Chapter 5

Near Infrared Spectroscopy (NIRS) and Functional Near Infrared Spectroscopy (fNIRS)

Raymundo Cassani

Raymundo Cassani is a Research Developer and Research Assistant at the The Neuro (Montreal Neurological Institute-Hospital), McGill University. He received the BEng degree in Communications and Electronics and the MSc degree in Microelectronics from the Instituto Politécnico Nacional, México, in 2007 and 2012 respectively. In 2018, he obtained his PhD from the Institut National de la Recherche Scientifique, as a member of the Multimodal Signal Analysis and Enhancement Lab (MuSAE Lab), where he held the positions of Postdoctoral Fellow and Research Associate. In 2021, he joined the Dynamic Neuroimaging Lab (neuroSPEED). His research includes signal processing applied to biomedical signals, such as EEG, MEG, fNIRS, ECG and EMG, all of this with applications in health diagnostics, human-machine interaction, entertainment and neurotechnologies.

Contents

5.1 Introduction

Functional near-infrared spectroscopy (fNIRS) is a non-invasive optical technique used for the study of the brain activity. fNIRS is an application of the near-infrared spectroscopy (NIRS) to measure the concentration changes of deoxy-hemoglobin (HHb) and oxy-hemoglobin (O_2Hb) in the blood vessels in the cerebral cortex, thus providing an insight on the metabolic demand in the cortex, which is an indirect measurement of the cortical activity.

In this chapter, a brief history of the use of optical methods for the study of biological tissues is presented, placing special interest in the study of the brain. After, the basics of NIRS are presented in detail, followed by fNIRS as the natural use of NIRS to study the brain activity in real time, its principles, characteristics, comparison with other neuroimaging modalities, and its medical and research applications.

5.2 History of NIRS and fNIRS

The use of optical methods for the study of human tissues can be dated back to the 19th century. Among the relevant discoveries of the epoch, in 1876, the German physician Karl von Vierordt developed the a noninvasive and painless technique to evaluate the amount of oxygen carried in the blood, this technique was based on the observed spectral changes of red light penetrating tissue when the circulation is interrupted; unfortunately, his work remained ignored for nearly half a century [1, 2].

In the 1930s, von Vierordt's works on the use of optical methods for the study of tissue oxygenation were replicated by Ludwig Nicolai, and extended by Karl Kramer and Karl Matthes, who introduced the use of two wavelenghts of light, red and near infrared (NIR) to determine the levels of deoxy-hemoglobin (HHb) and oxy-hemoglobin (O_2Hb) for human tissue. This is possible due to the fact that HHb preferentially absorbs more red than NIR light, while O_2Hb presents the opposite behaviour. Thus, the degree of absorption of red or NIR light provides information about the concentrations of HHb and O_2Hb i.e., [HHb] and [O_2Hb] respectively [1] [2]. As such, in the 1940s, red and NIR light were used to determine determine the oxygen levels in muscles, this approach is known as oximetry [3].

It was also in that decade that Glen Millikan developed the first portable human ear oximeter to study the cases of black-outs in fighter pilots at high altitude during WWII [3, 4]. In the early 1960s Karl Norris and co-workers introduced NIR spectroscopy (NIRS) as a technique to analyze the composition of a given sample with the use of NIR light [1]; while the main application for the work developed by Norris was the study of agricultural samples, since then, the use of NIRS has been proven of incredible value to study the chemical composition of samples in pharmaceutical, medical and industrial applications.

The groundbreaking advance towards the use of NIRS to study the brain came in 1977 when through a series of *in vivo* trans-illumination experiments Frans Jöbsis demonstrated that human tissues are relatively transparent to NIR light in the 650-950 nm wavelength range, in other words, this range of wavelengths provide an "optical window" into the body [5]. In this way, his discoveries showed the possibility of continuous non-invasive

[1] Note the use of square brackets to indicate that these are concentrations

monitoring of [O_2Hb] and [HHb] in muscles and internal organs such as the brain through skin and bone [6]. It was in 1985, when Jöbsis and colleagues presented two works which were the to use NIRS to study the cerebral oxygenation in sick newborn infants [7], and during anesthesia and surgery [8]. As such, Jöbsis is considered to be the initiator of medical NIRS [4]. The use of NIRS to measure oxygenation changes in the brain cortex due to the execution of mental tasks was presented 1993 by four different research groups [9, 10, 11, 12], these works are considered the starting point in functional NIRS (fNIRS) research.

The pioneer fNIRS studies used simple NIRS devices that allowed the measurements in only one or few cortical locations; the introduction of simultaneous measurements in multiple cortical locations led to the use of fNIRS to provide topographical information [4]. Nowadays, fNIRS is regarded in neuroscience as a relevant technique for the study of the brain activity, this is due to the fact that fNIRS presents characteristics that can complement other neuroimaging methods.

5.3 NIRS Overview

NIRS is a technique where a given material sample is illuminated with NIR light (wavelength 650-950 nm); then, the light that is not absorbed by the sample, is quantitatively analyzed with the aim of study the composition of the sample. This is possible as each compound (or chromophores) in the sample presents a characteristic absorption pattern for NIR light, this absorption has its origin in the molecular structure and properties of the compound [13].

