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Reconfiguration and renewal of a multimodal fNIRS-Environment

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Abstract

At the Institute of Neural Engineering in Graz, Austria, the non-invasive near-infrared spectroscopy (fNIRS) technology is used to measure concentration changes of oxygenated and deoxygenated hemoglobin (oxy-Hb, deoxy-Hb) as a result of metabolic processes since 2011. From thereafter the setup increased in complexity and size. Dr. Bauernfeind was the main contact person when measurements concerning fNIRS should be performed but he left the Institute in mid 2015 taking most of his knowledge with him. It seemed to be the best time for investigating the single devices and used software and it revealed that updates from manufacturers as well as simplifications of hardware were available and possible. Improvements include within software the usage of Lab Streaming Layer (LSL) for data acquisition and within hardware exemplary the reduction of device amount from 11 to 6. Further the retained functionality and behavior in context to previous setup should be approved through a mental arithmetic task and an apnea task.

Finally it is again possible to measure with the fNIRS setup at the Institute activities of the cortex with better mobility, modularity and usability.

Keywords. Near-infrared spectroscopy fNIRS, update, validation, mental arithmetic, apnea

Kurzfassung

Am Institut für Neurotechnologie, Austria, ist zur Messung der Konzentrationsänderungen von oxygeniertem und deoxygeniertem Hämoglobin (oxy-Hb, deoxy-Hb) als Folge von metabolischen Prozessen die nichtinvasive Nah-infrarotspektroskopie (fNIRS) Technolgie seit 2011 in Verwendung. Seither ist das ursprüngliche Setup in Komplexität und Größe gewachsen. Hauptansprechperson für die Durchführung von Messungen in Zusammenhang mit fNIRS war Dr. Bauernfeind, jedoch verließ er Mitte 2015 das Institut und nahm den Großteil seines Wissens mit. Dies wurde zum Anlaß genommen die einzelnen verwendeten Komponenten zu untersuchen und diese zu vereinfachen sowie zu aktualisieren. Verbesserungen umfassen zum Einen die Einbindung des Lab Streaming Layer (LSL) zur Erfassung der Messdaten und zum Anderen die Verringerung der Anzahl verwendeter Geräte von 11 auf 6 hardwareseitig. Zur Überprüfung der Funktionalität und um das Verhalten in der aktualisierten Version zu bestätigen wurden zwei Tasks durchgeführt, Kopfrechnen und Apnoe.

Als Ergebnis ist es nun mit dem neuen fNIRS Setup am Institut möglich, Aktivitäten des Kortex mit besserer Mobilität, Modularität und Anwendbarkeit zu messen.

Schlüsselwörter. Nah Infrarot Spektroskopie (fNIRS), Update, Bewertung, Kopfrechnen, Apnoe

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Abbreviations

API	Application programming interface
BP	Blood pressure
CAR	Common average reference
CBF	Cerebral blood flow
CBV	Cerebral blood volume
$CMRO_2$	Cerebral metabolic rate of oxygenation
CW	Continuous wave
DAQ	Data acquisition
deoxy-Hb	Deoxygenated hemoglobin
ECG	Electro cortico gram
EEG	Electroencephalography
FD	Frequency domain
fNIRS	Functional near-infrared spectroscopy
GDF	General data format
GUI	Graphical user interface
HR	Heart rate

HRV Heart rate variability

ICSP In-circuit serial programming

IDE Integrated development environment

ISP In-system programmer

LSL Lab streaming layer

MW Mayer wave

NI National Instruments

NIR Near-infrared

NIRS Near-infrared spectroscopy

NTP Network time protocol

oxy-Hb Oxygenated hemoglobin

RF Respiratory frequency

SDK Software development kit

SNR Signal-to-noise ratio

SRS Spatial resolved spectroscopy

TCP Transmission control protocol

TOF Time-of-flight

TTL Transistor-transistor logic

UDP User datagram protocol

XDF Extensible data format

1 Introduction

At the Laboratory for BCI of the Institute of Neural Engineering in Graz, Austria, beside electroencephalogram (EEG) based devices also a multi-channel functional near-infrared spectroscopy (fNIRS) measurement device called NIRScout (NIRx Medizintechnik GmbH, Berlin, Germany) is in use since first quarter of 2011. From the beginning, starting with a custom made one source/detector pair described in [11] up to previous mentioned commercial available multi-channel device, Dr. Bauernfeind was the first contact person for measurements based on fNIRS. During different works he developed a fNIRS setup with the ability to acquire the blood pressure (BP), respiration out of which respiratory frequency (RF) could be determined, electrocardiogram (ECG) and additionally oxygenated and de-oxygenated hemoglobin (oxy-Hb, deoxy-Hb) were measured with NIRScout device. Post-processing of data happens within custom developed software based on well established calculation methods to increase signal to noise ratio (SNR) of fNIRS data. During the development process extent of software and hardware increased continuously with their capabilities such as removal of slow arterial pressure changes also known as Mayer-Traube-Hering waves or short Mayer waves (MW).[22]

All those extensions demanded their tribute. Performing one measurement requires a series of special knowledge concerning operation of different devices and software. Since Dr. Bauernfeind left the institute in mid 2015, time has come to update and simplify the setup.

1.1 Fundamental Basics

In the following chapters basic knowledge on topics in relation with this work will be illuminated in advance for an enhanced understanding of selected methods.

1.1.1 Anatomical and Physiological Basics

While a human body is alive, in every moment physiological parameters such as its BP, pulse, respiration, blood flow are regulated partly voluntarily or involuntarily resulting in for example MW, which is described later more detailed. Since all of our cells consume oxygen and other nutrients continuously, the results of a measurement can vary. Additionally, if work is done by the subject, the results can change even more. For brain especially the cerebral blood flow (CBF), cerebral blood volume (CBV) and the cerebral metabolic rate of oxygenation ($CMRO_2$) are responsible for changes in oxy-Hb and deoxy-Hb. The connections were described in detail by Wolf et al. in [59] and summarized in Table 1.1. All changes of physiological parameters were considered to appear isolated, which happens rarely within the human body. For example neuronal activation measured with fNIRS is described initially with an increase of deoxy-Hb, also called "initial dip" shown in Figure 1.1, reasoned with a rise of metabolic rate and therefrom $CMRO_2$. The lack of decreasing oxy-Hb described in Table 1.1 is attributed to a fast increase of CBF and CBV in this phase. Thereafter the main activation gets visible with rising oxy-Hb and decreasing deoxy-Hb as a result of an ongoing increase of CBF and CBV which leads to a rise in total hemoglobin. Finally after stimulation oxy-Hb and deoxy-Hb turn back to a steady state. The initial dip is listed due to completeness but is not found within all fNIRS studies.

Some possible backgrounds for changes in CBF, CBV and $CMRO_2$ are described in the following with no claim to completeness. CBF and CBV change if either venous, arterial or capillary vessels singular or in combination increase or decrease their diameter, called vasodilation and vasoconstriction. For example a possible reason of a vasodila-

Table 1.1: Arrows up indicate an increase in physiological parameters and an arrow down vice versa. An isolated increase in CBF, CBV or $CMRO_2$ result in displayed in- or decrease of oxy-Hb or deoxy-Hb.

	oxy-Hb	deoxy-Hb
CBF ↑	↑	↓
CBV ↑	↑	↑
$CMRO_2$ ↑	↓	↑

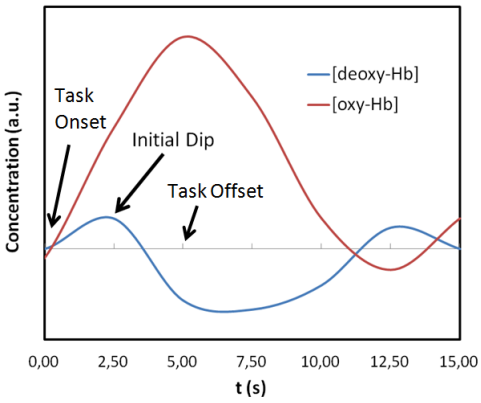


Figure 1.1: Exemplarily activation of a fNIRS signal. After the task onset at $t = 0s$ deoxy-Hb express the "initial dip" at $t = 2.5s$ followed by the main activation process, oxy-Hb increase and deoxy-Hb decrease. After the end of the task at about $t = 5s$ both return back to baseline. (modified from [9])

tion is an increase of CO_2 blood saturation, also called hypercapnia, described in [47]. Another reason, found in subjects after steep inhalation with following apnea, is an increase of intra thoracic pressure reducing blood flow back to the heart within veins. That leads to reduced cardiac output which is followed by an increase of BP reasoned with a vasoconstriction.[2, 33]

A rise in BP can be a result of increased vascular resistance due to vasoconstriction and vice versa. This is regulated to normal values through the arterial baroreflex acting as a negative feedback system needing some seconds for compensation. Due to the behavior of such a system with a time lag, it shows resonance with a duration of about 10s leading to pulsations in BP, which are stated as MW's earlier introduced as low frequency changes in BP.[54]

1.1.2 Background of NIRS

The attenuation of light crossing an absorbing material is the basis for fNIRS measurements. The scalp and also the skull are nearly completely translucent to near infrared light providing the possibility to reach deeper regions. On its way through the tissue it is scattered and attenuated by the chromophores oxy-Hb and deoxy-Hb. This circumstance could be described with the Lambert-Beer's law shown in Equation 1.1. A $[-]$ is the attenuation, I_0 $[mW]$ identifies the incident intensity and I $[mW]$ the intensity of light exiting the absorber. Further α $[\frac{l}{mol \cdot m}]$ describes the specific extinction coefficient, c $[\frac{mol}{l}]$ the concentration of absorbing substance and d $[m]$ the path length of light through the material. This equation is valid for light passing the medium without scattering. Figure 1.2 represents this case graphically. In the other case the extended Lambert-Beer's law displayed in Equation 1.2 is needed with a differential path length factor x for increased distance between incident light source and detector because of scattering and a factor K due to scattering loss. With short measuring periods K could be neglected because of its time invariance in such cases.

$$A = log\left(\frac{I_0}{I}\right) = \alpha \cdot c \cdot d \tag{1.1}$$

$$A = log\left(\frac{I_0}{I}\right) = \alpha \cdot c \cdot x \cdot d + K \tag{1.2}$$

The next step is to calculate the attenuation change ΔA between two time points t_1 and t_2, displayed in equation 1.3, dependent on the occurring concentration change.

$$\Delta A = log\left(\frac{I_0}{I(t_2)}\right) - log\left(\frac{I_0}{I(t_1)}\right) = \alpha \cdot \Delta c \cdot x \cdot d \tag{1.3}$$

For differentiating between two substances, in this case oxy-Hb and deoxy-Hb, two wavelengths are needed which leads to equations 1.4 and 1.5. Within fNIRS setup at the institute wavelength $\lambda_1 = 760nm$ and $\lambda_2 = 850nm$ are used for determination of

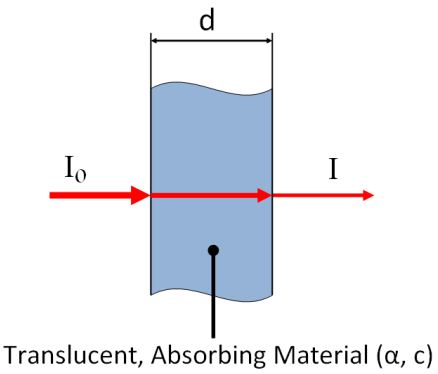


Figure 1.2: The attenuation of incident light with an intensity I_0 by a translucent, absorbing material of specific extinction coefficient α and substance concentration c is represented within this figure.

substance concentrations.

$$\frac{\Delta A_{\lambda_1}}{x_{\lambda_1} \cdot d} = \alpha_{(\lambda_1, oxy-Hb)} \cdot \Delta c_{oxy-Hb} + \alpha_{(\lambda_1, deoxy-Hb)} \cdot \Delta c_{deoxy-Hb} \tag{1.4}$$

$$\frac{\Delta A_{\lambda_2}}{x_{\lambda_2} \cdot d} = \alpha_{(\lambda_2, oxy-Hb)} \cdot \Delta c_{oxy-Hb} + \alpha_{(\lambda_2, deoxy-Hb)} \cdot \Delta c_{deoxy-Hb} \tag{1.5}$$

Finally equation 1.6, written in matrix notation and converted from equations 1.4 and 1.5 to achieve concentration changes, becomes the basis of fNIRS.[9]

$$\begin{bmatrix} \Delta c_{oxy-Hb} \\ \Delta c_{deoxy-Hb} \end{bmatrix} = \Delta \boldsymbol{C} = \boldsymbol{\alpha}^{-1} \cdot \Delta \boldsymbol{A} = \begin{bmatrix} \alpha_{(\lambda_1, oxy-Hb)} & \alpha_{(\lambda_1, deoxy-Hb)} \\ \alpha_{(\lambda_2, oxy-Hb)} & \alpha_{(\lambda_2, deoxy-Hb)} \end{bmatrix}^{-1} \cdot \begin{bmatrix} \frac{\Delta A_{\lambda_1}}{x_{\lambda_1} \cdot d} \\ \frac{\Delta A_{\lambda_2}}{x_{\lambda_2} \cdot d} \end{bmatrix} \tag{1.6}$$

Penetration depth of the light is determined by the distance between source and detector. The path between them is mostly described banana or crescent shaped only reaching some millimeters of cortical surface for measurements.[9, 23]

As previously described concentration changes due to physiological processes affect oxy-Hb and deoxy-Hb leading to varying attenuations of the tissue. Different techniques such as continuous wave (CW), time-of-flight (TOF) or frequency domain (FD) displayed

in Figure 1.3 are used to receive data with fNIRS and were described in detail by Delpy and Cope in [20]. Also previously addressed spatially resolved spectroscopy (SRS) could be used for this purpose.

