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Review

A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology

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ABSTRACT

This year marks the 20th anniversary of functional near-infrared spectroscopy and imaging (fNIRS/fNIRI). As the vast majority of commercial instruments developed until now are based on continuous wave technology, the aim of this publication is to review the current state of instrumentation and methodology of continuous wave fNIRI. For this purpose we provide an overview of the commercially available instruments and address instrumental aspects such as light sources, detectors and sensor arrangements. Methodological aspects, algorithms to calculate the concentrations of oxy- and deoxyhemoglobin and approaches for data analysis are also reviewed.
From the single-location measurements of the early years, instrumentation has progressed to imaging initially in two dimensions (topography) and then three (tomography). The methods of analysis have also changed tremendously, from the simple modified Beer-Lambert law to sophisticated image reconstruction and data analysis methods used today. Due to these advances, fNIRI has become a modality that is widely used in neuroscience research and several manufacturers provide commercial instrumentation. It seems likely that fNIRI will become a clinical tool in the foreseeable future, which will enable diagnosis in single subjects.

Contents

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Introduction

Continuous light has been used to non-invasively investigate human tissue such as the breast, head and testes by transmitting the light through the body as early as at least in the 19th century (Bright, 1831; Curling, 1856; Cutler, 1929). More specifically, already in 1862 Hoppe-Seyler from Germany, described the spectrum of oxy-hemoglobin (O_2Hb) (Perutz, 1995) and in 1864 Stokes from the United Kingdom added the spectrum of deoxy-hemoglobin (HHb) and consequently discovered the importance of hemoglobin for the oxygen transport (Perutz, 1995). In 1876 von Vierordt, also from Germany, analyzed tissue by measuring the spectral changes of light penetrating tissue when the blood circulation was occluded (Severinghaus, 2007; von Vierordt, 1876) and in 1894 Hüfner from Germany spectroscopically determined absolute and relative amounts of O_2Hb and HHb in vitro (Hüfner, 1894). After decades of no relevant research in this field, in the 1930s the work on spectroscopic determination of tissue oxygenation was continued by several researchers. For example Nicolai, Germany, repeated the study of von Vierordt (Nicolai, 1932a,b), and Matthes and Gross, Germany, demonstrated for the first time the spectroscopic determination of O_2Hb and HHb in human tissue using two wavelengths, one in the red and near-infrared region (Matthes and Gross, 1938a,b,c).

In terms of quantification, an important first step was the discovery of the Beer–Lambert law first by the French mathematician Bouguer in 1729 (Bouguer, 1729). It is often attributed to the Swiss Lambert, although he cited Bouguers work in 1760 himself (Lambert, 1760). The law was extended by the German Beer to quantify concentrations in 1852 (Beer, 1852). Since the Beer–Lambert law is only valid in non-scattering media, it cannot be applied to biological tissue. Relatively recently therefore the modified Beer–Lambert law (MBLL) was developed by the British Delpy (Delpy et al., 1988), to take into account the light scattering. The MBLL is often used by many instruments described in this review. Further important steps were also analytical solutions of the diffusion equation (e.g. Arridge et al., 1992; Patterson et al., 1989) to quantitatively describe light transport in tissue.

Based on the insight of the relative transparency of the tissue including the skull in the near infrared range in 1977 Jobsis from the USA first demonstrated the feasibility to continuously and non-invasively monitor the concentration of O_2Hb and HHb ([O_2Hb] and [HHb]) in the brain (Jobsis, 1977). Therefore he is considered to be the initiator of near-infrared spectroscopy (NIRS).

His discovery led to designing and building of several NIRS instruments (Ferrari and Quaresima, 2012). All these instruments were continuous wave (CW) instruments. The term "continuous wave" means that the instrumentation is solely based on a light intensity measurement, i.e. near-infrared light is sent into the tissue and the intensity of the re-emerging (i.e. diffusely reflected) light is measured. This is in contrast to time resolved techniques such as time and frequency domain techniques, which, additionally to the intensity measurements also measure the time of flight, i.e. the time that the light needs to travel through the tissue. For a visualization of the three different techniques please refer to Fig. 1.