For an absorbing compound dissolved in a non-absorbing and non-scattering medium, (i.e., its optical properties: absorption and scattering coefficients are zero), the relationship between the attenuation (also known as optical density) of light with a wavelength λ passing through the medium and the concentration of the absorbing compound is given by the Beer-Lambert law (BLL) (REF):

$$A(\lambda) = -\log_{10}\left(\frac{I_{out}(\lambda)}{I_{in}(\lambda)}\right) = \epsilon(\lambda)cd, \tag{5.1}$$

where A is the measured attenuation, I_{in} is the intensity of the incident light, I_{out} is the intensity of the transmitted light through the medium; ϵ is the wavelength-dependent molar extinction coefficient of the absorbing compound measured in $M^{-1}cm^{-1}$; c is the molar concentration of the absorbing compound in the solution measured in M; and d is optical pathlength, this is to say, the distance between the points where the light enters and leaves the medium measured in cm. For non-scattering media $\epsilon = \alpha log_{10}(e)$, with α as the molar absorption coefficient. The product αc is corresponds to the absorption coefficient (or factor) μ_a measured in cm^{-1}. In case of more than one compound, the total attenuation is the summary of the attenuation for each compound.

Among the main characteristics that render NIRS a powerful technique for the study of human tissues we can find:

1. Human tissues are relatively transparent to light in the NIR spectrum (650-950 nm).
2. The incident NIR light is either absorbed by chromophores such as fats, proteins, melanin, hemoglobin, etc., or scattered in the tissues.
3. The quantity of light that is absorbed depends on two variables: the concentration of the compounds and their absorption coefficient for a given wavelength. In this sense, for fix concentration a given compound will present an absorption spectrum that indicates how the light is absorbed for different wavelengths. Figure 5.1 shows the absorption spectra of important compounds present in human tissues.

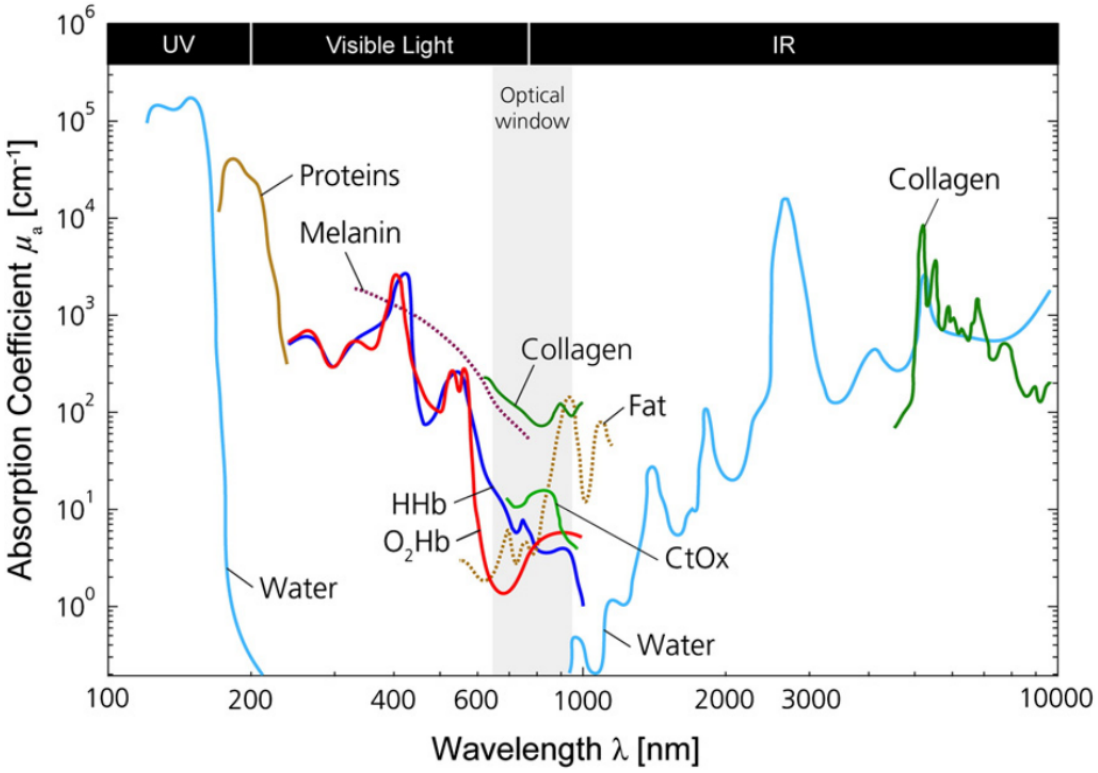

Figure 5.1: Absorption spectra for different chromophores present in human tissues, from [2]

4. Various compounds present high absorption coefficients in the NIR range, but they are present in relatively low concentrations relative to hemoglobin, making hemoglobin the main absorbing compound. It is important to mention that NIR light has been used also to study cytochrome-c-oxidase (CtOx), an enzyme involved in cellular respiration. Hemoglobin absorption spectrum depends on its oxygenation status; as such, two compounds of special interest for clinical purposes are deoxy-hemoglobin (HHb) and oxy-hemoglobin (O_2Hb). As HHb and O_2Hb possess different absorption spectra, it is possible to estimate the concentration of these compounds, thus allowing to derive information on blood oxygenation. The absorption spectra inside the "optical window" for HHb, O_2Hb and water are presented in Figure 5.2. Note that major absorption of of NIR in the tissues is due to the hemoglobin located in small vessels (capillary).