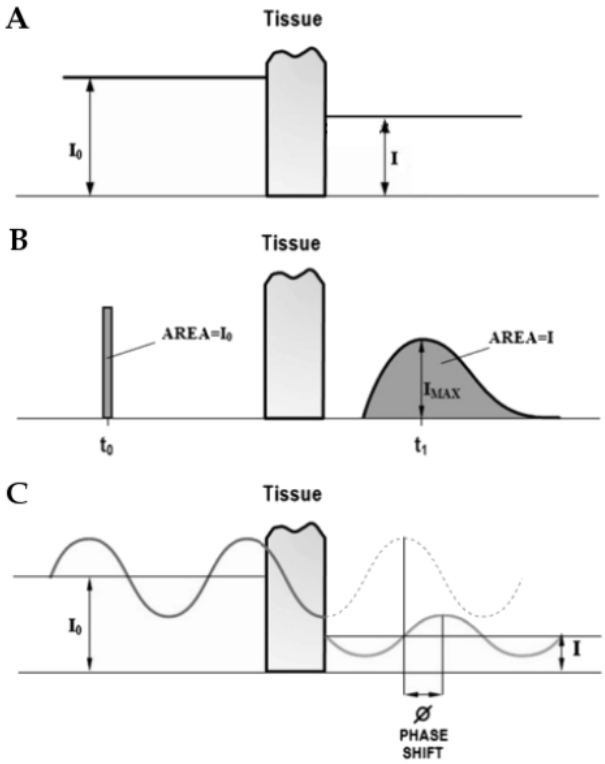


Figure 1.3: The figure show a schematic description of the A) CW, B) TOF and C) FD NIRS technique. On the left side of the tissue the incident and on the right side the exiting NIR light intensity is displayed.(modified from [8])

The CW method uses a continuous active near infrared (NIR) light source during a measurement. If more than one source is used it is possible to determine the sent wavelengths by sending them alternating or by modulating them with distinctive frequencies. The NIRScout device uses the second type with modulated frequencies in kHz range.[41] With this method it is not possible to determine the absolute concentrations of oxy-Hb and deoxy-Hb but with the previously described extended Lambert-Beer's Law it is possible to calculate relative concentration changes.

The TOF technique provides the possibility to determine absolute concentrations.

With short pulses of NIR light in the range of picoseconds and time correlated single photon counters it is possible to determine the penetration depth of NIR through TOF measurements. If a bolus measurement should be done the CW method is not able to distinguish between dye concentrations within the brain as a result of the bolus and concentrations within the surrounding tissue. With knowledge of the penetration depth the location of the dye can be investigated more precisely.[21, 57]

The FD method is also able to measure absolute concentrations of oxy-Hb and deoxy-Hb. An amplitude modulated sinusoid NIR light source at frequencies up to 200MHz is sent through the tissue. Afterwards the concentrations can be calculated from the amplitude change, phase shift or modulation of exiting NIR light. A drawback of this method in comparison to the CW method is the higher technical complexity because of intensity, phase and modulation related light source and detector. Also the penetration depth is reduced with the FD technique.[8]

At last the SRS is described, which is often used by devices based on the CW method due to their simple structure. Basically it relies on different distances between one NIR light source and one or more detectors. A change of this distance also variates the penetration depth which reduces the influence of superficial brain tissue because it affects all detector distances equally. With this information the influences can be removed.[8]

1.1.3 Lab Streaming Layer

LSL is a relatively young, free and online available option to acquire and record data time synchronized with centralized systems described in [32]. It inherits the transport reliability of transmission control protocol (TCP) as well as the time synchronization accuracy from an algorithm similar to so called "Clock Filter" algorithms used in the network time protocol (NTP) which is achieving accuracies below milliseconds. Additionally LSL handles network communication between client and host so integration in existing projects is rather simple. For opening new streams a big variety of applications according to different data sources are provided by community behind the project. An example is the

transfer of serial data acquired via COM port to LSL packages. A host PC with one or several active LSL applications acquires data from different sources and provides the resulting streams inclusive a time stamp created by an internal clock to the network. Every additional host PC connected to the network is also able to feed further streams into it. Similar, one or several client PC can now record all LSL data provided by the network which are selected with a recording tool. Recording itself can be done individually but it is suggested to use recording tool "LabRecorder".[61] It is based on Python using "RecorderLib" [61] library supporting Python and C++. As a result such recorders store data within an extensible data format (XDF) [17] file for which several libraries of different programming languages are provided to read data at a later point of time to perform post processing or visualization. An additional benefit is the property of LSL to buffer data on client and host site to reduce risk of data loss during connection errors.[32]

After investigating a connection from a LSL application to LabRecorder by the network sniffing tool "Wireshark" [19] it turns out that LSL is based on the user datagram protocol (UDP) at transport layer. This circumstance and lower level layers are shown in Table 1.2. From LSL documentation no conclusion can be made about the used layer structure as previously described, but with the assumption, that it uses UDP for data transport and NTP for time synchronization the transport reliability, similar to TCP, must be a part of LSL libraries.

A LSL stream pushes single- or multichannel data to the outlet without taking care of listeners. The data consists of uniform value types such as integers, floats, doubles or strings, with regular or irregular sampling rate and more. According to the network settings it is possible to record the outlet stream by creating an inlet within the same workstation or a connected PC. Again several settings are available to define how to acquire the data, for example with reliable transmission or optional type conversion. To select only the desired outlet streams, it is possible to resolve them by content-based-queries, as exemplarily by name, content-type or ID.[32]

Table 1.2: The Table represent the layer structure of a supervised LSL connection. It revealed that LSL is based on UDP.

Layer (Nr.)	Extracted
Application (5-7)	Data
Transport (4)	UDP
Network (3)	IPv4/6
Data link (1, 2)	Ethernet II

1.2 Related Work

fNIRS is already a well established method for non-invasive detection of oxy-Hb and deoxy-Hb within brain tissue during the execution of a wide range of different tasks performed by subjects [25, 26, 28, 29, 31, 60] or to diagnose and also monitor diseases such as epilepsy, strokes, idiopathic headache and even more to investigate their origin in the brain as described in [1, 16, 27, 43, 49, 53, 56]. In contrast to medical usage scientists doing their research are interested on unprocessed raw data from fNIRS measurement devices because of the possibility to adapt pre- and post-processing methods according to the current state of scientific knowledge achieving more accurate and repeatable results. Problematic for comparability between studies is mostly the lack of details in context with used filters, excluded trials or channels and internal preprocessing found in publications. As an example within the study of M. Pocivalnik et al. [46] the devices NIRO 300 (Hamamatsu®, Japan) measuring the "tissue oxigenation index" and INVOS5100 (Somanetics®, USA) measuring the "regional oxygen saturation" were compared. Even if both devices rely on spatially resolution spectroscopy, which is known to be unable to calculate absolute concentration values similar to CW technique, it reveals that data is hardly comparable between two different devices and studies.

Physiological artifacts reducing SNR are produced by very low frequency changes around 0.04 - 0.13Hz in BP called MW [42, 44, 45], respiration with a frequency range of 0.2 - 0.4Hz and also the heart rate (HR) itself with about 0.8 - 1.2Hz during a measurement. Those artifacts could be removed by a variety of filters listed in [36], as for

example moving average, FIR filter or pulse regression to remove HR/respiration artifacts, detrending or least mean square adaptive filtering for mayer wave correction, also leading to different post processing methods between different studies in some cases and therefrom to varying results.

An artifact, that is difficult to remove due to its hard detectability, is motion resulting in tilting or lifting sources and/or detectors during a measurement which loose their contact to the scalp. Robertson et al. investigated in [48] recursive least squares adaptive filtering, wavelet-based filtering, independent component analysis and two-channel and multiple-channel regression methods for reducing motion artifacts. They claim that independent component analysis and multiple-channel regression methods are the best to increase SNR but also wavelet filtering seemed to be a proper way if sharp spikes are within the signal. If applicable, the easiest way to reduce motion artifacts is to minimize motion itself by matching study design.

1.3 Current Setup

Figure 1.5 shows the current setup which consists of following devices:

- **Laptop 1: Paradigm presentation**
  Internal description "BCIPC107". It is a HP Compaq nw8000 with an Intel Pentium 1,8GHz processor and 1GB RAM of working memory. The operating system is Windows XP with 32 bit. It is used for paradigm presentation with Matlab code.

- **Laptop 2: Physiological data acquisition**
  Internal description "BCIPC121". It is a HP Compaq nw8000 with an Intel Pentium 1,8GHz processor and 1.5GB RAM of working memory. The operating system is Windows XP with 32 bit. It is used for acquisition of physiological data and analog trigger signals from g.CBox through a NI DAQ-Card.

- **Laptop 3: NIRS acquisition**

  Internal description "Lap1". It is a Lenovo ThinkPad R500 with an Intel Centrino 2.2GHz processor and 4GB RAM of working memory. The operating systems are Windows 7 with 64 bit, Ubuntu and Windows XP. It is used for acquisition of fNIRS data from NIRScout device with all necessary programs installed within operating system Windows 7.

- **PCMCIA DAQ-Card (National Instruments GmbH, Salzburg-Bergheim, Austria)**

  NI DAQ-Card 6024E. Acquires data from g.CBox. The g.CBox works as a connector box from the NI DAQ-Card to analog and digital input and output pins as well as a biosignal amplifier input pin.

- **CNAP^{TM} Monitor 500 (CNSystems Medizintechnik AG, Graz, Austria)**

  Measures noninvasive continuously the BP of a subject during experiment. [18]

- **g.CBox (g.tec Medical Engineering GmbH, Schiedlberg, Austria)**

  Acquires trigger signals from arduino duemilanove [3], respiration and ECG from g.tec amplifier and BP from CNAP monitor.

- **g.tec amplifier (g.tec Medical Engineering GmbH, Schiedlberg, Austria)**

  Sends acquired respiration and ECG data to g.CBox.

- **Sync.box**

  Basically an arduino duemilanove located in a plastic housing with several pins lead out for better accessibility. An integrated development environment (IDE) [4] for programming is provided on-line for free. This devices provide an in circuit serial programming (ICSP) header which allows to load compiled source code as a hex file via serial connection to the microprocessor but it is not possible to read it out afterwards. In case of the arduino duemilanove its microprocessor is an ATMEGA328P (ATMEL Corporation, San Jose, California, USA). It distributes an

analog trigger signal to the g.CBox and a digital binary 4bit value to the NIRScout device.

- **NIRScout (NIRx Medizintechnik GmbH, Berlin, Germany)**
  It provides 16 LED sources with wavelengths of 760nm and 850nm and 24 Si photo diodes coupled through fiber optics to the head of a subject. One source-detector pair creates a channel. In Figure 1.4 sources are shown with a black, detectors with a gray and resulting channels with a white background. As can be seen source 1 and detector 1 create channel 1, source 1 and detector 2 create channel 2 and so on. The number of channels depends on the number of used sources and detectors as well as on their arrangement.[41]

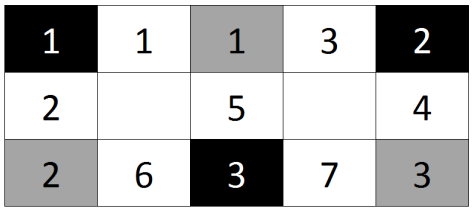


Figure 1.4: Squares with black background describe sources (LED), gray ones describe detectors (optode) and white ones are the resulting channel.

- **1st and 2nd Monitor**
  Display of Laptop 2 is broken so the 1st monitor is only a compensation of this issue. The 2nd monitor is used by the operator to supervise the paradigm progress and is connected to Laptop 1.

As previously mentioned the current setup at the institute has increased over the years in hard- and software. This setup is schematically displayed in Figure 1.6. Three laptops and big device effort are needed to perform one measurement to benefit from all of its capabilities. According to the experiment a Matlab code must be adapted to display paradigm on TFT monitor (black path in Figure 1.6) located within fNIRS box connected to laptop 1. For time synchronization at the beginning and end of each run, a trigger

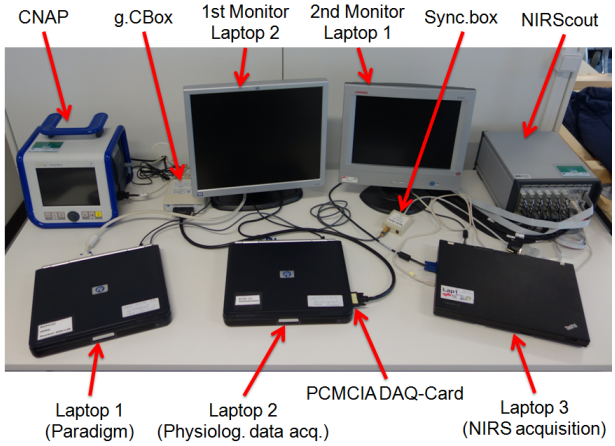


Figure 1.5: The figure shows components of current setup outside NIRS-box. Inside fNIRS-box: g.tec amplifier, wirings for BP and fNIRS measurement.

is sent three times with approximately one second spacings additionally to single trigger signals for determining the start of a new trial and their condition. Those trigger signals created by Matlab code are sent to arduino duemilanove through a virtual COM port of laptop 1.

