Development, set-up and first results of the Graz one-channel near-infrared spectroscopy system

Entwicklung, Aufbau und vorläufige Ergebnisse des Grazer Einkanal Nahinfrarot Spektroskopie Systems

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Running title:

Graz one-channel near-infrared spectroscopy system
Abstract

Near-infrared spectroscopy (NIRS) is a non-invasive optical technique for the assessment of functional activity in the human brain. This work describes the set-up of the Graz one-channel NIRS-system designed as prototype for an optical brain-computer interface (BCI) and reports on first measurements of deoxyhemoglobin (Hb) and oxyhemoglobin (HbO$_2$) changes during mental arithmetic (MA). We found relative stable and reproducible hemodynamic responses in a group of 13 healthy subjects. Nevertheless, the finding of a decrease of the HbO$_2$ and increase of the Hb concentration measured by optode placement over the prefrontal cortex was unexpected related to the typical hemodynamic responses (increase of HbO$_2$, decrease of Hb) during cortical activation known from literature.

Keywords:

Near-infrared spectroscopy (NIRS); optical brain-computer interface (BCI); mental arithmetic (MA); oxyhemoglobin (HbO$_2$); deoxyhemoglobin (Hb).

Abbreviations

MA, mental arithmetic; NIRS, near-infrared spectroscopy; BCI, brain-computer interface
Zusammenfassung


Schlüsselwörter:

Nahinfrarot-Spektroskopie (NIRS); optisches Brain-Computer Interface (BCI); mentale Arithmetik (MA); Oxyhämoglobin (HbO2); Deoxyhämoglobin (Hb).
1 Introduction

1.1 General

A Brain-computer interface (BCI) allows users who suffer from neuromuscular impairments the possibility to communicate or interact solely through thought processes. Neural activity, detected by electroencephalography (EEG), within the cortex is a typical physiological signal often used for common BCI-systems [24]. On the other hand non-invasive near-infrared techniques can also be used to detect functional activity of the cerebral cortex [2] and are an alternative to electrical signals for BCI communication. The intention of the present work was to develop a near-infrared-spectroscopy (NIRS) based optical BCI which is more practical, user-friendly [2] and overcomes the limitations and restrictions of EEG acquisition, such as the influence of electrooculogram (EOG), electromyogram (EMG), electrode failures and conductivity problems.

1.2 Near-infrared-spectroscopy

The NIRS is a non-invasive optical technique for the assessment of functional activity in the human brain. The technique uses the optical window in the near infrared light spectrum which was developed by Jöbsis [13] in 1977. Within this spectral range (about 630 - 1300 nm), light can penetrate the cranium and reach sufficient depth [17] to allow an investigation of the metabolism in the cerebral cortex [13]. Near-infrared light, which invades the tissue at a particular place at the head, interacts with the tissue in several ways. The beam becomes diffuse through scattering of the photons in the tissue. The scattered photons follow a random path through the tissue, resulting in the absorption of a part of these photons (e.g. through chromophores such as deoxyhemoglobin (Hb) and oxyhemoglobin (HbO$_2$)). Another part is back-reflected and leaves the head several centimetres away from the source location [17]. Theoretical and experimental investigations of Okada et al. [17] have shown that the photons
travel in a crescent-shaped path from the source to the detector. If the back-reflected photons may be detected over a longer time period it is possible to draw conclusions about metabolic changes in the tissue area that is penetrated by the photons. These changes, such as increased or decreased blood flow or changes in tissue oxidation are associated with brain activity and modify the tissue-characteristics. This means, that the absorption and scattering of the photons is changed and hence affect the detected light. Therefore a qualitative measure of brain activity can be obtained.

1.3 Cerebrovascular coupling

Cerebrovascular coupling is a term for the interaction between the neuronal (electrical) activity, cortical blood circulation and oxygen consumption of the brain tissue. As described in the work of Wolf et al. [23], there are three main factors which affect the Hb- and HbO$_2$-concentration in the investigated brain area and consequently the attenuation of the near infrared light. These factors are the cerebral metabolic rate of oxygenation (CMRO$_2$), the cerebral blood flow (CBF) and the cerebral blood volume (CBV).