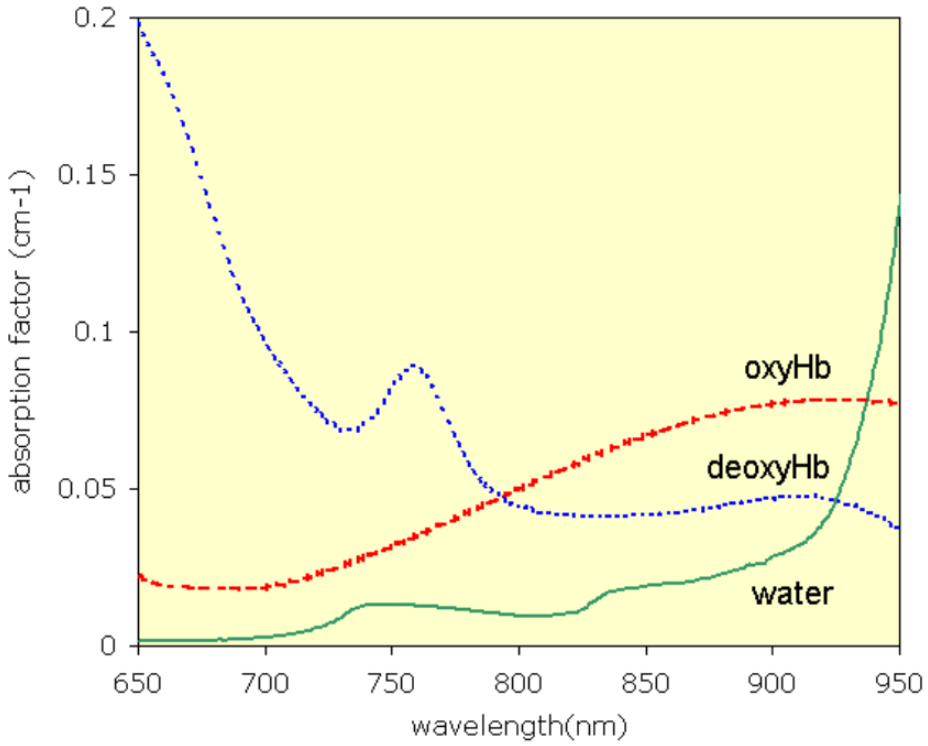

Figure 5.2: Absorption spectra for HHB, O_2Hb and water in the NIRS optical window (650 - 950nm), from [14]

5. Due to the composition of human tissues, the scattering of NIR is 100 times more probable than its absorption, this is to say, NIR light can be be transmitted through many centimetres of tissue. Moreover, because of the complex light scattering in different tissues, the optical pathlength is longer than the physical distance between the entry and the exit of the NIR light.

The BLL formulation presented in Eq. (5.1) assumes a non-scattering medium (scattering coefficient μ_s equal to zero), and this is not the case of human tissues. Thus, to account for scattering media, diverse methods have been developed, from these methods the modified Beer-Lamber law (MBLL), [15], is the most used method. The MBLL allows to convert the measured attenuation of the NIR light into concentrations of compounds.

$$A(\lambda) = -\log_{10}\left(\frac{I_{out}}{I_{in}}\right) = \sum_i \epsilon_i(\lambda) c_i DPF(\lambda) d + G(\lambda), \tag{5.2}$$

where index i indicates the compounds under study, commonly HHb and O_2Hb; DPF is a differential pathlength factor that compensates for the increased distance the light travels as μ_s is different from zero; finally G is a time-invariant unknown geometry dependent factor. Finally, by knowing [HHb] and [O_2Hb] it is possible to infer the level of oxygenation of the studied tissue.

To study oxygenation levels of the brain, a source of NIR light and a detector are placed on the scalp, the distance between source and detector is defined by the desired penetration depth of NIR light, the penetration depth is approximately half of the distance between source and detector.

NIR light is emitted by the source (two wavelengths are used). In its travel from source to detector, NIR light is mainly absorbed by HHb and O_2Hb, reaching finally the detector. Thus the measured attenuation of the NIR light correspond to the concentrations of HHb and O_2Hb in the tissue below and between the source and detector. Additionally, NIR light is diffused in all direction inside the head tissues (scalp, skull and subarachnoid space filled with cerebrospinal fluid), as a result the spatial distribution of NIR light through the layers is a banana-shape region, this region is illustrated in Figure 5.3.