Afterwards the arduino sends an analog high for every trigger signal to an input of g.CBox and also a 4 bit digital value to the transistor-transistor logic (TTL) input of NIRScout device according to displayed condition. All trigger signals are represented in red within Figure 1.6.

Increasing SNR is one of the main tasks for getting representative results from the experiments. Preparatory work to achieve this aim is partially solved by recording BP (measured by CNAP^{TM} monitor), ECG and respiration (both measured by g.tec amplifier). With the amplifier acquired data streams are sent to g.CBox, put through and received by laptop 2 containing NI DAQ card. As previously described, the data streams also contain trigger signals for time synchronization with fNIRS data in post processing. Again a custom made Matlab code is used for storing incoming data in a file with current widely used general data format (GDF).[50] Furthermore, during a measurement the cursor of laptop 2 must be moved continuously because the Matlab code is speed optimized

and will hang up if there is no side process.

Laptop 3 is responsible for acquisition of fNIRS data and triggers are recorded with software NIRStar version 10.8.3 from NIRScout. Additionally it is not allowed to connect laptop 1 or 2 to internet because it is suspected that they will not work as expected any longer after possible installation of operating system updates.

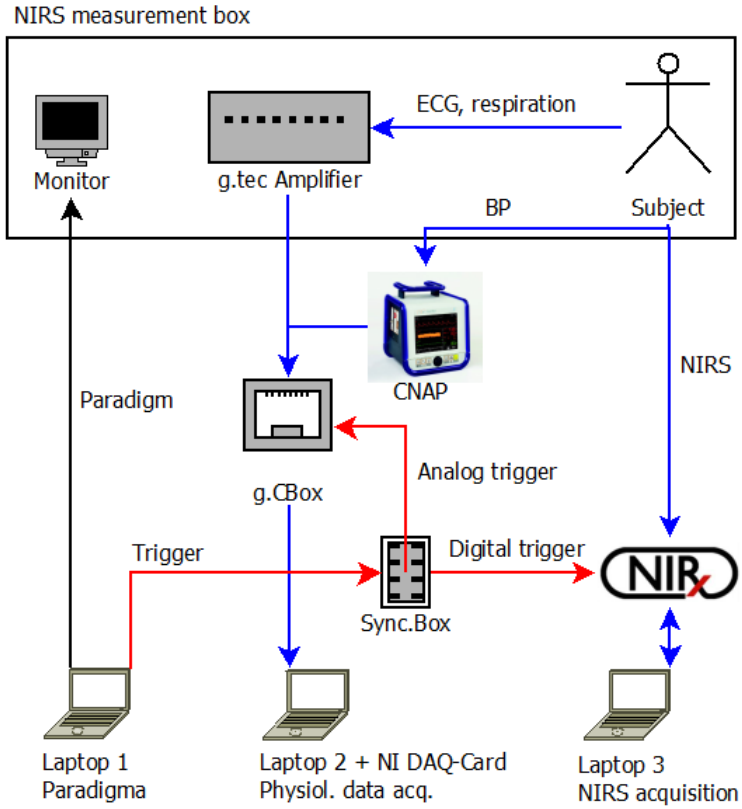


Figure 1.6: Three laptops are used within the current setup. Laptop 1 shows the paradigm (black path) on a TFT monitor within the fNIRS box and sends trigger signals (red paths) to an arduino which distributes them. Laptop 2 acquires digitalized analog data (blue path) produced by NI DAQ within g.Cbox from BP, respiration and triggers. Laptop 3 acquires fNIRS data (blue path) and also trigger signals.

Post processing of data happens within individual created Matlab code by Dr. Bauernfeind using BioSig Toolbox [51]. This Toolbox supports artifact processing, provides adaptive signal processing, includes an interface to different data formats as for example GDF and contains much more additional characteristics.[52] Before previously recorded data

can be evaluated with the software, several settings such as storage location of GDF and fNIRS data from different runs, amount of trials and their duration, number of different conditions, type of artifact reduction, possible SNR improvements and more must be made. On the basis of continuously increasing extent of software inevitably clarity, structure and readability of code got negatively affected. As an example, the fNIRS sample frequency is described within the code with differing variable descriptions without obvious reason.
Nonetheless it represents a very good up to time processing tool for acquired fNIRS data with a lot of settings, useful plots and features.

1.4 Motivation

After Dr. Bauernfeind left the institute most of the knowledge in context with current setup went with him. Published papers [10–14] as well as his dissertation [9] do not provide enough information about the usage of the current system. For example the original code used within arduino already got lost. The fNIRS environment is also not compatible with newly introduced LSL used in other research areas at the institute. Since no measurements or projects are planned currently, it is the most appropriate time to simplify, update and document the current NIRS setup for future use.

1.5 Objectives

First of all, the devices that are no longer supported by up to date software should be replaced with new devices and a higher modularity for interaction with other measurement setups should be reached. To control the functionality and correct interaction between newly arranged devices within the setup, experiments should be performed to reveal functionality and behavior.
Therefore, this master thesis is split up into two parts according to previously described

tasks.

1.5.1 Update of Current fNIRS Setup

Transportation of the whole setup to patients located at rehabilitation centers or hospitals is currently demanding because of its time effort reasoned by decomposition and composition of the setup at different locations. Also the usage of the different devices and their software requires a lot of special knowledge which is not instinctively acquirable. To achieve improvements in those areas no restrictions are previously set with exception of the obligation to use LSL for acquisition of data, due to its advantageous behavior of adding time stamps instantaneous beside recorded data points. With those time stamps it is possible to create time synchronized data streams, which are recorded from different devices with different sampling rates as described in [32]. The goal of this limitation is to adapt all following post processing software currently used to the new file format XDF, created by LSL stream recording software.

1.5.2 Experimental Validation

To secure that none of the reformations have influences on quality and functionality of the setup two experiments must be performed. The first experiment is a repetition of well known mental arithmetic task. Main reason therefore is to check the functionality of the whole setup in working configuration without aim to achieve statistically evaluable data. The second one is a test to check if oxy-Hb and deoxy-Hb rise or fall according to real conditions. For this purpose a subject changes its oxy-Hb and deoxy-Hb concentrations by breath holding as long as possible but maximal one minute.
Both tasks should be done with already prepared experimental caps holding 16 sources and 15 detectors resulting in 47 channels.

2 Methodology

2.1 Update of Current fNIRS Setup

As mentioned before, the current setup consisted of different devices with special usage and compatibility in between. The used software was out of date and required an update with referring hardware adoptions. Figure 2.1 schematically shows the achieved simplification of current fNIRS setup. Two of three laptops were not allowed to be linked to the world wide web due to the compatibility issues in combination with the used hardware. To reduce computational effort two laptops BCIPC107 and BCIPC121 were removed and the third laptop (lap1) has been equipped with the new operating system windows 7, 64bit. Because lap1 does not support PCMCIA slot cards, NI DAQ has been removed with all of its following components, g-CBox and g.tec amplifier. Due to replacement of both devices the use of arduino duemilanove was switched from sending trigger signals to acquiring BP via one of its 6 analog input pins.

The black path in Figure 2.1 displays paradigm presentation into the fNIRS box. The blue path represents the acquisition of ECG and respiration data. The BP is displayed as green path and the red one describes the acquisition of fNIRS data. The trigger signals are sent internally either directly as additional LSL stream or indirectly via NIRStim software. All collected data is converted into a LSL stream and can be further recorded or processed instantly within the same laptop or streamed into a network as presented

with a dotted black path. Afterwards it is possible to combine it with data from other setups as for example EEG or only for distribution of processing workload to other PC.

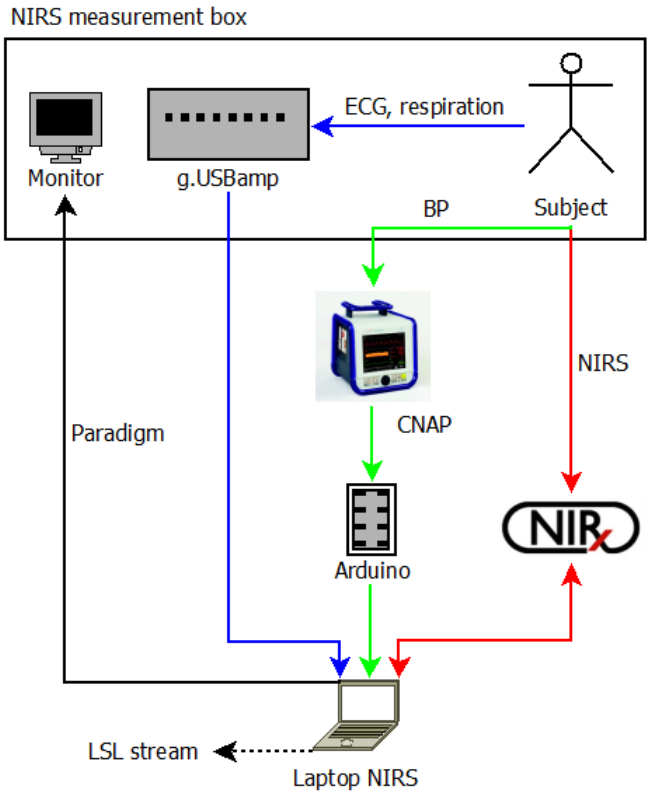


Figure 2.1: Final hardware setup for fNIRS measurements at the institute. A g.USBamp (g.tec Medical Engineering GmbH, Schiedlberg, Austria) acquire the ECG and respiration data. The CNAP^{TM} Monitor acquire the BP and send it to an arduino which acts as analog-digital converter. Inside the NIRS measurement box a monitor presents the paradigm. The acquisition of NIRS data is performed by NIRScout device. All data streams are collected by one Laptop and are put through into a network as LSL stream.

2.1.1 Blood Pressure Acquisition

To comply with good scientific practice, the nowhere else than on the Sync.box (arduino duemilanove) stored program, performing distribution of trigger signals, was saved with a second arduino of model type uno. It is used as in-system programmer (ISP) according to the instructions provided by the tutorial on arduino web page.[5] Using that configuration

it is possible to read the program which is stored as a .hex file within the processor of the Sync.box and save it with the documentation.

AUX out of BP monitor provides an output voltage between 0V to 5V on channel 1, which was covering a BP range from 0mmHg to 500mmHg with a sampling frequency of 100Hz[18]. The used microprocessor within arduino duemilanove is an ATMEGA328P which provides an analog to digital converter with a resolution of 10bit resulting in a resolution of about 0.488mmHg in BP[6]. To calculate the measured voltage an internal reference for comparison is provided, which is stated to be 5V if default settings are used. Due to inaccuracies 5V are not precisely achievable.
For most accurate acquisition a calibration of analog input values according to on-line description was performed with the arduino. 100 samples were taken from the analog input while a 5V reference voltage was attached to an analog input. The calculated mean of those samples was used to define the reference voltage within the acquisition code attached in A.1 where it is used to calculate the actually measured voltage value.[35] As reference voltage to calibrate the arduino a Thurlby Thandar TS3022S (Aim-TTi, Huntington, United Kingdom) power supply was used to create a constant direct current voltage of 5V in combination with a multimeter MY64 (Precision Mastech Enterprises CO., Hong Kong, China) to check set voltage value.
Finally, the program code attached in Appendix A.1 (the acquisition of BP and sending of data as a serial stream to a PC) was created with arduino IDE. Sampling frequency was set to 250Hz which is more than twice the sampling frequency of BP monitor.

Furthermore, the "Serial.write()" command is only able to send one byte or an array of bytes per call and also LSL application is not able to concatenate two or more corresponding bytes before recording them via LabRecorder.py. This leads either to increased processing effort within evaluation software or to limitation in measurable range of BP. The second opportunity was chosen to keep the functionality as simple as possible for possible migration of BP acquisition setup to other projects than fNIRS.

2.1.2 Respiration and ECG

The previously used g.tec amplifier has been replaced by a g.USBamp amplifier. With this replacement also g.CBox and PCMCIA DAQ card became obsolete because g.USBamp performs amplification and conversion within the device and sends acquired data via USB to the attached PC. It is required to install device drivers previously.

Both, respiration and ECG require their own ground and reference level according to their signals. However, the g.USBamp provides one ground and one reference pin grouped together with four channels. For all 16 channels of the g.USBamp four ground and four reference pins are available. In conclusion this means that for a respiration and ECG measurement two channels, two reference and two ground pins are used. Because ground and reference is always grouped together with four channels, eight channels are blocked by this measurement. Further ECG is measured with the first block on channel 1 and respiration with the second block on channel 5. All described circumstances are displayed in Figure 2.2.

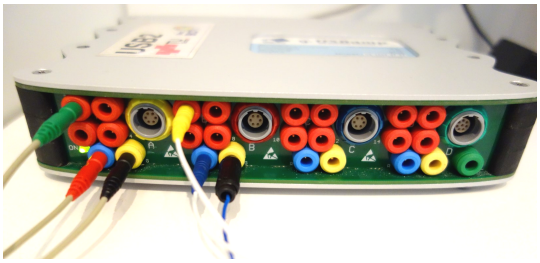


Figure 2.2: ECG is measured with with the first and respiration with the second block. The channels are defined with red pins, reference with blue and ground with yellow pins.