During neuronal activation, changes in the CMRO$_2$, CBV and CBF partially occur at the same time. Figure 1 shows a schematic diagram of a typical hemodynamic activation response of the Hb- and HbO$_2$-concentration to a stimulus. The chronological sequence can be split into three stages [15]:

(i) The increase of CMRO$_2$ causes an increase in Hb, described by Malonek and Grinvald [16] and designated as “Initial Dip”. In this stage the dominating factor is the CMRO$_2$.

(ii) In stage two, an increase in the CBF is the dominating factor and causes a decrease in the Hb-concentration and an increase in the HbO$_2$-concentration. The increase in the CBF superimposes the “Initial Dip” described in stage one [16].
After the end of the stimulus (t₁) the CBV remains transiently as the most dominating factor while the CMRO₂ and CBF return more swiftly to the baseline. This causes an “overshoot” in the Hb-concentration and an “undershoot” in the HbO₂-concentration [8].

- Figure 1 -

One goal of this paper is to introduce the components of the Graz one-channel NIRS-system and to report first results of Hb and HbO₂ changes during different mental arithmetic (MA) tasks. Another goal is to investigate the intra-and intersubject variability of the mental response.

2 Methods and materials

2.1 NIRS measurement

Biological tissue is a highly scattering medium. Therefore, the photons’ path length increases as a result of scattering events. This elongated path length leads to higher scattering losses. In order to describe the light absorption process the modified Beer-Lambert Law [6]

\[ A = \log \left( \frac{I_0}{I} \right) = \alpha c x d + K \]

needs to be used, where A is the attenuation, Io [mW] is the light intensity entering the tissue, I [mW] is the light intensity exiting the tissue, \( \alpha \) [mol⁻¹ m⁻¹] is the specific extinction coefficient of the absorber, \( c \) [mol] is the concentration of the absorption, \( x \) is the differential path length factor (estimated factor, based on empirical studies), \( d \) [m] is the geometrical distance between emitter and detector and \( K \) a term influenced by the geometry of the measurement accounting the scattering loss and can be seen as time-invariant in a small time interval. HbO₂ and Hb, which are the two chromophores of interest in this work, have different attenuation spectra (Figure 2). The concentrations of all other absorbers such as e.g. water and lipids and the absorption of the surface tissue are assumed to remain constant.
during the measurement. Therefore the detected signal intensity depends on the sum of the absorption of HbO\(_2\) and Hb.

![Figure 2](image)

One method that can be used for NIRS measurement is the Continuous Wave (CW) method, where two wavelengths are necessary to calculate the two concentrations of interest. With this method only relative absorption changes can be detected. The concentration changes of HbO\(_2\) and Hb between two time points (t1 and t2) are calculated by the following equation:

\[
\Delta C = \alpha^{-1} \Delta A = \alpha^{-1} \begin{pmatrix}
\Delta A_{670} \\
\Delta A_{890}
\end{pmatrix} = \begin{pmatrix}
\alpha_{670,\text{Hb}} & \alpha_{670,\text{HbO}} \\
\alpha_{890,\text{Hb}} & \alpha_{890,\text{HbO}}
\end{pmatrix}^{-1} \begin{pmatrix}
\log \frac{I_{670}(t_1)}{I_{670}(t_2)} \\
\log \frac{I_{890}(t_1)}{I_{890}(t_2)}
\end{pmatrix} = \begin{pmatrix}
\Delta C_{\text{Hb}} \\
\Delta C_{\text{HbO}}
\end{pmatrix}
\]