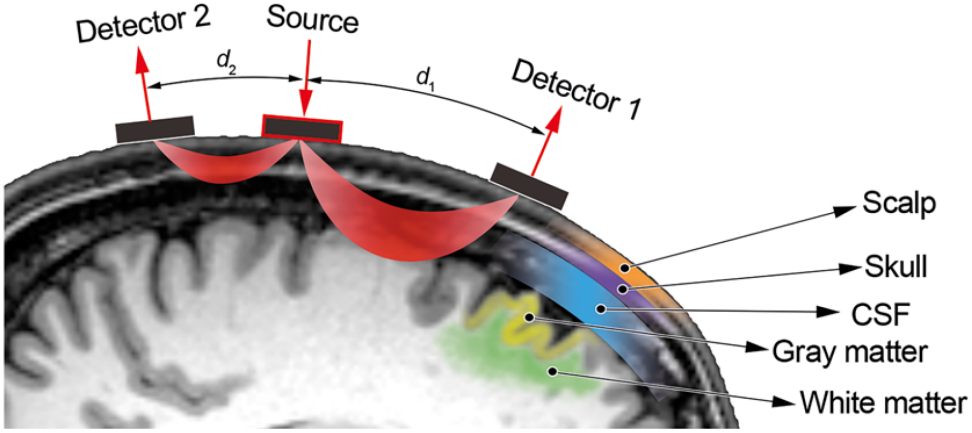

Figure 5.3: Path followed by NIR light through the different layers of the head. Depth is proportional to the distance between source and detector. From [16]

Interestingly, in the brain, the level of oxygenation depends on the blood flow which in turn is dependent on the neuronal activity. In this sense, with the use of NIRS it is possible measure changes in oxygenation in the brain and from these variations to infer the levels of neural activity by its demand for oxygen, this approach is known as functional NIRS (fNIRS).

5.4 fNIRS Overview

Functional near-infrared spectroscopy (fNIRS) non-invasive neuroimaging technique that uses NIRS to analyze the oxygenation due functional activation in the brain. fNIRS is often referred by other names such as optical topography or near-infrared imaging (NIRI).

When in a specific region of the brain there is an increment of neural activity, the consumption of oxygen and glucose increase, to keep with that demand, local blood vessels dilate, resulting in an increment of blood flow in that region occurs. As the increment of oxygen transported to the region typically exceeds the local neuronal rate of oxygen utilization, there is an overabundance of cerebral blood oxygenation (increase in [O_2Hb], and decrease in [HHb]) in active areas between 3-6 s after the neural activity [17].

This relationship between the local increment of oxygenated blood flow due to brain activity is know as neurovascular coupling, or hemodynamic response, and it is depicted in Figure 5.4. By using NIRS, fNIRS exploits the neurovascular coupling phenomenon to infer changes in the neural activity in a given region by analysing the local changes in blood oxygenation [18, 4]. This measurement of the brain activity with indirect variables is similar to approach used in functional magnetic resonance imagery (fMRI) presented in Chapter 4, where the oxygenation level dependent (BOLD) signal is an indicator of neural activity.

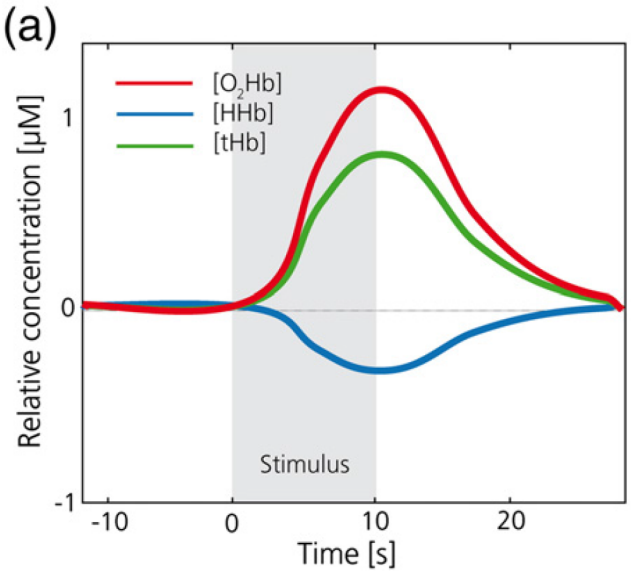

Figure 5.4: Typical neuronal hemodynamic response, from [2]

With the use of Eq(5.2), it is possible to infer the temporal changes in [HHb] and [O_2Hb]. Thus for an interval $\Delta t = t_1 - t_0$, the relationship between the temporal changes in the [HHb] and [O_2Hb] and the changes in the measured attenuation are given as:

$$\Delta A(\Delta t, \lambda) = -\log_{10}\left(\frac{I_{out}(t_1, \lambda)}{I_{out}(t_0, \lambda)}\right) = \sum\nolimits_i \epsilon_i(\lambda)\Delta c_i DPF(\lambda)d, \tag{5.3}$$

where $\Delta c_i = c_i(t_1) - c_i(t_0)$ represents the temporal changes in the compounds concentrations. Typical values for ϵ and DPF can be found in the fNIRS literature.

As fNIRS allows to characterize the brain hemodynamics in a non-invasive, portable, comfortable, and potentially wearable way, it has become an useful tool to study either in physiological or pathological conditions, this is reflected in the steadily grown that fNIRS research has presented in the last two decades with the number of publications being double every 3.5 years [19]. A general overview on fNIRS devices is provided below, followed by a comparison of fNIRS with other neuroimaging techniques, and current uses of fNIRS.