2.1.3 fNIRS

Acquisition of fNIRS data is done with NIRStar software handling illumination pattern of sources as well as sending data within TCP packets to one or more clients. Additionally the installation package contains drivers for NI DAQ USB card 6218M used within NIRScout.

2.1.4 Software Update

After frequent contact with support of NIRx Medizintechnik GmbH the used NIRStar fNIRS acquisition software has been updated from version 10.8.3 to 14.1. The update came with an application programming interface (API) called "NIRx SDK-2015_64bit" for communication with inbuilt functionality to send acquired data via the transmission control protocol (TCP) to a client within the same network. It supports Matlab, C++ and LabView code. Figure 2.3 shows the relationship between the later described NIRStar-LSL Interface for conversion of fNIRS data into a LSL stream. For communication between the new application that was created with C++ and NIRStar software the library TomographyAPI.h is used. It provides the functionality to connect or disconnect to NIRStar or to send data and version requests.[39]
Furthermore, NIRStim, a software to present simple paradigms consisting of pictures, text or sound, was made available. It works in cooperation with NIRStar, sending trigger signals internally via system variables from NIRStim to NIRStar, during the presentation of a paradigm.

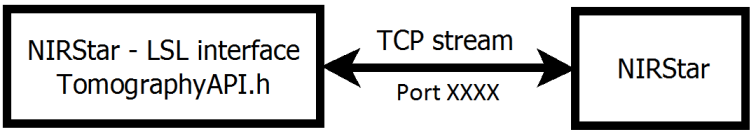


Figure 2.3: NIRStar sends a TCP stream through a previously defined port. For access from outside the library TomographyAPI.h added within "NIRx SDK-2015_64bit" API must be integrated to the created interface code.

Additionally to NIRStim a second option for paradigm presentation has been created using Matlab code, which is able to represent every type of stimuli programmable and executable using Matlab. Trigger signals are sent over a further LSL stream designated just for "paradigm", only. The primary code consisting of proven routines to create a stable serial connection was provided by D. Steyrl and slightly adapted to usage of LSL as well as to the use of paradigm for experimental setup.

All essential LSL streams are recorded with an application named "LabRecorder". It

required the SDK Python with version 2.6 or 2.7 and additionally the correct version of pyside according to Python which provides Qt library to support its inbuilt graphical user interface (GUI).
Furthermore, during this thesis a user manual [7] has been created and stored on the institutes file system, which is describing the installation order of the software and how to perform a measurement. Therefore these steps will not be repeated within this work.

Regarding the evaluation software created by Dr. Bauernfeind, the main changes were made within the file *load_NIRx.m*, which should be able to load XDF files created by LSL. During this task, additionally the code has been cleaned up and simplifications were applied, for example the deletion of duplicate variables differently named or removal of not used variables. In addition to those simplifications new functionalities, such as a notch filter applied on g.USBamp data or additional settings like the possibility to plot all or no figures while execution, which decreases processing duration, were added.

2.1.5 LSL Interfaces

Creation of LSL streams is done by so called applications. For the updated fNIRS setup three of those apps are needed to convert from BP acquisition received serial data, ECG and respiration data from g.USBamp and fNIRS data optionally including trigger signals if NIRStim was used. Two of the three applications were already made available by community behind LSL, thus only for conversion of fNIRS data a new app called "NIRStar - LSL Interface" has been created. Most applications are also able to load a previously created configuration file containing all settings necessary for respective measurement.

Basic LSL libraries are free available online [32] and were integrated into a new C++ project created with visual studio 2013 distributed by Microsoft Corporation, Redmond, USA. Additional also the free available software extensions Qt5 (The Qt Company, Espoo, Finland) for creation of a GUI and BOOST (BOOST C++ libraries,

http://www.boost.org/community/), which contains useful libraries as exemplarily for thread creation and handling, were integrated within the project. Because fNIRS data is not directly accessible for conversion through a COM port or anything similar, the provided TCP stream created by NIRStar is used to convert it to LSL. Through the additionally delivered API and its libraries, it is possible to establish a new connection to the TCP stream, reading the amount of used fNIRS channels, starting transmission of data and more.[39]

The procedure for opening a TCP and LSL stream, conversion of acquired data into LSL packets and displaying necessary information within a GUI is done in C++ code *main.cpp*, *mainwindow.cpp*, *mainwindow.h* and *mainwindow.ui*. Those files were saved on the micro SD card attached to this work instead of listing in appendix due to their size. While *mainwindow.ui* contains all information about the GUI such as width and height of buttons and bars, *mainwindow.cpp* contains the core functions to establish a connection to the TCP stream created by NIRStar, defining actions for buttons of the GUI, thread handling and of course LSL stream creation.

The file *mainwindow.cpp* from line 284 to 294 deals with the streaming latency on the order of 0.8s if 4 to 7 and 2s if 1 to 3 NIR light sources are used, as described at page 37 of NIRStar manual [40], which seems to be the result of processing. If more or equal to 8 sources are used 0 streaming latency should be achievable. From line 357 to 360 the created time lag is subtracted from real clock time which is used for LSL time synchronization. Code 2.1 shows the described lines from the file *mainwindow.cpp*. In contrast to other used applications errors could pop up, as for example if no connection could be established on the chosen port or the connection got lost after its establishment. This app does not require a configuration file because the only possible setting is the port value of the TCP stream, but this does not change until the standard port is changed within NIRStar.

Installation and usage of the API is straight forward and is described within [39]. For the used laptop (lap1) additional microsoft visual studio runtime environments [7] is required

to reach the full functionality.

Code 2.1: The streaming latency is handled within the file *mainwindow.cpp*. From line 284 to 294 the time lag created by NIRStar is defined and from line 357 to 360 the used clock for LSL synchronization is adapted.

```
        ...
284     // Define time correction. Sources >=8 -> 0s; 8 > sources >= 4 ->
286     // 0.8s; 4 > sources >= 1 -> 2s
287     if (sources_ >= 8)
288       timelag = 0;
289
290     else if ((8 > sources_) && (sources_ >= 4))
291       timelag = 0.8;
292
293     else
294       timelag = 2;
295
        ...
356
357       if (frame_count){
358         now = lsl::local_clock() - timelag;
359         data_outlet.push_sample(data, now);
360         marker_outlet.push_sample(timing_bytes, now);
361       }
        ...
```

The acquired BP data available as serial stream from arduino duemilanove is converted with the "Serial Port Connector" application to a LSL stream. Sampling rate is set to 250Hz, the stream name is defined with "CNAP-BP", baud rate of arduino is 115200 for fast communication and COM port is set up according to the used one at the laptop. All other remain default settings.

Within the application creating an LSL stream from g.USBamp data several settings,

such as the number of used channels, the sampling rate or the channel labels can be made. For an fNIRS measurement two channels of g.USBamp are needed to measure respiration and ECG. As previously described both parameters are measured on different channels 1 and 5. The LSL application is not able to exclude unused channels 2 to 4 in between which means that they are also recorded during a measurement. As RF is within a range of 0.2 - 0.4Hz and ECG in 1 - 2Hz initial set sampling rate of 256Hz is above nyquist-shannon sampling theorem and is left unchanged. Furthermore, the check boxes "Common Ground" and "Common Reference" are initially unset because respiration and ECG do not share them. All settings are stored within the configuration file "gUSBamp.cfg".

Those three applications are started with the app "LSLConfigurator" created by M. Schlesinger during his Master Thesis. It allows to open two or more applications simultaneously inclusive their perhaps required configuration file and link them immediately to their targets. Thus this setup calls only one application to open three LSL streams, one for fNIRS data from NIRScout through NIRStar, a second for BP measured with CNAP^{TM} Monitor 500 which is digitalized by arduino duemilanove and a third for ECG and respiration acquired with g.USBamp. A graphical description is given in Figure 2.4. A possible fourth stream is sent from Matlab paradigm software including trigger signals which is not shown in the Figure 2.4.

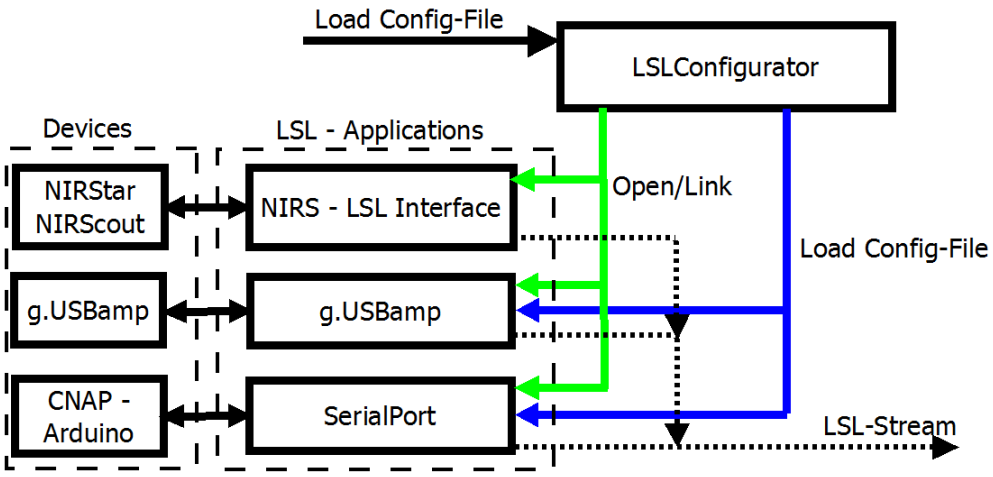


Figure 2.4: The figure illustrates connections between LSL applications and devices as well as the calling app "LSLConfigurator" which is able to open, configure and link a defined list of applications saved in a configuration file. The LSL apps create a data stream which is sent to the network. Within this work only to g.USBamp and SerialPort app a configuration file is transfered from LSLConfigurator

2.2 Experimental Validation

2.2.1 Subjects

Four healthy, right handed volunteers (three male, one female) performed the mental arithmetic task. All of them were students with an age between 25 and 27 years, did not smoke, wear no eyeglasses or lenses. One took medicine against hypertension. Additionally, one healthy, right handed male volunteer at the age of 28, non-smoker and not wearing eyeglasses or lenses, performed the validation task. This task was done under supervision due to the higher risk of getting unconscious. All gave informed consent about the experiment and were instructed previously to the tasks.

The subjects were seated comfortably in an armchair within the silenced fNIRS box containing a TFT monitor, gUSBamp to record ECG and respiration, sensors for measuring BP and fNIRS. Furthermore, they were instructed to avoid head movements due to

artefacts within fNIRS and to avoid movement of the left arm and especially the fingers, used for measuring continuous BP.

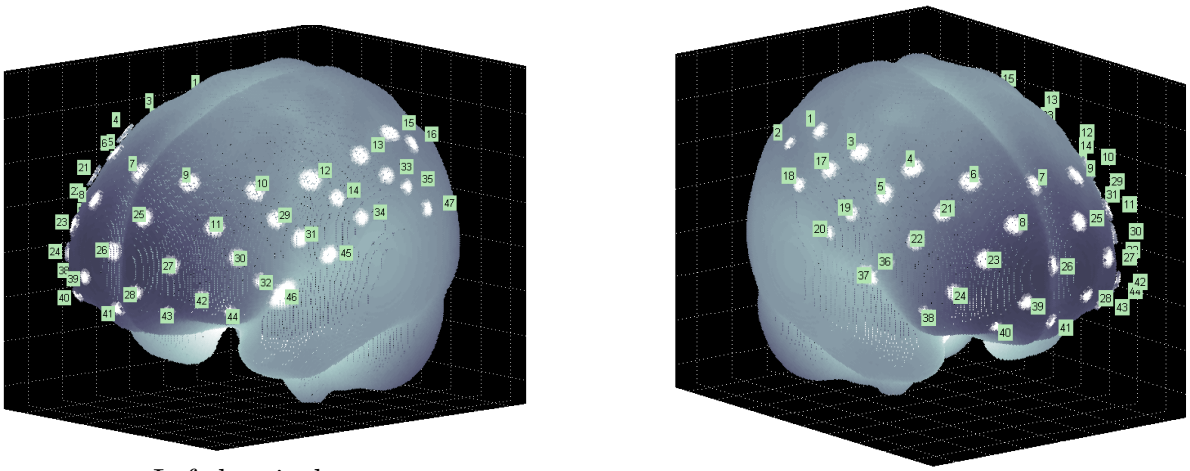
47 channels were recorded during a measurement with 16 LED light sources and 15 optodes. The source-detector arrangement is shown in Figure 2.5 with the same color definition as in Chapter 1.3. Between every source-detector pair a 3cm distance was kept by previously prepared experimental cap. Channel 41 was placed at position Fz which was determined by 10% of measured distance between nasion and inion above nasion. The resulting slight shift to the left has its origin in the available amount of sources which were limited by NIRScout device. A visual presentation of the channel positions on the head is given in Figure 2.6 recorded with zebris system ELPOS (Zebris medical GmbH, Allgaeu, Germany). This was measured during a previous study and thankfully provided by E. Kurz.

16				15	46	15	44	14	43	14	41	13	40	13	38	12	37	12	
47				45		32		42		28		39		24		36		20	
11	35	11	34	10	31	10	30	9	27	9	26	8	23	8	22	7	19	7	18	6
16		33		14		29		11		25		8		21		5		17		2
6	15	5	13	5	12	4	10	4	9	3	7	3	6	2	4	2	3	1	1	1

Figure 2.5: Channel 41 was placed at position Fz which results in a slight shift to the left reasoned by available amount of sources.

