIRI system.

Two different signals related to brain activity can be assessed by NIRI: a fast neuronal signal is caused by a change in the optical scattering properties of the neurons upon activation and occurs within milliseconds of the stimulation [2]. A few seconds after activation, the hemodynamic response of the cortex can be measured: the increasing oxygen consumption in the activated cortical area results in an increase of the perfusion (causing a change in hemoglobin concentration and blood oxygenation) and therefore a change of the optical properties of the tissue [3]. A system potentially capable of measuring both effects in a clinical setup must fulfill three requirements. First, it must feature a high temporal resolution at low signal noise since the effects are usually small compared to the total signal intensity and the other physiological influences. Second, it must enable sampling at numerous locations for these effects are not systemic but localized. Third, such a system must provide good clinical usability and ease of transportation, to enable measurements on patients for the assessment of pathologies. A detailed discussion can be found in [1].

This paper describes an easily applicable and transportable, palm-sized wireless NIRI system which measures optical changes of tissue at a sampling rate of 100 Hz.

2. Instrumentation

2.1 Overview

The wireless NIRI sensor was designed using commercially available electronic components which were mounted onto a four-layer rigid-flexible printed circuit board (PCB) (figure 1). The flexible parts of the PCB in combination with a highly flexible casing made of medical grade silicone enable the sensor to be aligned to curved body surfaces such as e.g. limbs or the head. Figure 2 displays a schematic diagram of the system. It consists of the battery driven NIRI sensor which is connected wirelessly to a host computer, preferably a notebook or a personal digital assistant. The size of the sensor device is 92×40×22 mm, the weight including battery is 40 g.

2.2 Optical system

Four light sources and four detectors constitute the optical system. Each light source consists of two pairs of serially connected light emitting diodes (LED) (760 nm nominal wavelength, 757 nm effective wavelength, ±25 nm spectral half width, 3.5 mW nominal power and 870 nm nominal wavelength, 857 nm effective wavelength, ± 40 nm spectral half width, 5 mW nominal power). To achieve a high integration density, four bare-chip LED dies were grouped together and sealed by a medical grade translucent epoxy. The light sources are driven current controlled and time multiplexed with an on-time of 120 μs per sample and a forward voltage of 4 V per diode. Although LEDs have a broader emission spectrum than lasers, they have several advantages: they can be applied directly on the body surface without need for lenses or fibers and they are inexpensive. Furthermore, they are harmless for the eye, which is an important advantage in a clinical environment. Four PIN silicon photodiodes in combination
with transimpedance amplifier stages are used as detectors. The time multiplexed acquisition enables the background light intensity to be subtracted from the total incident light intensity, which is the superposition of LED and background light.

2.3 Power supply

To integrate highly accurate analog electronics along with power supply electronics for different voltage levels, special attention was given to the design of the power supply circuitry to avoid electric crosstalk, which was achieved by choosing appropriate shielding planes, passive filters and switched power supply circuits with switching frequencies magnitudes higher than the signal frequencies. There are four voltage levels present, namely 1.8 V for the wireless communication module supply, 3 V for the analog signal circuitry, 3 V for the digital logic and 8 V to drive the LEDs. The power is provided by a rechargeable 3.7 V lithium-polymer battery with integrated safety circuitry, which allows a continuous data acquisition for 180 minutes at full light emission power.

2.4 Data acquisition

The light intensity signal, provided by the transimpedance amplifiers of the detectors as voltages, is converted to a digital value by a 8051-architecture type microcontroller (Silicon Labs, Austin TX, USA) with an integrated 12 bit analog to digital converter. The system clock is provided by a 3.6864 MHz crystal. In principal, 16 different possible light paths at two emis-
sion light wavelengths i.e. a maximum of 32 channels (4 sources × 4 detectors × 2 wavelengths) could be recorded. However, during the 10 ms time-slot given by the 100 Hz sampling rate the light intensity signals of only 12 user-defined channels are acquired at the moment. This number can be improved by increasing the clock frequency to allow faster analog-digital conversion at the cost of higher power consumption or by decreasing the sampling rate.

2.5 Wireless data transmission

The digitalized light intensity data is serially transmitted to an integrated class 2 Bluetooth™ communication module (CSR, Cambridge, UK), which transmits the data wirelessly to the host computer using the Bluetooth serial communication layer Rfcomm and applying a simple protocol specifically defined for this application. Operating in a demanding environment such as an ICU, the operating range of the sensor is about 5 m. On the host system the data is fed into a JAVA™ and C++ based data processing software.