5.4.1 Devices

The miniaturization and affordability of sensors and circuitry has led to the a great advance on fNIRS technology, from the single-channel fNIRS devices used in the early 1990s to current fNIRS devices that can simultaneously measure +200 channels providing detailed topographic maps of the undergoing brain activity. Moreover, depending on their main application, fNIRS devices can be portable and wearable, opening the doors to acquisition of fNIRS signals in places other than the typically clinic environments. Despite of the great diversity of fNIRS devices, some of the relevant characteristics to take into account for selection of one are: illumination method, light wavelengths used, technologies used to emit and detect light, and the number of channels.

5.4.1.1 Illumination type

According to the type of illumination used in fNIRS devices, these can be divided in three categories: continuous-wave (CW), time-domain (TD), and frequency-domain (FD).

CW (or continuous-intensity) fNIRS devices are the simplest and most used fNIRS systems. As it name indicates, these devices continuously emit NIR light, typically at two or more wavelengths, the back scattered light is detected and the light attenuation is measured. From the changes in the light attenuation, the changes in [HHb] and [O_2Hb] are registered with respect to a zero at the start of recording. This is due to the fact that the absolute baseline concentrations cannot be resolved, as CW fNIRS devices are not able to separate and quantify the contribution of absorption and scattering. However, in experiments where the functional activity is evaluated relatively to a baseline, the absolute concentrations are not needed. The absolute concentrations of [HHb] and [O_2Hb] can be obtained with TD and FD fNIRS devices [16, 2].

In TD (also know as time-resolved) fNIRS devices, a short duration ($\sim$100 ps) light pulse is emitted, and the temporal point spread function (impulse response) of the light after it has passed through the tissue is analyzed. The scattering process broadens the duration of the pulse, while the absorption modifies its intensity, as such the optical properties (μ_a and μ_s) of the tissue can be estimated. [16, 1]

The FD (or phase modulation) fNIRS devices follow a similar approach TD devices, but in frequency domain. Light is modulated in intensity (amplitude modulation) at radio frequencies, after passing through the tissue, amplitude and phase shift of the emerging wave are measured. With these parameters it is possible to determine the optical properties of the tissue, as the phase contains information about the time of flight, and the amplitude about the absorption [1, 20].

Figure 5.5 presents the main three different types of illumination used in fNIRS devices. Regardless the illumination technique, NIR light is emitted and received by sources and detectors respectively. Collectively, sources and detectors are referred as optodes.

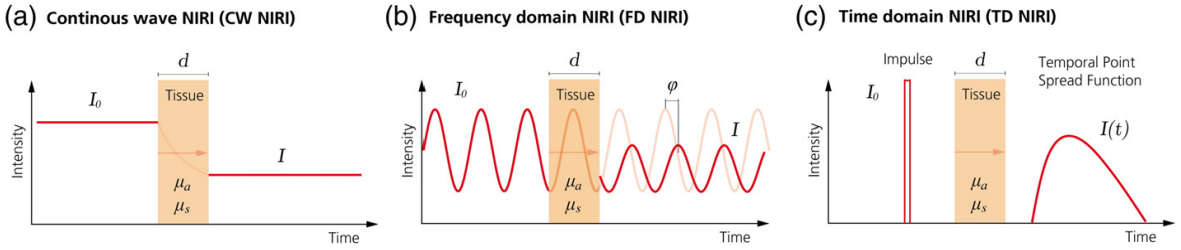

Figure 5.5: Type of illumination: CW, FD and TD. From Fig [2]

5.4.1.2 Optodes: sources and detectors

Two types of NIR light sources are used in fNIRS devices: laser diodes and light emitting diodes (LEDs). Both diodes are made of semiconductors and use the electroluminescence phenomenon. Laser diodes have some advantages over LEDs, e.g., LEDs provide incoherent light with a broad bandwidth up to 50 nm, while laser diodes emit coherent light with narrower bandwidths. On the other hand, LEDs allow more flexibility in the wavelength selection, are smaller and less expensive; for these reasons LEDs are commonly used as alternative to laser diodes [2].

Regardless the source of NIR, the emission component has to be careful design to avoid fluctuations in the intensity and wavelength of the radiated light, as these introduce noise on the detector size. The transduction from light to an electric signal is based on the photoelectric effect, the most common semiconductor devices used as detectors in fNIRS devices are: photodiode, avalanche photodiode and photomultiplier tube. To transfer the light from the sources to the scalp and from the scalp to the detectors, there are two options: either the optodes are placed directly on the scalp, or the light is channelized between the scalp and the optodes by optic fibers. The first approach present the advantage of being more robust to movements from the subject.

5.4.1.3 Number of channels

Each pair of source-detector can investigate the space between them, thus this pair constitutes a fNIRS channel. fNIRS devices have drastically evolved from single-channel measurements in the 1990s to current devices with more than 200 channels. The theoretical maximum of channels is the product of the number of sources and the number of detectors. However, in practices, due to the placement, not all detectors can receive light from all the sources, thus diminishing the total number of channels. Nowadays, there is not a agreement on the placement of the optodes on the scalp, however, as general practice locations are borrowed from the international 10-20 system used in EEG (Chapter 2).

Moreover, the selection of source-detector distance depends on properties of the NIR light that is used (intensity and wavelength), as well as the age of the subject and the head region measured. Longer source-detector distances allow to explore deeper regions of

the brain but lead to low signal-to-noise ratio (SNR). Typical values for source–detector distances are 3-3.5 cm for adult studies and 2-2.5 cm for infants [4, 16].