2.2.2 Subject Preparation

Setup of fNIRS caps was, as well as the visual presentation of channel position, reused from E. Kurz. First circumference of subjects head was measured resulting in best fitting size of used cap. Channel 41 was positioned at Fz and remaining ones according to well established 10-20 system by Jasper et.al. in [30]. Visible hairs were as well as possible pushed aside to decrease distinction of NIR light by them.



Left hemisphere. Right hemisphere.

Figure 2.6: With zebris mapped channel positions placed on left and right brain hemisphere. Diameter of points describe gaussian standard deviation resulting from mapping accuracy. The data was kindly made available by E. Kurz from an earlier measurement with same channel setting.

Furthermore, to capture ECG, three adhesive electrodes KENDALL^{TM} H135SG (Covidien Deutschland GmbH, Neustadt/Donau, Germany) connected to suitable cables were used. The first was sticked to the right side of sternum, second one underneath left costal arch and third to right hip.

Next, the sensory belt for respiration was located in the middle of the subjects chest but not directly above the electrodes to prevent the subjects from pain.

After the CNAP^{TM} monitor was powered on and system checks were performed an appropriate sized double finger cuff for the subject was attached to the monitor according to user manual [18]. To ensure no disturbance during measurement, integrated alarms were switched off.

2.2.3 Laptop Configurations

To simplify the measurements all necessary programs got shortcuts on the desktop of lap1. Within NIRStar a consecutive order to activate light sources was chosen as illumination

pattern which prevents crosstalk, but leads to a sampling frequency of about 4Hz with current amount of used sources and detectors. Further, the integrated calibration within NIRStar checking signal quality was executed and possible bad channels were tried to be fixed by improving connection of sources and detectors to skull. Also CNAP^{TM} monitor was started at this point of time because the calibration phase can take several minutes.

Depending on the used software to present the paradigm either NIRStim or corresponding Matlab code was started. Finally, LSL configurator was opened and a config file was loaded to start the three needed applications. For a measurement first app is needed for the g.USBamp, secondly the serial to LSL converter for the arduino and third the TCP to LSL converter for NIRS data. To record those streams LabRecorder.py was opened with Python additionally.

2.2.4 Paradigm

Mental Arithmetic Task

This paradigm consisted of three runs, each containing 14 trials with one condition. A trial started with showing 2s a black fixation cross on light gray background. This is followed by a randomly selected (14 possible), written subtraction for a duration of 12s. Thereafter a resting period of 8s randomly shortened/elongated with max. $\pm$ 2s was displayed on a light gray background screen which closed the trial. Each of the 14 possible subtractions were used once within each run and consisted of a one digit number subtracted from a two digit number, for example "$93-8$". A graphical presentation is shown in Figure 2.7, left.

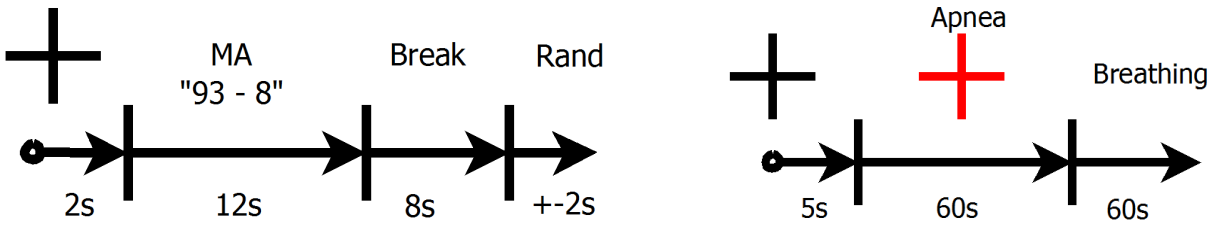
The subjects were asked to perform continuous mental subtraction as long as the operation was displayed on the screen, for example "$93-8=85 \rightarrow 85-8=77 \rightarrow 77-8=69 \rightarrow ...$". Displayed was only the initial subtraction without result, following subtractions should happen mentally. This paradigm was shown once with NIRStim software and three times with Matlab code previously described.

Similar paradigms were used by Dr. Bauernfeind in his works [13] and [12] but

instead of achieving statistical evaluable data this task was used for checking the correct recording functionality and interaction between different components of the updated setup.

Validation Task

To demonstrate the sustained functionality of the updated fNIRS setup a breath hold experiment was performed in the validation task. One run consisted of holding breath as long as possible but at last for maximal 60s followed by normal breathing for further 60s. Apnea was indicated with a red cross, leaded by a black fixation cross shown for a duration of 5s. Those steps were repeated two times continuously within one run and three runs were executed. Figure 2.7, right shows one trial graphically. The subject was also instructed to stop breathing after an inhalation not above normal volume because a higher inhalation could possibly lead to an increased intra thoracic pressure and resulting physiological response.



One trial of mental arithmetic. One trial of validation task.

Figure 2.7: Each figure shows one trial of respective task. The subtraction within mental arithmetic task is shown without the result as displayed in left Figure. Within validation task a red cross indicated to keep breath hold.

2.2.5 Evaluation Software Settings

To evaluate the data streams from previous tasks, the evaluation software and within this especially the files *Main_NIRx.m* and in the following *Grand_avg.m* were used. Due to the aim of this work not one setting was chosen to evaluate data but a random sample survey

was done trying the most frequently used filter settings if they retained their functionality within the new setup and do not produce errors. The possibility to remove single trials or to interpolate one channel through averaging surrounding neighbor ones was also used within some tests to check their functionality or to improve the SNR of a single channel as well as of the average from all channels. This feature also allows to average only trials with a specific condition. An currently ongoing fNIRS project with five conditions was used to check its functionality.

The filter and correction settings are selectable within *Main_NIRx.m*. Every setting was tested on its own by running the software once with activated and afterwards with deactivated filter or correction. MW correction source (systolic/diastolic BP or HR) and correction mode settings allow more than an on/off selection. The first was checked completely and the second only with options uncorrected, respiration corrected, MW corrected and respiration+MW corrected. A test with all possible settings was not performed.

Nonetheless later presented results were corrected with filters removing MW (based on diastolic BP) and respiration, also a baseline and a notch filter to remove main voltage 50Hz ripple and a low pass filter were applied. Further, a common average reference (CAR) filter removed BP expressions in fNIRS.

3 Results

3.1 Update of Current fNIRS Setup

Finally, a reduction of devices is easily visual recognizable as shown in Figure 3.1. The only devices remaining are CNAP^{TM} Monitor 500, arduino duemilanove, Lap1, NIRScout device and newly added g.USBamp within fNIRS box.

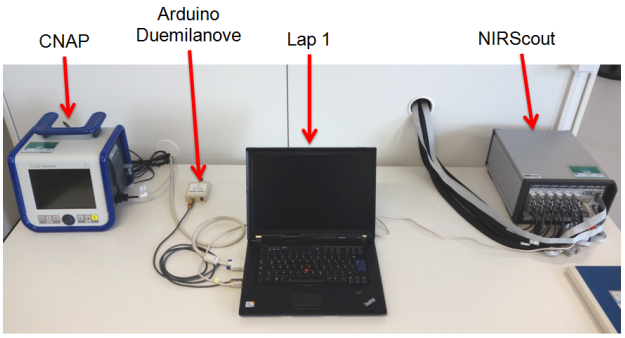


Figure 3.1: The figure presents final updated fNIRS setup containing CNAP^{TM} Monitor 500, arduino duemilanove, Lap1 and NIRScout device. g.USBamp is within fNIRS measurement box.

Calibration of the arduino duemilanove revealed a difference of +52mV between applied and measured voltage of 5V reference. This results in about 1% measurement inaccuracy if a range from 0V to 5V is assumed. Furthermore, BP from 0mmHg to 500mmHg is mapped to analog input range of arduino which ends up in an inaccuracy of about 5mmHg. The chosen opportunity to send BP within one byte result in

a measuring range from 0 to 255mmHg with a resolution of 1mmHg. Also the 16MHz of the arduino duemilanove are not able to hold a sampling rate of 250Hz. Instead an effective sampling rate of 199.227Hz was measured during experiments with LSL.

The signal run times for CNAP^{TM} monitor and NIRScout device were requested by their manufacturers to investigate possible delays influencing the data processing. According to the workload of CNAP^{TM} monitor the signal run time vary between 50ms to 60ms. For the NIRScout device the reply included the information that according to a linear, single illumination pattern of NIRScout sources only a sampling frequency of about 4Hz, equal to 250ms, is achievable. Furthermore, the information was given that all channels are measured once within this time and are sent afterwards as one package. This leads to a signal run time of a quarter second for each measurement of all channels. It was also claimed that transmission durations produced by TCP could be neglected due to their minority.

The created GUI of NIRS - LSL Interface is shown in Figure 3.2. By clicking the "Link to NIRStar" button the interface should connect to above entered TCP port and display the used version of API. By default the port is the same as the one used in default settings of the NIRStar software.

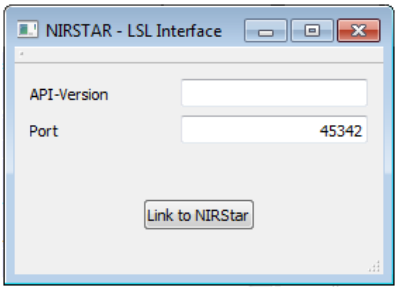
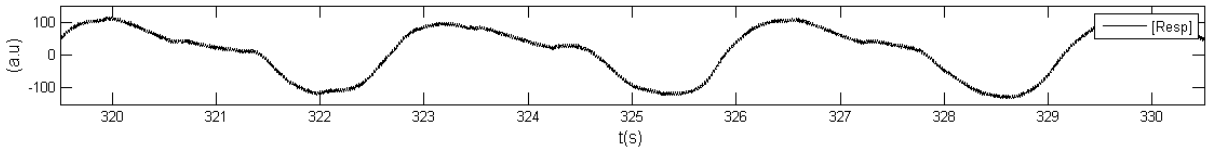


Figure 3.2: The GUI of NIRStar - LSL Interface shows the used API version provided by NIRx Medizintechnik GmbH and adjustable port number (initial port is 45342) containing the fNIRS TCP stream. With button "Link to NIRStar" the interface connects to the TCP stream and converts the incoming data to an LSL output.

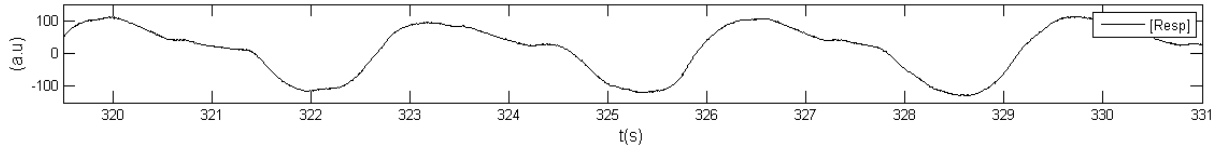
3.1.1 Evaluation Software

Regarding to the evaluation software, the used *load_NIRx.m* file which is responsible for loading fNIRS data stored within GDF files is copied, adapted and named to *load_NIRx_XDF.m* for reading XDF files.

Other results in the evaluation software are difficult to measure because the performed changes only reveal within code. For example approximately 30 lines of code in the file *Main_NIRx.m* and about 80 lines in the replaced *load_NIRx.m* could be removed. All up, both files consist of about 500 lines of code. Exemplarily Figure 3.3 shows the application of a notch filter within first file on respiration data which was disturbed by 50Hz mains voltage ripple acquired with the g.USBamp. Second file kept most of its functionality but since GDF and NIRStar files are replaced by XDF the used procedure for loading and handling different data streams has changed.



Respiration inclusive 50Hz ripple.



Applied notch filter on respiration.

Figure 3.3: Figures contain an excerpt of a subjects respiration during a measurement. Upper one shows respiration inclusive 50Hz artifact produced by mains voltage and second one shows the same signal with applied notch filter.

With the evaluation software different figures are displayable. Concerning data measured with g.USBamp and BP with CNAP^{TM} monitor two figures are created. The first one, exemplarily shown in Figure 3.4, contains the whole signal length measured from one subject showing the BP surrounded by determined diastolic and systolic values, the respiration, the HR and the ECG from which the HR was calculated from. Also all not manually excluded trials used for averaging could be identified within those diagrams by

the green logic level signal with value one equal to active and zero equal to inactive trials.