3. Theory

To calculate the concentration changes of HHb and O2Hb from the light intensity data, an approach based on the modified Beer-Lambert law is applied. By choosing light wavelengths in the near-infrared spectral range, the contribution of non-hemoglobin chromophores to the change in light absorption can be neglected. By evaluating Beer-Lambert's Law at two wavelengths \( \lambda_1 \) and \( \lambda_2 \) one can derive the temporal changes of HHb and O2Hb concentrations. However, with the present instrumentation both the initial light intensity and the scattering properties of the tissue remain unknown and a quantification of absolute hemoglobin concentrations is therefore impossible. The Beer-Lambert law and its application in in-vivo near-infrared spectroscopy is discussed in [4].

By properly choosing \( \lambda_1 \) and \( \lambda_2 \) one ensures that the condition number of the linear system of equation which is constituted by the Beer-Lambert law is as favorable as possible and hence disturbance of the results by measurement- and computation-accuracy errors is minimized. In the present case, the wavelengths 760 nm and 870 nm were chosen. The absorption spectra are weighted by the spectral distribution of the light sources to account for their non-monochromatic characteristic.

The value for the differential path length factor (DPF) can be found in the literature yet the values vary. Essenpreis et al have published a DPF value of 4.48 ± 0.41 at 800 nm measured in the adult forearm assessing a gender mixed group [5], while Duncan et al found a significant gender dependence of the DPF (4.57 ± 0.74 for females and 3.75 ± 0.57 for males at 807 nm) [6]. For the arterial occlusion experiment described hereafter, the DPF values published in [6] were interpolated according to the DPF as a function of wavelength published in [5]: we used 4.48 for 760 nm and 3.81 for 870 nm. For the reconstruction of the cortical hemodynamic signals a DPF of 7.75 for 760 nm and 7.25 for 870 nm was chosen [7]. The absorption coefficients for the O2Hb and HHb were taken from [8].

4. Experimental setup

4.1 Signal drift and noise measurements

The wireless NRI device was tested on a solid silicone phantom with absorption coefficients of 0.125 cm\(^{-1}\) and 0.123 cm\(^{-1}\) and scattering coefficients of 4.9 cm\(^{-1}\) and 4.3 cm\(^{-1}\) at the wavelengths of \( \lambda = 690 \) nm or \( \lambda = 830 \) nm respectively. The intensity-signal noise and long-term signal drift were measured for both wavelengths and at a source-detector separation of 25 mm.

The drift of the low-pass filtered light intensity signal was measured after a warm-up delay of 120 seconds (filter \( f_{\text{cutoff}} = 0.1 \) Hz, total signal duration 30 minutes). To quantify hemodynamic responses of the cortex due to functional stimuli, the signal is usually averaged over numerous time segments with a typical length of 20 s to 120 s. Hence the drift was examined by sliding a window with a width of 120 s over the signal. The drift was defined to
be the slope of a linear least-squares regression of the signal within the sliding window normalized with the initial signal value.

The signal noise was measured on the phantom at a LED emission intensity of 80% of the maximum intensity, which is a typical setting for in-vivo experiments.

A signal to noise ratio (SNR) of the brain activity experiment described below was calculated by dividing the power of the resulting signal of the second most superior source-detector pair by the noise power measured on the silicone phantom.

### 4.2 In-vivo experiments

To validate the functionality of the sensor in-vivo and to show the comparability of the results with those of existing instrumentation, an arterial occlusion experiment similar to the experiment described in [1] was performed. The wireless sensor was positioned longitudinal over a forearm muscle (musculus brachioradialis) of a healthy male volunteer. After acquiring 60 seconds of baseline data, a pneumatic pressure cuff attached to the upper arm was inflated to a pressure of approximately 300 mmHg to prevent venous blood backflow and arterial blood inflow into the forearm for 180 seconds. The NIRI sensor monitored the oxygen consumption of the muscles at rest. The total hemoglobin concentration in the tissue is expected to remain constant, while O$_2$Hb deoxygenates to HHb. After the occlusion period, the cuff was released to allow normal blood flow in the arm for a resting period of 180 seconds. The experiment was repeated consecutively to get five occlusion periods. The measurements were performed in a semi-dark environment with the subject sitting comfortably on a chair. The subject was given the ability to abort the experiment at any time by releasing the pressure cuff and switching off the measurement devices himself.