Overlapping channels can be assessed by using multiple source–detector distances over the scalp, this provides a tomographical representation of the distribution of the changes in concentration of O_2Hb and HHb over the cortical surface. This channel configuration is referred to as diffuse optical tomography (DOT), where much denser arrays of channels are used that sample overlapping brain volumes [16]

5.4.1.4 Costs

Most of fNIRS devices in the market are CW-based, and their cost is linked to the number of channels, optodes technology, and portability. These devices can cost from U$10,000 to U$100,000. In general TD- and FD-based devices are more expensive than CW devices as they require sophisticated equipment. A list of the main manufactures of fNIRS devices can be found in: `https://fnirs.org/resources/instruments/`. Moreover, open documentation and design files for a portable CW NIRS device can be found in `http://www.opennirs.org/`.

5.4.2 Signal processing

The changes in [HHb] and [O_2Hb] are obtained by evaluating Eq(5.3) for two different wavelengths, and solving:

$$\begin{bmatrix} \Delta\,[\mathrm{HHb}] \\ \Delta\,[\mathrm{O_2Hb}] \end{bmatrix} = (d)^{-1} \begin{bmatrix} \epsilon_{\mathrm{HHb}}(\lambda_1) & \epsilon_{\mathrm{O_2Hb}}(\lambda_2) \\ \epsilon_{\mathrm{HHb}}(\lambda_2) & \epsilon_{\mathrm{O_2Hb}}(\lambda_1) \end{bmatrix}^{-1} \begin{bmatrix} \Delta A(\Delta t, \lambda_1)/DPF(\lambda_1) \\ \Delta A(\Delta t, \lambda_2)/DPF(\lambda_2) \end{bmatrix} \tag{5.4}$$

The raw fNIRS signals, i.e., the intensities recorded by the detectors, ($\Delta A(\Delta t, \lambda_1)$ and $\Delta A(\Delta t, \lambda_2)$) are often corrupted by artifacts. Due to its nature raw fNIRS signal are distorted by activity in cardiac pulsation, respiration and Mayer waves. Movements of head and face have also negative effects in the quality of the signals as they may cause movement on the optodes. Lastly, ambient light may also be present in the signals as noise. All these artifacts can lead to inaccurate quantification of [O_2Hb] and [HHb] temporal dynamics, thus must be removed or rejected. [21, 2].

Currently, there are not standardized and widely accepted signal processing pipelines for fNIRS signals. However, common processing pipelines found in the fNIRS literature comprehend the following steps:

1. Raw fNIRS signals are visually inspected to identify large artifacts due to optode movement. In this step the presence of heart beat oscillations is a good sign, as it indicates the good optical coupling between the optodes and the scalp.
2. Raw fNIRS signals are converted to changes in $[O_2Hb]$ and [HHb] concentrations by solving Eq.(5.3) for $\Delta[\text{HHb}](t)$ and $\Delta[O_2\text{Hb}](t)$.
3. The physiological artifacts in the concentrations signals can be easily removed using the band-pass filters.
4. Finally, $\Delta[\text{HHb}](t)$ and $\Delta[O_2\text{Hb}](t)$ signals are use to perform statistical analysis, and/or feature computation [22].

Interestingly, some fNIRS works report the use of digital filtering on raw fNIRS signal, before the computation of the concentration signals. Moreover, given the similarities between the fNIRS signals and the BOLD signal, diverse methods to analyzes the latter have been used in fNIRS research. An extensive review in current methods for processing fNIRS signals can be found in [23].

5.4.3 Risks

In general, high intensity NIR light sources are desirable as they maximize the amount of light that reaches the detector, improving the SNR. Moreover high intensities allow longer source-detector distances, which in turn allow the study of deeper structures. However, high light intensity can lead to tissue heating due to the irradiation and/or conductive heat transport from the source, this not only may distort the measurements, but may endanger or at least cause discomfort to the subject [2, 14].

5.5 fNIRS Compared with Other Neuroimaging Modalities

Similar to other neuroimaging modalities such as fMRI (Chapter 4) and PET (Chapter 6), fNIRS provides and indirect measurement of the brain activity which is inferred from the metabolic footprints for the neural activity. As such, there is an inherent delay between the onset of the neuronal activation and the changes in the fNIRS signals. This delay is not present in methods that directly measure the electric activity of the brain, such as EEG (Chapter 2) and MEG (Chapter 3). Regarding spatial and temporal resolution, fNIRS falls in the middle of range that can be obtained with other modalities. Due to its optical nature, fNIRS does not produces nor is affected by electromagnetic interference, as such, it can be used in parallel with other modalities (e.g. EEG and fMRI) to have a more detailed characterization of the brain activity. Table 5.1 presents a comparison in different characteristics for fNIRS, fMRI, EEG, MEG and PET [16].