2.2 Hardware

Inspired by the work of Coyle [2] a one channel NIRS-system (Figure 3) was developed in the framework of a diploma thesis [1]. With this system characteristic hemodynamic responses during cognitive tasks can be measured in real-time. The developed NIRS-system uses the CW method and operates at two different wavelengths. Two light emitting diodes (LEDs) with a wavelength of 670 nm and of 890 nm (L6112-01 and L2656-03, Hamamatsu Photonics K.K., Japan) are used as light sources. The LEDs were placed in direct contact with the scalp. For light detection a single avalanche photodiode (C5460-01, Hamamatsu Photonics K.K., Japan), connected to the scalp via an optical fibre with a diameter of 2.5 mm, was used. The distance between LED-sources and detector was 3 cm, which corresponds to a penetration depth of approximately 2.5 cm [17]. In order to separate the light emitted from the two
sources, the amplitude of each LED was modulated with a sine oscillation. A dual lock-in amplifier (Model 7265, AMETEK Signal Recovery, USA) was used to obtain the intensities at the two modulated frequencies. These intensities correspond to the two LED wavelengths. The modulation frequencies have no influence on the absorption coefficients, since they are only determined by the wavelengths of the LED-lights. The output of the lock-in amplifier was recorded with 250Hz by a data acquisition card (NI PCI-6024E, National Instruments, USA).

- Figure 3 -

2.3 Artifact reduction and preprocessing

Artifacts which influence the recorded signals are the pulse, the respiration, Mayer waves [9], which are spontaneous low frequency oscillations about 0.1 Hz (see Figure 4A) and hair movements. The movement of hair, which is also an absorber of light in the near infrared range, may cause instability of the detected signal [2]. The frequency of the pulse waves is in the range between 1 Hz (60 bpm) and 2 Hz (120 bpm), compared to that, the activation responses of Hb and HbO$_2$ are much slower. Therefore a digital 0.4 Hz low pass butterworth filter of order 5 with an attenuation of 30 dB in the stop band was designed to remove the pulse and contingently hair movements. After calculating Hb and HbO$_2$ and downsampling to 10 Hz a 0.01Hz low pass filter was used to remove baseline drifts. Furthermore a 0.1 Hz notch filter was used to remove the Mayer waves. Effects of respiration were not removed totally. The whole artifact reduction and preprocessing procedure is shown in Figure 4B.

- Figure 4 -
2.4 Experiments

In the present work, different experiments with mental arithmetic (MA) tasks have been carried out. All experiments were complied with the World Medical Association Declaration of Helsinki. The aim of these experiments was to measure hemodynamic changes of Hb and HbO$_2$ caused by different MA tasks to find stable and reproducible activation patterns. The concentration changes of Hb and HbO$_2$ are calculated from the output signals of the Lock-in amplifier by using the equation of section two and averaged over the number of tasks.

Experiment 1

This experiment was conducted in the framework of a diploma thesis [1]. A group of 5 subjects (j8, l8, v4 y3, z24; 3 male, 2 female, all right-handed) with mean age of 28.4 ± 6.3 years (mean ± SD) were measured with the custom-made one-channel system. The subjects were seated in a comfortable arm-chair. The sources and the detector were placed on the frontal cortex (which is involved in arithmetic operations [10, 14, 21]) 1.5 cm to the left and right of position FP1 (see Figure 5A) according to the international 10/20 system for EEG recording. During the task, which was presented on a monitor, the subjects had to perform an arithmetic operation. After a visual cue the subjects had to subtract two three-figure numbers within 10 seconds (e.g. 793-247), afterwards a pause of 30 seconds followed. One recording consisted of 6 trials and lasted about 4.3 minutes. The timing of the experiment is shown in Figure 6. Each subject performed 4 recordings on two days, resulting in 24 trials, except subject j8 who performed 42 trials (7 recordings in 3 days).

Experiment 2

A group of 10 subjects (ac9, ak2, ak3, ak4, ak7, al9, am1, j8, x20, z24; 5 male, 5 female, all right-handed) with mean age of 26.6 ± 3 years (mean ± SD) was measured with the developed
one-channel system. The experimental setup was the same as in experiment 1 except the task. Instead of one single subtraction the subjects had to perform repetitive subtractions within a time slot of 10 seconds (e.g. 97-4=93, 93-4=89, 89-4=85,…….). For each subject 7 recordings on one day were performed, resulting in 42 trials each.