To demonstrate the feasibility of assessing hemodynamic cortical signals, such an experiment was performed on a male subject. The sensor was positioned on top of the motor cortex (C3 position according to the international ten-twenty system [9]). After a resting period of 20 s the subject tapped his right thumb and index finger for a period of 20 s, followed by an other resting period of 20 s. This was repeated consecutively 10 times. The signals during the stimulation periods were block averaged. Both experiments were approved by the local ethics committee.

### 5. Results and discussion

#### 5.1 General remarks

The subtraction of the background light intensity and the fact that the silicone casing of the sensor is completely opaque and covers the entire measurement area, prevent disturbance of the measurement by moderate background light. However, direct irradiation from light sources such as surgical lamps or infrared heating devices must be avoided.

Operating the sensor close (nearer than approximately 1 m) to sources of radio-frequency radiation such as mobile phones causes disturbance of the measurements and should be avoided. However the built-in Bluetooth device does not influence the measurement since the sending of data and signal acquisition are time-separated. Other sources of electromagnetic radiation inside buildings such as personal computers and wireless network routers do not to disturb the sensor signal. Due to the error correction and frequency hopping, which are intrinsic to the Bluetooth protocol, other devices using the Industrial Scientific Medical (ISM) band e.g. other Bluetooth or IEEE 802.11 devices do not disturb the wireless transmission quality. So far, also no disturbance of other electronic devices by the wireless NIRI sensor was observed. This observation is supported by results published in [10], where Bluetooth was evaluated as a cable replacement in intensive care and surgery: neither disturbance of medical equipment by Bluetooth nor vice versa was reported.
5.2 Signal drift and noise measurements

The light intensity signals (in analog-digital conversion units) for the phantom were approximately normally distributed around constant intensity values between 13154 and 15614 units (the overall dynamic range of the signal is 0 to 16348 units) with standard deviations (SD) of 3.01 to 3.71 units or approximately 0.02 % of the light intensity, independent of the wavelength. For the presented brain activity experiment, the light intensity was between 1500 and 1900 units and the amplitude of the changes of the intensity values due to the arterial pulsation was approximately 20 units for both wavelengths and can be clearly detected (figure 3).

The signal to noise ratio (SNR) for the brain activity experiment was 32 dB for the 760 nm source and 37 dB for the 870 nm source. This difference can be explained by the fact, that the power of the 870 nm signal is higher, while the noise is the same for both source types.

The results of the phantom drift measurements are listed in table 1. Compared to the signal intensity changes of approximately 4 % for the 760 nm light sources and 8 % for the 870 nm light sources in the described brain activity experiment, the drift can be neglected.

<table>
<thead>
<tr>
<th>Wavelength</th>
<th>mean [1 / 120s]</th>
<th>max [1 / 120s]</th>
</tr>
</thead>
<tbody>
<tr>
<td>760 nm</td>
<td>0.024 %</td>
<td>0.077 %</td>
</tr>
<tr>
<td>870 nm</td>
<td>0.027 %</td>
<td>0.087 %</td>
</tr>
</tbody>
</table>

Table 1. Drift characteristics

5.3 In-vivo experiments

Figure 4 shows the O$_2$Hb and HHb concentrations in the muscle for the arterial occlusion experiment with a nearly time-linear decrease of the muscular O$_2$Hb of 6 to 7 μmol l$^{-1}$min$^{-1}$ and a time-linear increase of the HHb at the same rate, which is consistent with the results that were published e.g. in [1].

Fig. 3. The raw signal measured during the hemodynamic experiment, sampled with 100 Hz time resolution for a 760 nm and a 870 nm light source.
Figure 5 displays the O$_2$Hb and HHb concentration measured at the head during the finger tapping experiment. For the reconstruction, 9 of 10 stimulations were averaged, one was excluded due to a severe motion artifact. Four vertically aligned light paths are shown, the source-detector separation is 25 mm. The superior and the inferior paths show less activation than the central ones, probably because they were located away of the activated cortical area. During stimulation, an increase in the O$_2$Hb concentration of 0.2 to 0.3 μmol l$^{-1}$ and a decrease in the HHb concentration of 0.05 to 0.1 μmol l$^{-1}$ were observed.
6. Conclusion

A lightweight and inexpensive miniaturized wireless NIRI device with good clinical applicability has been realized. First experiments show that the measurement accuracy is comparable to well established NIRI instruments. The device is easy to handle and the battery lifetime is sufficient for many desirable applications.

Acknowledgement

The authors wish to thank the Swiss Federal Veterinary Office for funding this research project (project number 2.06.01).