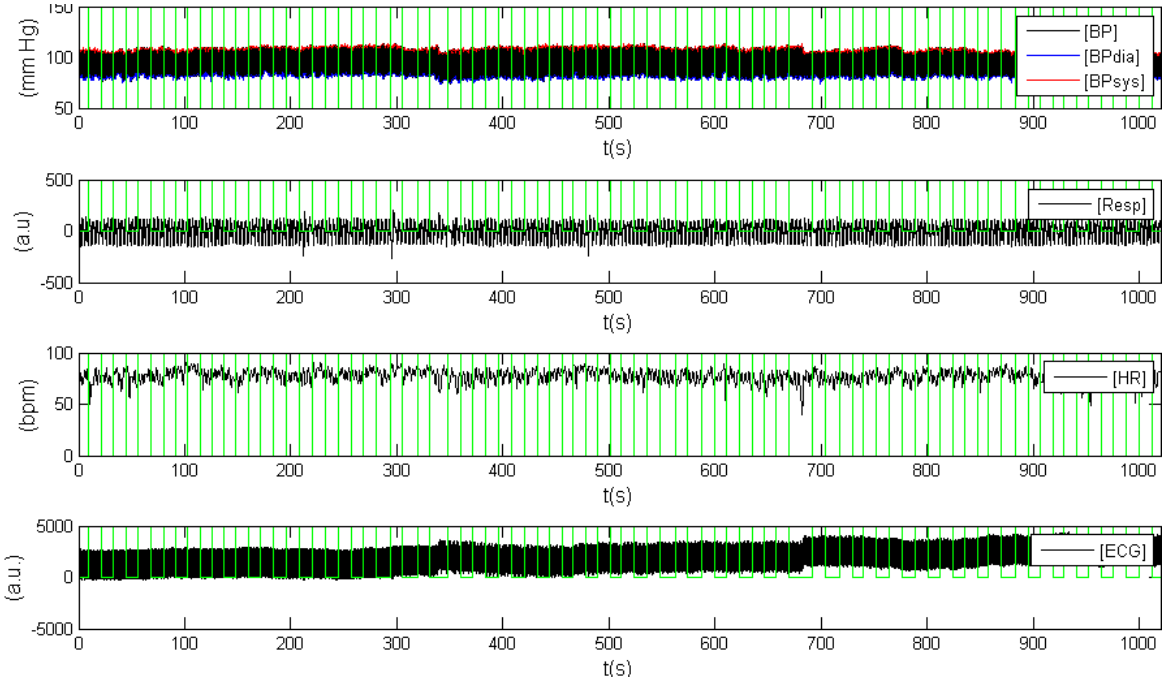


Figure 3.4: First shows BP in black, diastolic in blue and systolic BP in red solid line. Second shows the respiration, third the HR and last the ECG. The green solid line indicates an active trials.

The second figure averages the data of systolic and diastolic BP variability as well as the heart rate variability (HRV) calculated from HR over all active trials. Figure 3.5 exemplarily shows the second one.

Next two figures in Figure 3.6 display the frequency spectra, the upper one without any correction and the lower with applied, previously set correction methods for every channel with the same alignment as they were displayed in Figure 2.5. This is also used within later described presentation of fNIRS concentration changes in 3.10. A third one shows the average over all previously cleaned spectra, exemplarily shown in Figure 3.7.

Further three figures show concentration changes of fNIRS signals. One displays the whole recorded data of one, an in the settings chosen channel, again in combination with a logic level signal indicating trial activations (see Figure 3.8). Another presents the averaged concentration changes of the same channel over all activated trials within a

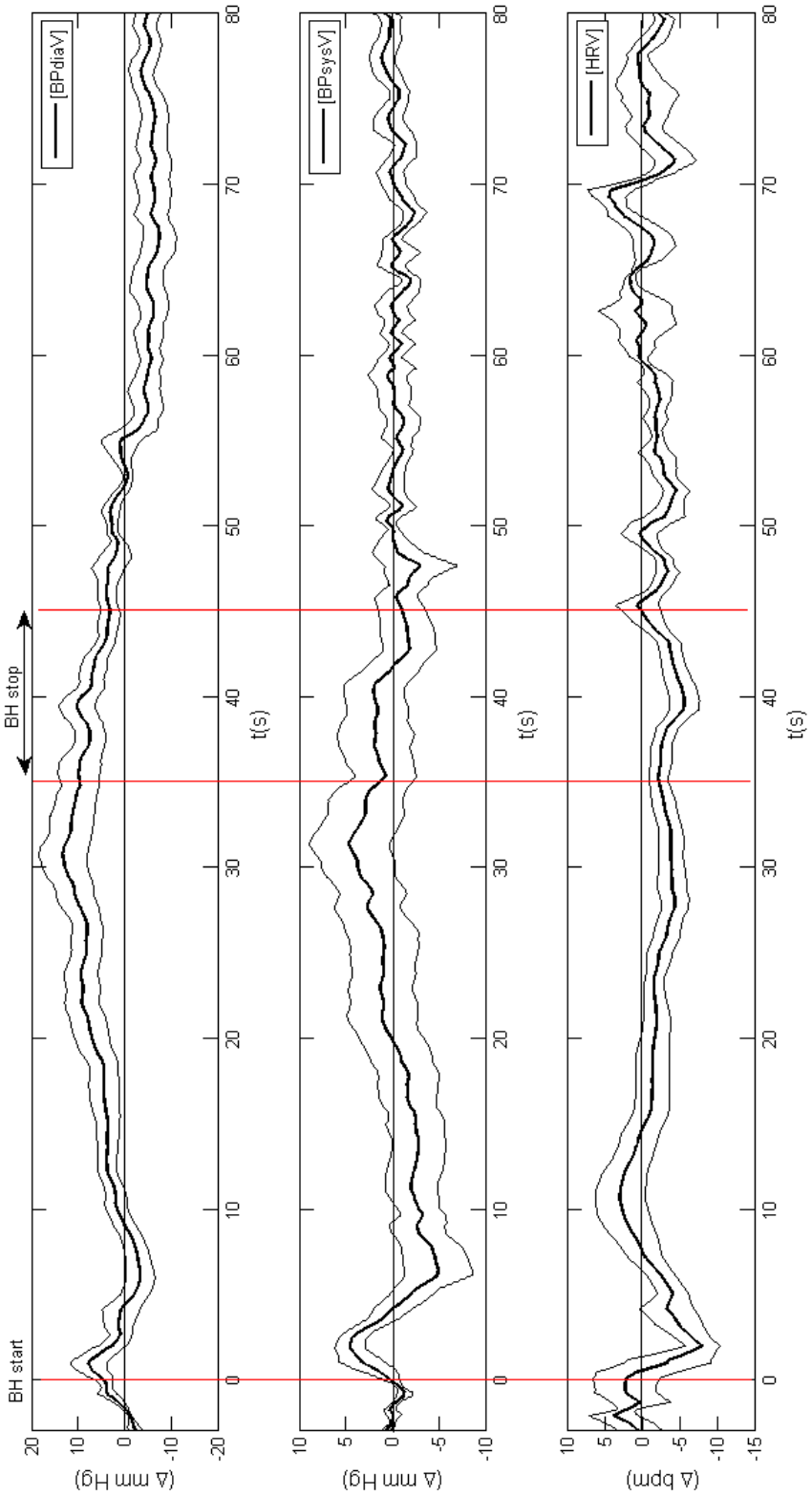
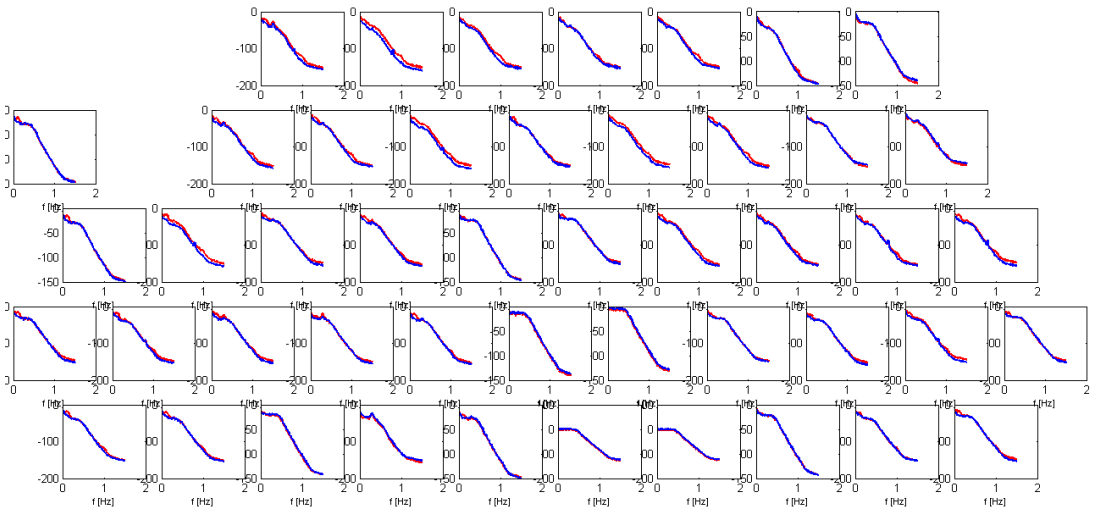
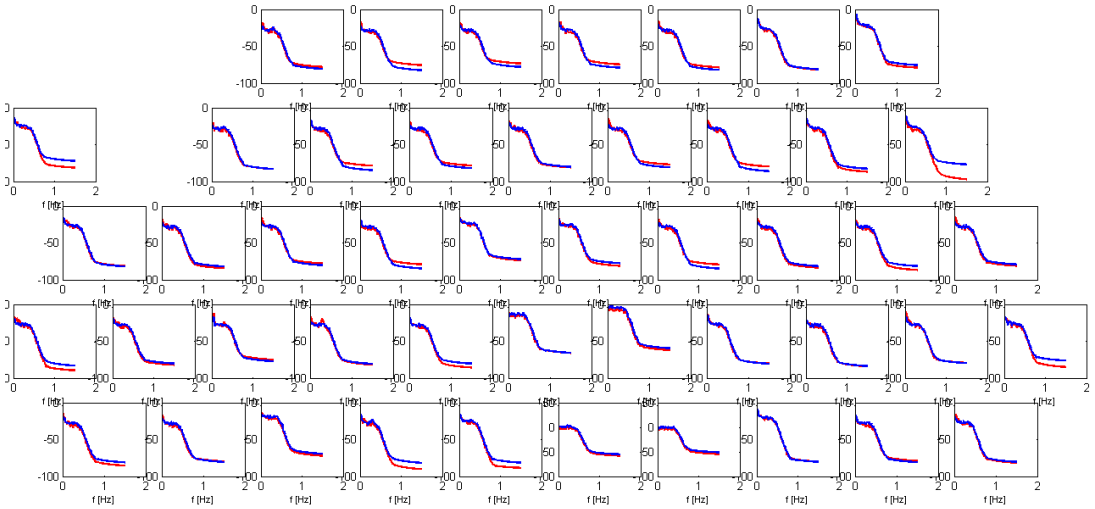


Figure 3.5: The calculated variabilities of BP and HR averaged over four trials measured with CNAP^{TM} and g.USBamp. Start of breath hold was at 0s, stop between 35s and 45s both marked with red vertical lines. Thick black solid lines describe respective averaged data surrounded by standard deviation as thin black solid line.



Unfiltered frequency spectra.



Frequency spectra with applied filters.

Figure 3.6: Frequency spectra of each single channel before and after filtering with low pass filter, CAR, baseline, etc.. Blue solid line identifies deoxy-Hb and red one oxy-Hb.

single Figure in 3.9. The last presents all channels averaged over active trials as shown in Figure 3.10.

The last plot was newly implemented and displays the concentration changes of oxy-Hb and deoxy-Hb as a topographic presentation mapped on a head like sketch. An example is given in Figure 3.11.

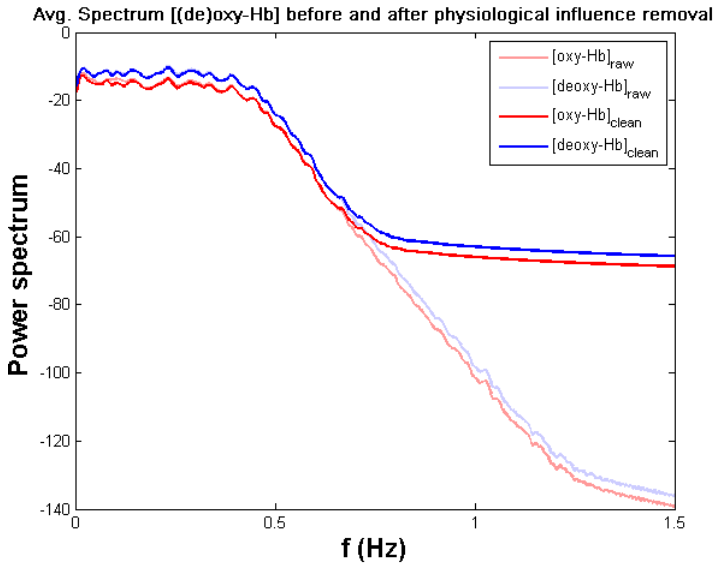


Figure 3.7: Frequency spectra averaged over all channels. Dark blue and red line identify filtered deoxy-Hb and oxy-Hb, bright blue and red line unfiltered spectra.