Experiment 3

In order to validate the achieved results four subjects (ak4, am1, j8, z24) out of the ten person group were additionally measured with a commercial multi-channel NIRS-system (ETG-4000, Hitachi Medical Corporation, Japan) performing the same paradigm as in experiment 2. The 24-channel array of this system was arranged in such a way that channel 2 was placed over the FP1 position, similar to the one channel-system (see Figure 5).

3 Results

Experiment 1

The mean concentration changes of HbO₂ and Hb (± SE) of the 5 subjects, based on 24 trials, with exception of subject j8 (42 trials), are displayed in Figure 7. The mental task was always performed between second 0 and 10 (marked as shaded area in Figure 7). All subjects showed a similar activation pattern, a decrease of HbO₂ and an increase of Hb concentration.
Experiment 2

The results of seven subjects (based on 42 trials each) are reported in Figure 8. Due to an exceptionally high intrarecord variability, contingently caused by fitful breathing during the experimental epoch (e.g. stop breathing during solving the mathematical task), three subjects didn’t deliver usable results and are not presented here. This needs further investigations because the used artifact reduction procedure shown in Figure 4B did not remove effects of the respiration in particular. The mean concentration changes of HbO₂ and Hb of the seven subjects are displayed in Figure 8. The diagrams displays, just as in Figure 7, the same significant decrease in HbO₂ and increase in Hb concentration in each subject excepted ak4 (Hb) decrease.

- Figure 8 -

Experiment 3

To validate the results from previous studies (experiment 1 and 2), four subjects which took part in experiment 2 (ak4, j8, am1 and z24) were measured with the multi-channel NIRS-system performing the same experimental paradigm. The result of one of these subjects (j8) is shown in Figure 9, the big illustration shows channel 2 which was placed over FP1 similar to the experiments with the one channel system. It could be demonstrated that independently of the used NIRS-system, the same time course of Hb- and HbO₂-concentration changes could be obtained.

- Figure 9 -

4 Discussion and conclusion
The experiments with slightly different MA tasks (one subtraction for experiment 1 and repetitive subtractions within the task for experiment 2 and 3) revealed relative reproducible results independently from the used systems (custom-made one-channel system and commercial multi-channel NIRS-system). Of special interest are the unexpected HbO$_2$ and Hb responses during MA. In the experiments with the developed one-channel system and commercial multi-channel NIRS-system (frontal optode placement), the HbO$_2$ decreased and the Hb increased. This is in contrast to the HbO$_2$ increase and Hb decrease reported in many studies e.g. following sensory stimulation [15], during hand movement execution and imagination [2, 3 and 4] or during mental tasks [11, 12, 22]. Only in the work of Hoshi [12] additional to the expected changes the same decrease in the HbO$_2$ and increase in the Hb concentration in the frontal region of the dominant hemisphere during MA, as reported in this paper, were found in 9 of 33 healthy subjects. These observations were confirmed with simultaneous positron emission tomography (PET) measurements. One reason for such unexpected HbO$_2$ and Hb responses could be that compared to, for example, the case of hand movement execution the neuronal activation is more complicated in MA. In the case of hand movement execution the activated neurons are located in the motor area in the crown of the precentral gyrus and fully penetrated by photons. While hand movement execution involves a relative circumscribed area of some cm$^2$ in the motor cortex [19] the situation is more complex in a MA task. The areas or neural networks involved in MA operations are distributed over prefrontal, intraparietal and other cortices [5, 14] and not located exact under the optodes placed over the frontal brain. Thus the frontal measured HbO$_2$ decrease and the Hb increase, respectively, may be explained as a “surround effect”, of an HbO$_2$ increase and Hb decrease in areas not accessible by NIRS. Such a surround effect was reported during EEG recordings and is known as “focal event-related desynchronization (ERD)/surround event-related synchronization (ERS)” [20] but was also observed in blood flow studies. So for
example a decrease in regional cerebral blood flow (rCBF) arises in the somatosensory cortical representation area of the body part whenever attention is directed to a distant body part [7].