Table 5.1: Comparison of fNIRS with other neuroimaging modalities.

	fNIRS	fMRI	EEG	MEG	PET
Neural activity measurement	Indirect	Indirect	Direct	Direct	Indirect
Signal	Hemodynamic response (HHB, HHb)	Hemodynamic response (BOLD)	Electric potentials on scalp	Magnetic fields in the head	Brain metabolism
Spatial resolution	∼1 cm	≥0.5 mm voxels	5-9 cm	∼1 cm	3-4 mm
Penetration depth	Brain cortex	Whole head	Brain cortex	Deep structures	Whole head
Sampling rate	Low $\leq$ 25 Hz	Low $\leq$ 3 Hz	Low $>$ 1000 Hz	Low $>$ 1000 Hz	Low $<$ 0.1 Hz
Robustness to motion	Yes	No	Yes	No	No
Participants	Everyone	Limited	Everyone	Limited	Limited
Outside Lab conditions	Yes	No	Yes	No	No
Wearable?	Yes	No	Yes	No	No
Long term monitoring	Yes	No	Yes	No	No
Cost	Low	High	Low	High	High

Despite being present for over two decades, in fNIRS research there is a lack of standardization of instrumentation, methods for signal processing, statistical analysis, feature computations, etc. This situation is expected to change with growing adaption of fNIRS, and the existence of organizations such as the Society for functional Near Infrared Spectroscopy (SfNIRS).

5.6 fNIRS Uses

As a result of its characteristics, fNIRS is regarded as a flexible tool that has proven to be suitable for the study of brain development, cognitive and affective states, and physiological and pathological conditions.

In the field of neurodevelopment, fNIRS outstands among other neuroimaging modalities as it is suitable for the study of brain activity in infant participants (often neonatal), as they do not require to be still as in fMRI and MEG recording sessions; also, no radioactive tracers are needed as in PET, and brain activity can be acquired with higher spatial resolution than EEG.

Pioneer works in the field aimed to detect the neuronal response evoked by stimulus in the visual and auditory cortices. More recent applications include the study of object processing, social communication, motion processing, action observation, regulation of emotions and face processing [24, 19]. As the other neuroimaging modalities, for the study of the adult brain, fNIRS has been used to find correlates between the cortical activation, and cognitive and affective states. Some of the states explored with fNIRS include: workload, attention, perception, working memory, valence and arousal, among others. These states have also been study with other modalities such as EEG. The comparison between fNIRS and EEG does not show a clear advantage of one modality over the other, but suggests that by combining them it is possible to exploit their complementarity to achieve better outcomes.

Most of the works on fNIRS and states are performed offline, however, research on the online is carried on with the goal of proving a passive brain-computer interface (BCI), this is to say, a system that monitors the cognitive (or affective) state of the user, and adapts itself accordingly, to enrich the interaction between the user and the system. The simultaneous use of fNIRS and other modalities, opens the doors for the use of hybrid BCIs (Chapter 12), which aim to improve its performance by combining modalities [25, 19, 26]. Lastly, fNIRS has been used to study and reach a better understanding of different psychiatric disorders, for example, schizophrenic illnesses, affective disorders, and developmental syndromes such as attention-deficit hyperactivity disorder, and autism. Moreover, fNIRS has also been used for to study normal and pathological aging, neurodegeneration, epilepsy, cerebrovascular disease, among others [19, 16].

5.7 Future

Technological advance in fNIRS hardware, will lead to a widespread use of fNIRS not only in research but in clinical applications. Moreover, TD and FD fNIRS devices are expected to be more affordable, allowing the measurement of the optical properties in the tissues. Current advances in signal processing and machine learning will have an enormous impact in the development of fNIRS-based systems to diagnosis of diseases and disorders, and in human machine interfaces. An important challenge is the definition of guidelines and standards for the acquisition, processing, and analysis of fNIRS signals. This will allow a direct comparison between works from different research groups, and as consequence, better and refined methods to extract valuable information from the fNIRS recordings.

5.8 Conclusion

With is origins in the discovery of the optical window that the human tissues offer to NIR light, fNIRS has been used for over 20 years as an interesting tool for the study of brain activity. In comparison with other neuroimaging modalities, fNIRS characteristics such as cost, portability and time resolution, give fNIRS an advantage over modalities such as fMRI and PET. On the other hand, fNIRS presents advantages over EEG and MEG such as spatial resolution and robustness to electromagnetic interference. As such it has attracted the attention of researchers, and it is expected to be used as a valuable clinical tool.

Endnotes

[1] M. Ferrari and V. Quaresima, "Near Infrared Brain and Muscle Oximetry: From the Discovery to Current Applications," *Journal of Near Infrared Spectroscopy*, vol. 20, pp. 1–14, Feb. 2012.

[2] F. Scholkmann, S. Kleiser, A. J. Metz, R. Zimmermann, J. Mata Pavia, U. Wolf, and M. Wolf, "A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology," *NeuroImage*, vol. 85, pp. 6–27, Jan. 2014.

[3] J. W. Severinghaus, "Takuo Aoyagi: Discovery of Pulse Oximetry:," *Anesthesia & Analgesia*, vol. 105, pp. S1–S4, Dec. 2007.

[4] M. Ferrari and V. Quaresima, "A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application," *NeuroImage*, vol. 63, pp. 921–935, Nov. 2012.

[5] F. Jobsis, "Noninvasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters," *Science*, vol. 198, pp. 1264–1267, Dec. 1977.

[6] C. A. Piantadosi, "Early development of near-infrared spectroscopy at Duke University," *Journal of Biomedical Optics*, vol. 12, no. 6, p. 062102, 2007.