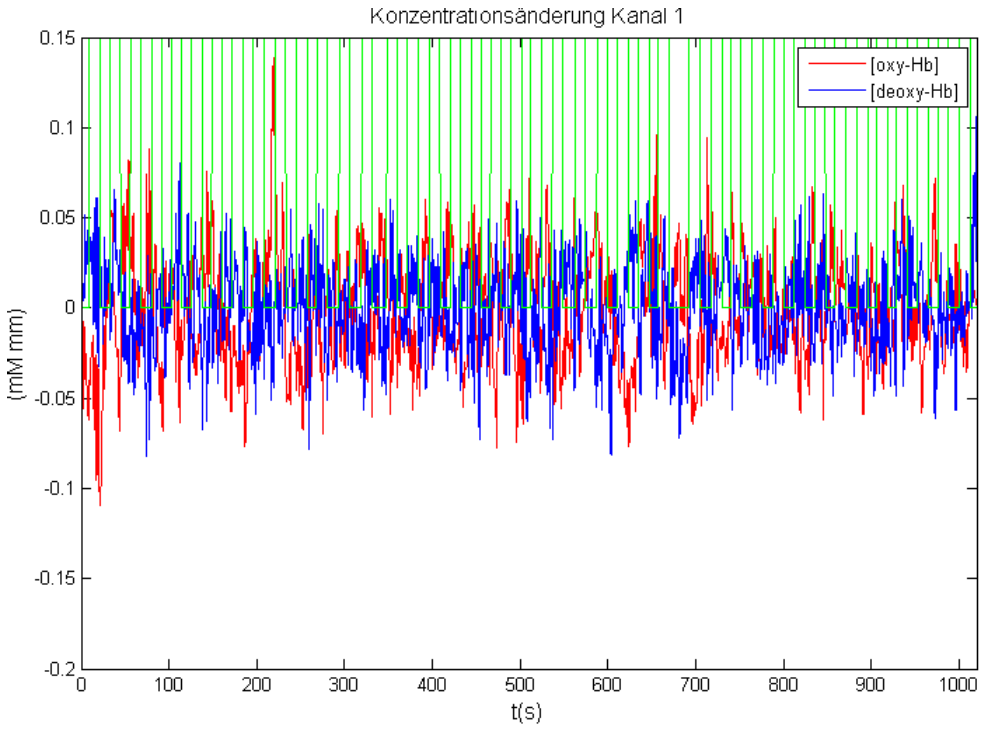


Figure 3.8: Raw fNIRS signal of channel 1. Deoxy-Hb is shown in blue, oxy-Hb in red and active trials in green.

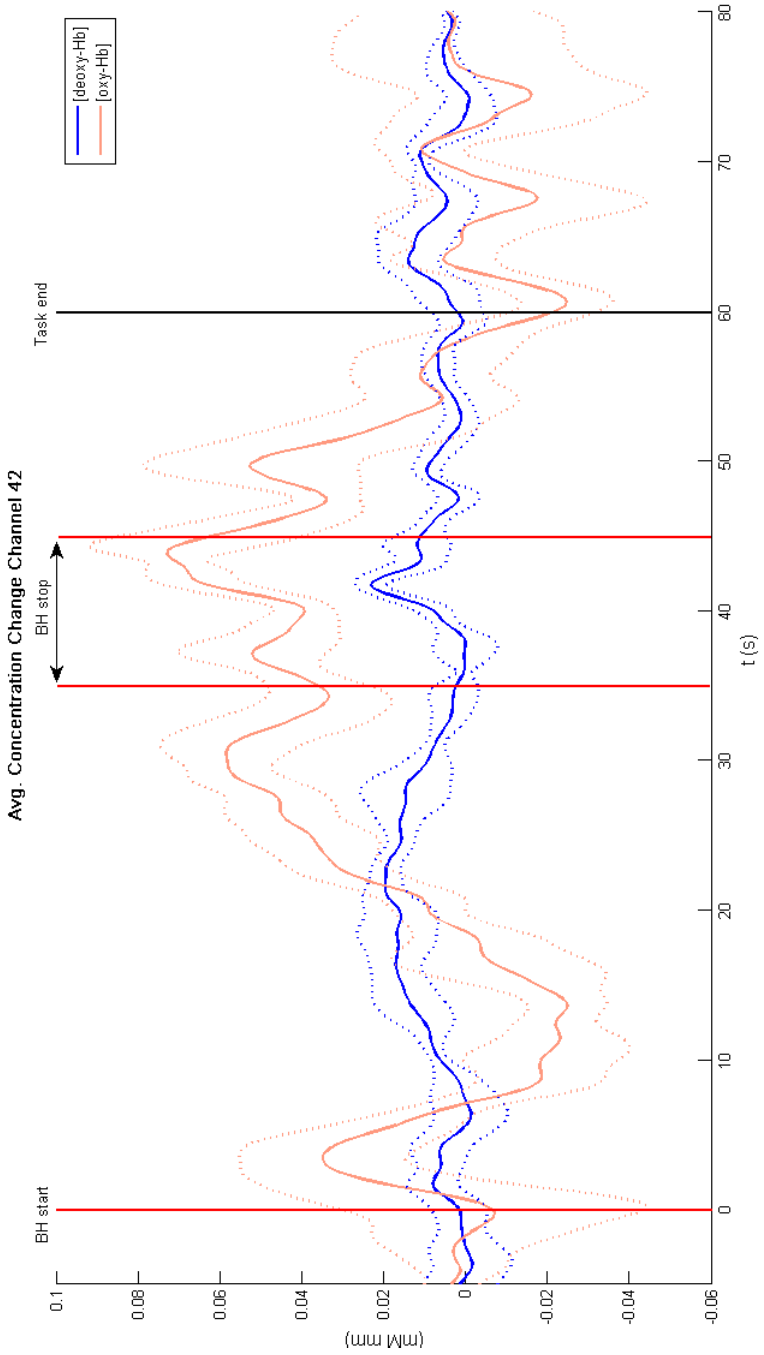


Figure 3.9: The concentration change of channel 42 averaged over 4 trials: Start and end of breath holding is marked with red, trials end with black vertical line. Blue solid line identifies averaged deoxy-Hb, red solid line averaged oxy-Hb and dotted lines in same colors describe standard deviation as a result of averaging through four trials.

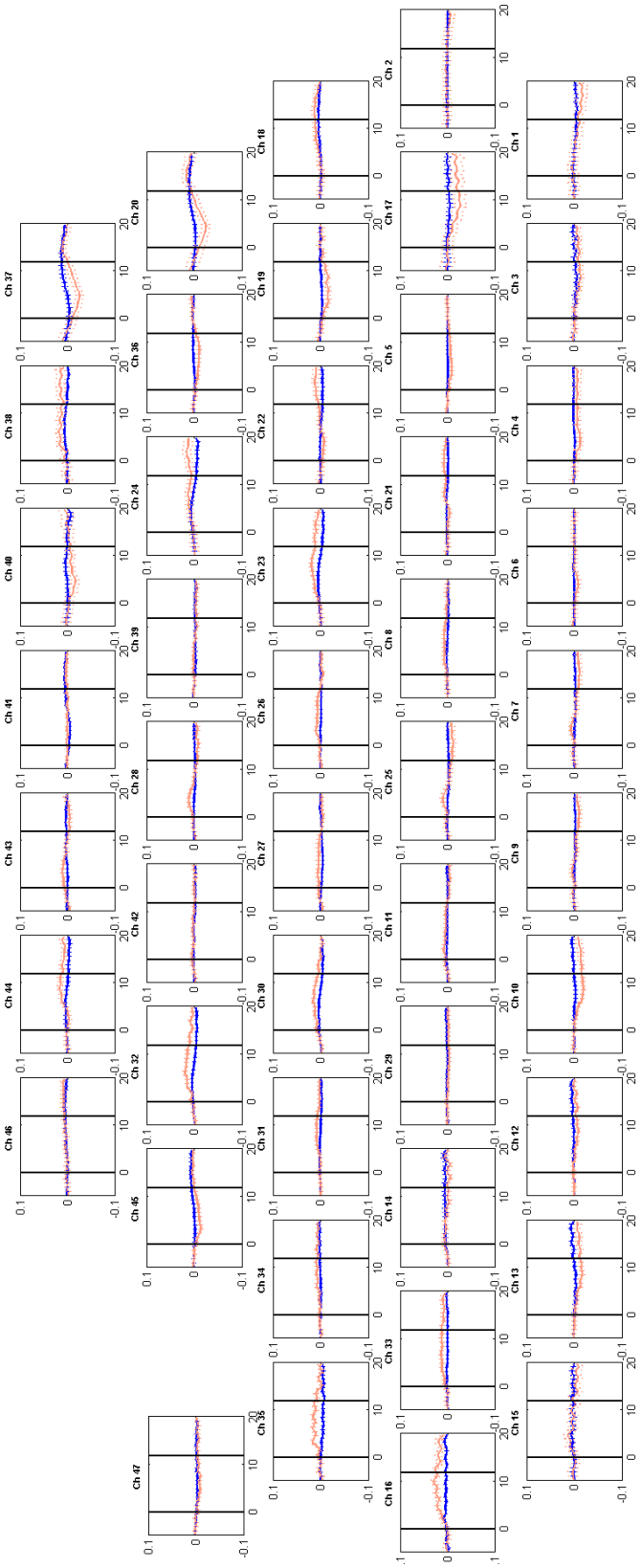


Figure 3.10: The figure displays the concentration change of all channels fNIRS data measured from one subject. First black vertical line at 0s indicate the beginning and second one at 12s the ending of a trial. The red solid line identifies oxy-Hb and the blue deoxy-Hb. Dotted lines describe the standard deviation of each signal.

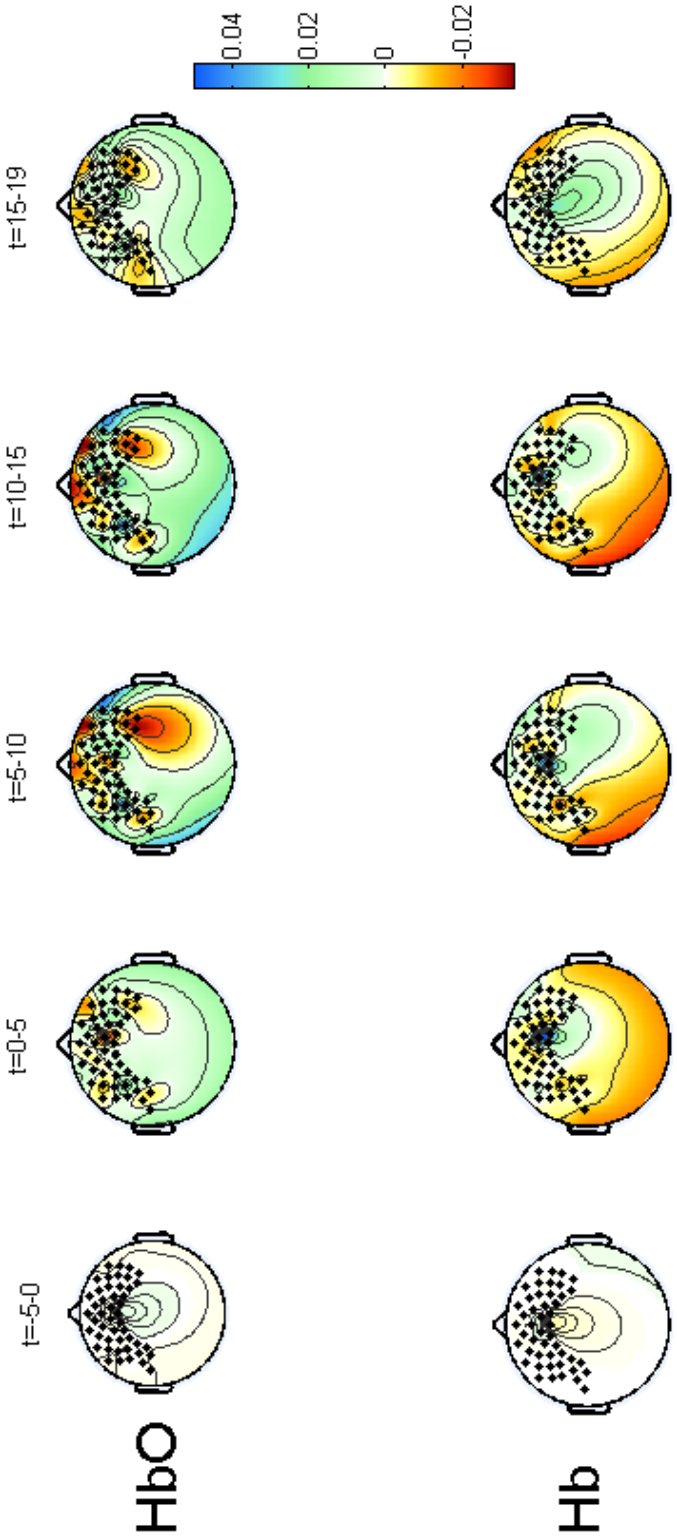


Figure 3.11: Through runs averaged concentration changes within five different time steps are mapped topographic on a schematic head. Red indicates low and blue high concentration.

3.2 Experimental Validation

To check the functionality and behavior of the updated fNIRS setup two different tasks were performed, a validation task consisting of holding breath and a mental arithmetic task where subjects must perform a continuous subtraction. Results of both tasks are presented in the following chapters. No statistically evaluation is performed because of the small amount of data reasoned by the lack of need for accomplishment of the objectives.

3.2.1 Mental Arithmetic Task

The first performed mental arithmetic measurement was done with NIRStim software but was incorrect because of inversely connected ECG cables. Before post processing ECG data was multiplied with (-1) to remove that issue. All trigger signals were detected correctly and paradigm presentation worked well. For the continuing three measurements Matlab code for paradigm presentation was used.

Figure 3.10 displays concentration changes of all channels as previous described measured from one subject, averaged over active trials. Visible range leads from 5s before to 20s after trial begin. Channels 6, 7 and 8 resulting from defect source 3 were interpolated with nearest surrounding ones. Also channel 2 was interpolated due to its bad signal quality. Further the 1., 14., 15. and 30. to 42. trials were removed also related to increased noise within signals.
CAR, baseline, respiration, notch, low pass filters and MW correction, determined through diastolic BP, were activated.

3.2.2 Validation Task

The data measured in the validation task has been evaluated with the same settings as for the mental arithmetic task. Respiration data allowed determination of breath hold start and stop and consequently absolute apnea duration which is listed in Table 3.1.