However that may be, from the relative low intrasubject variability in the time course of the hemoglobin response during MA and the reproducibility of the response within different MA experiments, there is evidence, that the MA task will be suitable for design a “BCI based brain switch”. A strong limitation for the BCI is however the nature of the hemodynamic response in the order of some seconds (see Figure 1). An advantage, compared to EEG-based BCI systems, in the relative simple application of the optodes especially suitable for home applications.

Additionally effects of the respiration in the results could be found in three subjects, because these subjects aligned their respiration with the given task. In these cases they particularly stop breathing during the calculation. This caused additional changes in Hb and HbO$_2$ and superimposed the changes caused by activation. Therefore the results of these subjects have been discarded.

The next steps towards a real-time system are the enhancement of the signal-to-noise ratio of the hemoglobin response by reducing influences e.g. from respiratory and blood pressure control systems (e.g. blood pressure waves of 3rd order) and to apply advanced methods for single-trial detection. An important topic is also the search for optimal optode positions by using a commercial multi-channel system.

Summarized, the NIRS is a cost-effective and non-invasive technology for physiological monitoring and perhaps suitable for future BCI applications. With the presented results it is possible to demonstrate that the developed one-channel NIRS is suitable to record metabolic responses in a MA task with frontally placed optodes. Our next step is to investigate the
suitability of on-line response detection after applying different methods of signal-to-noise enhancement.

5 Acknowledgements

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6 References


[18] Oregon Medical Laser Center, Optical Properties Spectra, online available (29.05.07) http://omlc.ogi.edu/spectra/hemoglobin/summary.html


**Figure 1:** Schematic graph of a typical activation response of HbO$_2$ and Hb to a stimulus (Modified from [3]). The activation starts at time $t=t_0$ and ends at time $t=t_1$. Section (i) shows an increase (“Initial Dip”) of Hb, which is followed by a decrease of Hb in section (ii). In the same time range as Hb decreases HbO$_2$ increases. Section (iii), after the end of activation ($t_1$) the two concentrations return to baseline.

**Figure 2:** Spectrum of Hb and HbO$_2$ in the range from 200nm through to 1000nm. The shaded area indicate the tissue window, the two lines at 670nm and 890 nm the used LED wavelengths. Data taken from [18].

**Figure 3:** Components of the NIRS-system developed at Graz University of Technology [1]. The system consists of: two light emitting diodes (670 nm and 890 nm) used as light sources, a single avalanche photodiode for light detection, a dual lock-in amplifier to separate the two intensities and a data acquisition card to record the output of the lock-in amplifier with a sample frequency of about 250 Hz.

**Figure 4:** (A) Spectrum of the optical signal (670nm) with the influence of heart rate with frequencies around 1.2 to 1.6 Hz (equivalent to 72 to 96 bpm), respiration around 0.2 Hz (30 breaths per minute) and the Mayer waves with a frequency around 0.1 Hz. (B) Artefact removal and preprocessing procedure to remove pulse wave, hair movement, baseline drift and Mayer wave.

**Figure 5:** Optode placement of the one channel custom-made system (A) and multi-channel NIRS-system (B). The multi-channel array was arranged in such a way that channel 2 was placed over the FP1 position, similar to the one channel-system.
**Figure 6:** Time course of the MA task. After a pre-waiting period of about 11 seconds 6 trials have been performed. The time course of one of these trials is shown separately. Two seconds before the task started a green bar appeared. After the cue (e.g. 793-274 for experiment 1 or e.g. 78-7 for experiment 2 and 3) the subject had to perform (repetitive) subtractions for 10 second until the green bar disappeared afterwards a pause of 30 seconds was given.

**Figure 7:** Mean concentration changes (mean ± SE) of subject j8 (enlarged diagram), l8, v4, y3 and z24 during performing the MA experiment 1. The shaded area indicates the time period of the MA task. HbO$_2$ is plotted in light gray and Hb in black.

**Figure 8:** Concentration changes from 7 subjects during the MA experiment 2 (based on 42 trials for each subject).

**Figure 9:** Mean concentration changes of 24 channels of subject j8 (42 trials) during the MA task in experiment 3. The enclosed figure shows channel 2 which was placed over the FP1 position, similar to the one channel-system.