The disadvantage of CW systems is that they cannot fully determine the optical properties of tissue (i.e. light scattering (μ_s') and absorption (μ_a) coefficients) and therefore the [O_2Hb] and [HHb] cannot be determined absolutely. However, with a few reasonable assumptions it is possible to quantify changes in [O_2Hb] and [HHb]. Therefore, during the first years, NIRS instruments were mostly trend monitors, employed to study various physiological conditions and clinical interventions. Much research was aimed at obtaining absolute values either by physiological maneuvers (e.g. Edwards et al., 1988; Wyatt et al., 1990) or enhancing the instrumentation (e.g. Matcher et al., 1994, 1995b; Wolf et al., 1997). Later time resolved techniques were developed and became available and enabled to determine absolute values. This will not be discussed further, because it is not within the scope of this review.

1993 was a crucial year in the development of *functional* NIRS (fNIRS) of the brain. In the same year four research groups published results and demonstrated that it is possible to non-invasively investigate brain activity using fNIRS (Chance et al., 1993; Hoshi and Tamura, 1993; Kato et al., 1993; Villringer et al., 1993). Brain activity leads to an increase in oxygen consumption, which is accompanied by an increase in cerebral blood flow due to neurovascular coupling. This leads to a change in the local [O_2Hb] and [HHb] (Wolf et al., 2002), which can be detected non-invasively by fNIRS. These first measurements were carried out with simple instruments, which measured at one or a few locations. Since brain activity in response to a stimulation occurs only at specific locations in the brain, when measuring just at one location it is often difficult to find the correct position on the head

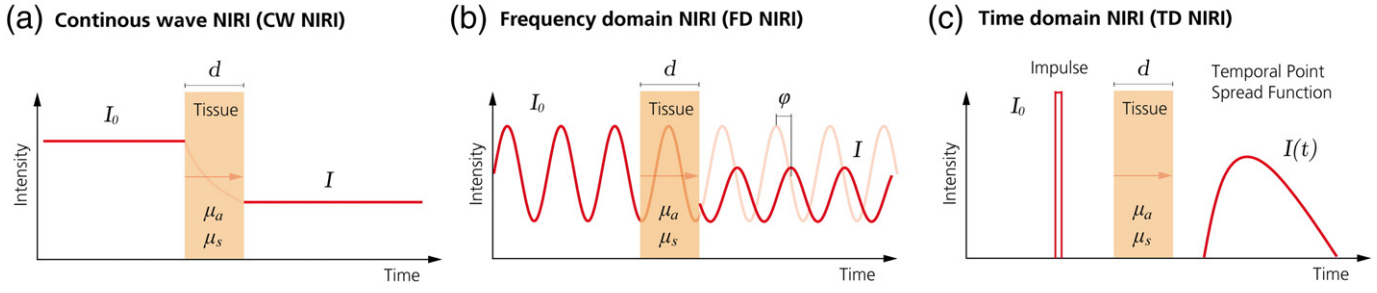

Fig. 1. Illustration of the three different NIRI techniques. The continuous wave technology emits light at a constant intensity and then only measures the changes in the intensity of the light that passed through the tissue. The frequency domain technology modulates the emitted light intensity and then measured the intensity of the detected light as well as the phase shift, which corresponds to the time of flight. The time domain technology emits an extremely short pulse of light into the tissue and measures the arrival times of the photons that emerge from the tissue. This technology yields the highest amount of information, but it is also the most complex technology. I_0: incident light signal, I: transmitted light signal, d: thickness of the medium, μ_a: absorption coefficient, μ_s: scattering coefficient, φ: phase delay, and $I(t)$: temporal point spread function of the transmitted light signal.