For further processing of fNIRS data trials 3 and 5 were excluded to decrease range of breath hold duration for averaging which leads to a smaller standard deviation. As previously described, Figure 3.5 displays systolic/diastolic BP and HR variabilities. First red vertical line indicates beginning of breath holding, second and third the range of starting to breath again. Figure 3.9 shows averaged oxy-Hb and deoxy-Hb surrounded by their standard deviation. Breath hold begin and end are again marked with red lines similar to Figure 3.5 but inclusive a black vertical line indicating the end of breath hold task, determined by paradigm.

Table 3.1: Durations of holding breath in each trial, determined through respiration measurement.

Trial Nr.	BH Duration (s)
1	43
2	41
3	58
4	49
5	61
6	35

4 Discussion

First of all the knowledge and its delivery to students at the Institute should be highlighted which works very well and was also a positive influence. Further, especially for this work it was beneficial to have no direct pressure on achieving the goals, due to the missing projects in context with the fNIRS Environment which created a good atmosphere to realize the objectives. This should be kept in mind if a further actualization is upcoming during the next years.

Although the environment at the Institute is very good, a drawback is the status of fNIRS. By counting people working with EEG versus with fNIRS it is obvious that EEG is preferred. To keep the quality as high as it is it is necessary to have also a powerful team that is used to fNIRS.

4.1 Update of Current fNIRS Setup

The replacement of g.tec amplifier and g.CBox by an g.USBamp and also the removal of both outdated HP compaq nw8000 laptops was an obvious solution to achieve a competing fNIRS Environment. Reuse of the arduino duemilanove results in buying an arduino uno to back up its program leading to the only costs in this project. But it comes with the possibility to further use a uno within other projects. Possible following improvements in hardware after this update are firstly the replacement of devices by newer ones, which is

not necessary in the near future and secondly an increase of available USB ports through an active hub because all ports provided from lap 1 are in use within the new fNIRS environment. Adding other USB devices for special studies will require additional ports.

The update of software is a continuous process, especially software from NIRx Medizintechnik GmbH was renewed during the work on this project leading to a further update afterwards. Despite of minor benefits the next software version is delivered with a new feature described next. Measurements within other studies revealed a 0.8Hz peak in frequency spectra with unknown origin. On demand at NIRx Medizintechnik GmbH it turned up that an internal issue is the reason for that peak but it will be removed by the newest version of NIRStar 14.2. Every institution has to decide whether it is reasonable to lose control on processing methods. Other improvements could lead to step backwards if they are not applied. In the end the chosen way must be well reasoned and all of its included features should be known.

Inaccuracy concerning arduino duemilanove acquired BP data before performing the calibration could had led to hypertension patients even if they were underneath the limits. Measurements were performed with lap 1 and the use of internal arduino 5V reference which is dependent on its power source. Any other setup than the one used for this measurement or other laptops could possibly lead to slightly different reference voltages resulting in inaccurate BP measurements. In [58] a valid voltage range from 4.40V to 5.5V for USB 3.0 is described which can change results significantly. Although this leads to inaccuracies in BP it will not affect fNIRS data because the calculation of MW is based on determination of low frequency changes in BP spectra, which is not affected by such systematic amplitude errors.

The achievable resolution of 10bit by the arduino instead of 12bit by DAQ PCMCIA slot card is a quite big reduction but not a problem for its purpose. Since the amplitudes of MW's are stated to be above 10mmHg in healthy young male, female and older male subjects by Taylor et. al. in [55], those reductions in resolution do not effect signifi-

cantly the calculation of MW artifact removal. Further the measurable range decreased to one byte as a result of the LSL application. The app was not able to concatenate two corresponding bytes, which is needed for values above 255. First it can be stated that systolic BP will rise in a negligible number of healthy and even hypertension subjects above 255mmHg and second if nonetheless two bytes should be sent it would take significantly more effort to rearrange them in evaluation software correctly afterwards.

Although the routine within the loop of code shown in A.1 from line 50 to 70 is kept very simple, only a maximum sampling rate of 200Hz instead of 250Hz is achievable with the arduino but with a sampling rate of 100Hz of CNAP^{TM} monitor it is within nyquist shannon sampling theorem. Due to the high baud rate of $115200\frac{bit}{s}$ and the usage of functions which do not take longer than one ms for processing, possible reasons for delays must be searched within the USB transmission and the already created LSL application for serial conversion. Since BP is a slow alternating signal and the predictable delays produced by the BP acquisition system will not affect the quality in a decisive way, no further investigations were performed.

For acquisition of ECG and respiration the now used g.USBamp is also an advance in comparison to PCMCIA DAQ card 6024E, g.CBox and g.tec amplifier. The resolution raised from 12bit to 24bit and the sampling rate from 200 samples per second to 38.4kHz. [24, 38]

The synchronization of data is handled by LSL, which was already investigated and approved by Dr. Scherer and one of his master students during a graduation work. Possible inaccuracies in synchronization could be a result of random time jitter in data acquisition of different devices but also linear drifts. Those are not investigated during this work due to their supposed marginality in duration compared to fNIRS signal speed. A possible time lag of g.USBamp was also ignored due to its common use in EEG measurements and their time requirements. Also arduino duemilanove was not considered because of its relative high sampling frequency in comparison to NIRScout

device and CNAP^{TM} monitor. The used linear illumination pattern of NIRScout sources is responsible for the achievable sampling frequency and therefrom the possible inaccuracies in synchronization. With the two paradigm displaying techniques also two different behaviors are created. If NIRStar is used with NIRStim software the trigger signals are always sent with acquired data packages from NIRScout device through TCP. For example within the experiment in this work NIRStar and NIRScout sent about every quarter second a TCP package to the LSL application. This produces the possibility that a trigger signal is received shortly after sending a data package by NIRStar and could lead to maximal about 250ms synchronization error in context with BP, respiration and ECG data. This error could not be removed trivially. A possible solution is to catch trigger signals with another application. A more simple solution is to use Matlab code for paradigm presentation which directly creates an separated LSL stream of triggers. The only inaccuracies in synchronization within this solution can result from triggers created by trial start, shortly sent after a package was acquired so that this one was lost. Same circumstances apply for the end of a trial but due to the fact that within studies averaging over trials offline mostly before start and end of a trial several seconds were added, this do not have influence on the result. Another positive effect can be achieved through averaging over bigger amounts of subjects and trials which will decrease standard deviation reasoned by even distributed statistically inaccuracies.

4.2 Experimental Validation

As previously mentioned, studies within this work do not achieve a statistically evaluable amount of measured subjects. Nonetheless it was enough to check retained functionality and behavior.

4.2.1 Evaluation Task

The Matlab code used for displaying the paradigm revealed that opening and closing of a LSL stream should not be done directly before or after sending packages because they can possibly get lost. Measurements with NIRStim are very comfortable with previously described synchronization restrictions.

A major achievement of this work is that the general usage of programs is easier due to the concentration within one PC but is also creating problems if the operator is switching between different programs during a measurement. In some cases subjects reported that the paradigm flickered during a run. This was reasoned by switching between programs to check their functionality, signal strength or the progress of paradigm by the scientist. The issue is produced by the operating system windows 7 and the scientist. Solutions could be a change to another operating system, run paradigm on a different computer than measurement software or training of researchers.

The evaluation software supports a multiplicity of settings, such as excluding or interpolating single channels or even excluding trials based on subjective decisions, which could possibly lead to forced results needed for a study. This fact is problematic because studies get dependent on researchers decisions and takes them in charge to describe detailed the evaluation settings to stay repeatable and comparable to different studies. More problematic is the fact that some times it is not known at the beginning where signals come from. Exemplarily earlier addressed 0.8Hz must be discussed. Without the information of NIRScout manufacturer it would not be trivial to find its origin because it is not described within manuals.

4.2.2 Validation Task

Although the durations of apnea vary widely and also two trials were excluded, the results of this task agree with the ones in [33, 34, 37]. This agreement must be viewed with caution because only one subject was measured within this work and slight differences

in methodology to other works exist but for following discussion the lack of subjects is neglected and data is accepted due to its high correlation to previous studies.

A CAR applied to this data would imply that the amplitudes of every channel come closer to zero which did not happen within this task. A possible explanation is that the diameter of blood vessels in the skin and brain vary widely at the measured areas which leads to changing blood flows all over the head and as a result to different oxy-Hb and deoxy-Hb concentrations. Also none equal SNR's between the channels, as a reason of bad mounted sources/detectors or even different gains within all channels, will have an affect on CAR. After handling those influences, which are difficult to control as previously described, also researchers change the signal distribution through removing or interpolating channels.

Finally, this task is proper to get a fast result and to check the behavior of the system with low effort, although the absolute values are not very meaningful due to the lack of physiological control and statistically significance. Better repeatable results could be achieved with a measurement phantom containing a chemical, scattering solution which reduce its oxygenation level after adding yeast as described in [15]. With that it should be possible to compare calculated values of the chemical reaction with the measured ones and increase the significance of such a task.

5 Conclusion

A reduction of one third in device effort is a great benefit for further use outside the institute. Combined with zero costs this solution is obviously a success. Nonetheless it should be thought about an investment into update of CNAP^{TM} monitor software to increase patient comfort through faster calibration speed and to benefit from other improvements included.

Understanding and adapting the evaluation software was a time consuming part of this work which should not be underestimated in further studies or theses although some code descriptions are added now. Especially debugging with the big functionality and selectable settings could hardly be done completely but in review it seems to retain all of its previous supported features and even some more.

The introduction of LSL for data acquisition and synchronization builds the core of the software update. Without this step the updated programs would not have brought a big benefit. It was a predictively one, creating more possibilities to cooperate with other setups as for example EEG, even if only single modules such as BP acquisition is needed.

Although the hardware was simplified significantly and LSL will become accustomed at the institute, the usage of software is not simplified in the same ratio. An improvement is that all programs can be started on one laptop without switching between different ones. Nonetheless the steps to perform a measurement are nearly equal to the previous setup but currently no significantly better solution was achievable.

Performing measurements worked well and obtained results confirm retain of functionality and behavior. Mental arithmetic and validation task were done with minor problems which could be fixed. Especially the validation task should be highlighted as example of problematic comparability between studies due to the rarely described methods and to the selectable settings. A statistically significant amount of subjects could remedy partially this circumstance but also other validation techniques described earlier.

After all it is to advice to train someone who should know the system similar as Dr. Bauernfeind to prevent scientists from interruptions during their work by updates of the system. With that in mind the first and hopefully not last update will keep the setup powerful at a high level for the next years.

5.1 Further Work

No absolutely necessary continuing work must be performed to accomplish the setup but possible bachelor or master thesis could work out a phantom to check the functionality of NIRScout sources and detectors inclusive the algorithms for oxygenation calculation within evaluation software in a repeatable standardized way. Another interesting work in respect to combine fNIRS with EEG based setups could be to determine the exact signal run times measured from detectors to recorders.

A Code

A.1 Arduino Duemilanove - BP acquisition

Code A.1: Created with Arduino IDE. The assumption that BP of most people range from 0 to 255 and resulting simplification in post processing lead to a read and sent value with size of one byte.

```
1  /*
2  CNAP Monitor data reader
3
4  Reads analog input signal from CNAP-Monitor and sends values via serial to Laptop
5
6  Adapted: CNAP_monitor_data_reader
7  First adapted 2016.01.21
8  by Dominik Bachmaier
9  University of Technology Graz
10 Institut for Knowledge Discovery
11 Laboratory of Brain-Computer Interfaces
12 8010 Graz, Austria
13 */
14
15 // Constants won't change:
16 // Define the analog input pin for cnap-recording (0-5 possible)
17 const byte PIN_CNAP = 0;
```

```
18 // Interval reading data from cnap and serial send in ms. CNAP captures with 100Hz
19 const int READ_INTERVAL = 4;
20 // Calibrated reference voltage measured at 19.01.2016 in mV
21 const unsigned long int VREF = 5052;
22 // Mask for low byte to split blood preassure value to low byte
23 const uint16_t MASK_LO = 255;
24
25 // Variables will change:
26 // Current time
27 unsigned long current_millis;
28 // Value of the analog Input pin for cnap-recording
29 unsigned int cnap_value_in = 0;
30 // Calculated blood pressure value
31 uint16_t bp_out;
32 // Last time the analog input pin was read
33 unsigned long analog_read_at_millis = 0;
34 // Blood pressure, assuming it won't be higher than 255mmHg.
35 byte bp;
36
37 // the setup routine runs once when you press reset:
38 void setup(){
39   // Opens serial port, sets data rate to 500000 bps
40   Serial.begin(115200);
41
42   // Set analog referance to default 5V
43   analogReference(DEFAULT);
44
45   // Delay while device settles
46   delay(1000);
47 }//end setup
48
49 // the loop routine runs over and over again forever:
50 void loop(){
51   // Current time
```

```
52    current_millis = millis();
53
54    // Read analog Input and send to serial
55    if( (current_millis - analog_read_at_millis) > READ_INTERVAL){
56      //Resets the counter for intervall of reading
57      analog_read_at_millis = current_millis;
58
59      //Read value of analog input pin
60      cnap_value_in = analogRead(PIN_CNAP);
61      //Convert from digital value to BP value 0-500mmHg (0-5V)
62      bp_out = round((VREF * cnap_value_in) / 10240);
63
64      // to read secure only lowes bits as byte
65      bp = bp_out & MASK_LO;
66
67      //Send high and low byte of BP to pc
68      Serial.write(bp);
69    }//end if(current_millis
70  }//end loop
```

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