[7] J. E. Brazy, D. V. Lewis, M. H. Mitnick, and F. F. J. vander Vliet, "Noninvasive monitoring of cerebral oxygenation in preterm infants: preliminary observations," *Pediatrics*, vol. 75, no. 2, pp. 217–225, 1985.

[8] E. Fox, F. F. Jöbsis-Vander Vliet, and M. H. Mitnick, "Monitoring cerebral oxygen sufficiency in anesthesia and surgery," in *Oxygen Transport to Tissue VII*, pp. 849–854, Springer, 1985.

[9] T. Kato, A. Kamei, S. Takashima, and T. Ozaki, "Human Visual Cortical Function during Photic Stimulation Monitoring by Means of near-Infrared Spectroscopy," *Journal of Cerebral Blood Flow & Metabolism*, vol. 13, pp. 516–520, May 1993.

[10] B. Chance, Z. Zhuang, C. UnAh, C. Alter, and L. Lipton, "Cognition-activated low-frequency modulation of light absorption in human brain.," *Proceedings of the National Academy of Sciences*, vol. 90, pp. 3770–3774, Apr. 1993.

[11] Y. Hoshi and M. Tamura, "Detection of dynamic changes in cerebral oxygenation coupled to neuronal function during mental work in man," *Neuroscience Letters*, vol. 150, pp. 5–8, Feb. 1993.

[12] A. Villringer, J. Planck, C. Hock, L. Schleinkofer, and U. Dirnagl, "Near infrared spectroscopy (NIRS): A new tool to study hemodynamic changes during activation of brain function in human adults," *Neuroscience Letters*, vol. 154, pp. 101–104, May 1993.

[13] A. Davies, "An Introduction to near Infrared Spectroscopy," *NIR news*, vol. 16, pp. 9–11, Nov. 2005.

[14] A. Bozkurt and B. Onaral, "Safety assessment of near infrared light emitting diodes for diffuse optical measurements," *BioMedical Engineering OnLine*, p. 10, 2004.

[15] D. T. Delpy, M. Cope, P. van der Zee, S. Arridge, S. Wray, and J. Wyatt, "Estimation of optical pathlength through tissue from direct time of flight measurement," *Physics in Medicine and Biology*, vol. 33, pp. 1433–1442, Dec. 1988.

[16] P. Pinti, I. Tachtsidis, A. Hamilton, J. Hirsch, C. Aichelburg, S. Gilbert, and P. W. Burgess, "The present and future use of functional near-infrared spectroscopy (fNIRS) for cognitive neuroscience: Advances in using fNIRS in cognitive neuroscience," *Annals of the New York Academy of Sciences*, Aug. 2018.

[17] R. Sitaram, A. Caria, and N. Birbaumer, "Hemodynamic brain–computer interfaces for communication and rehabilitation," *Neural Networks*, vol. 22, pp. 1320–1328, Nov. 2009.

[18] V. Quaresima and M. Ferrari, "Medical near Infrared Spectroscopy: A Prestigious History and a Bright Future," *NIR news*, vol. 27, pp. 10–13, Feb. 2016.

[19] D. A. Boas, C. E. Elwell, M. Ferrari, and G. Taga, "Twenty years of functional near-infrared spectroscopy: Introduction for the special issue," *NeuroImage*, vol. 85, pp. 1–5, Jan. 2014.

[20] D. Delpy and M. Cope, "Quantification in tissue near–infrared spectroscopy," *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, vol. 352, no. 1354, pp. 649–659, 1997.

[21] A. Girouard, E. T. Solovey, L. M. Hirshfield, E. M. Peck, K. Chauncey, A. Sassaroli, S. Fantini, and R. J. K. Jacob, "From Brain Signals to Adaptive Interfaces: Using fNIRS in HCI," in *Brain-Computer Interfaces* (D. S. Tan and A. Nijholt, eds.), Human-Computer Interaction Series, pp. 221–237, Springer London, Jan. 2010.

[22] S. Tak and J. C. Ye, "Statistical analysis of fNIRS data: A comprehensive review," *NeuroImage*, vol. 85, pp. 72–91, Jan. 2014.

[23] P. Pinti, F. Scholkmann, A. Hamilton, P. Burgess, and I. Tachtsidis, "Current Status and Issues Regarding Pre-processing of fNIRS Neuroimaging Data: An Investigation of Diverse Signal Filtering Methods Within a General Linear Model Framework," *Frontiers in Human Neuroscience*, vol. 12, Jan. 2019.

[24] S. Lloyd-Fox, A. Blasi, and C. Elwell, "Illuminating the developing brain: The past, present and future of functional near infrared spectroscopy," *Neuroscience & Biobehavioral Reviews*, vol. 34, pp. 269–284, Feb. 2010.

[25] M. Strait and M. Scheutz, "What we can and cannot (yet) do with functional near infrared spectroscopy," *Frontiers in Neuroscience*, vol. 8, May 2014.

[26] S. C. Bunce, K. Izzetoglu, H. Ayaz, P. Shewokis, M. Izzetoglu, K. Pourrezaei, and B. Onaral, "Implementation of fNIRS for monitoring levels of expertise and mental workload," in *Foundations of Augmented Cognition. Directing the Future of Adaptive Systems*, pp. 13–22, Springer, 2011.