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Measurement of cerebral blood flow and metabolism using high power light-emitting diodes

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ABSTRACT

In medical near-infrared spectroscopy (NIRS), particularly in the study of the brain, light illumination is commonly realised by lasers or laser diodes (LD). However, the rapid development of high-power light-emitting diodes (HPLED), increased optical output power and expansion of wavelengths of choice in particular, have made HPLEDs a feasible alternative, also for *in vivo* measurements of cerebral blood flow (CBF) and brain metabolism. These applications, however, require using sophisticated modulation techniques that enable distinguishing low-level light signals that are back-scattered from the cerebral cortex. They also rely on separating different wavelengths when the illuminating light is emitted simultaneously by several HPLEDs with different wavelengths.

In this paper, we study key properties of commercially available HPLEDs, with a focus on the study of the brain. Of particular interest here are optical output power and available wavelengths. Furthermore, we demonstrate a lock-in amplification technique suitable for use with HPLEDs in brain studies. Based on the presented measurement technique, we conduct experimental measurements on CBF in the cortex and analyse fluctuations in blood oxygen level at different combinations of wavelengths.

1. Introduction

NIRS has been utilised in the study of the human brain for more than two decades as a non-invasive tool for *in vivo* monitoring of tissue oxygenation in the cerebral cortex. Common measurement methods are based on the use of lasers or LDs, mostly because illumination power has to be sufficiently high to reach the cerebral cortex and to enable measuring the back-scattered light with a good signal-to-noise ratio (SNR). SNR can be only improved to a limited amount by increasing illumination power, because, due to safety considerations, there are standardized limits to optical power levels applicable to medical measurements. Nowadays, also HPLEDs have a level of optical output power that is sufficiently high in near-infrared range for illuminating the cerebral cortex with adequate SNR ratio [1,2]. Especially, in the case of continuous light illumination in *in vivo* measurements, a further increase in optical output power would not be even desirable, because possible warming of tissue, in consequence of increased optical power, could start to affect the measurement result [3].

HPLEDs can be driven at currents from hundreds of mili to several Amperes, provided that they are well connected to heat dissipation. HPLEDs are also very efficient in terms

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of radiant flux versus size, and most of them can be accommodated in an area of less than 2 cm^2. Moreover, the shape and size of the packaging allow attaching of different kind of lenses [4]. Other factors that have enabled a more effective utilisation of HPLEDs are improvements of their stability and widening the available spectrum [5]. At the moment, a wide range of available wavelengths exist, covering almost the entire spectrum of interest, particularly in medical NIRS measurements. In comparison to LDs, however, the main weakness of HPLEDs still is limited response time that restricts their utilisation in time domain (TD) and frequency domain (FD) based NIRS techniques.

In addition to light sources, also the detectors and receiver amplifiers are highly important for achieving a good SNR. By using a technique based on lock-in amplification, we may significantly enhance the sensitivity and SNR, because instead of amplifying the received signal over the entire frequency band of interest, we only amplify amplitude-modulated light signals at a specific reference frequency. As a result, a significant increase can be achieved in SNR performance. When an amplified reference signal is multiplied by the lock-in reference signal and then low-pass filtered, intensity changes of the remaining low-pass filtered output signal correlate with attenuation changes of the received light signal. Furthermore, the lock-in amplification technique enables separating several signals from each other. It is possible to label each wavelength of light for a specific modulation frequency, illuminate all wavelengths simultaneously and then separate them in the receiver by the lock-in technique. This technique is related to commonly utilised FD technique, which is based on modulating the intensity of the illuminating light and measuring both the attenuation and phase delay of the emerging light [6–8]. A more extensive explanation of the principle of the lock-in technique can be found in [9–11], for instance.

1.1. Blood metabolism and oxygenation measurements using NIRS

Blood is one of the most studied elements in the human body [12,13]. Since blood circulation is fundamental for the cardiovascular system, changes in the properties of blood reflect its function. NIRS studies of the brain often monitor oxygenation changes in the cerebral cortex, since local cerebral vascular and oxygen metabolic effects change during brain activity [14]. When some part of the brain, say, the motor cortex, is functioning in response to hand grip, brain oxygenation in the area increases. This increase can be measured by near-infrared spectroscopy (NIRS) based techniques [15].

The principle of NIRS is based on wavelength-dependent absorption. Each chromophore (molecules that absorb light) has a distinct absorption spectrum determined by its content and energy level structure. These individual spectra can be used as a profile for identifying individual compounds in a substance. Measuring the concentration of an absorbing species in tissue is commonly accomplished by applying the Beer–Lambert law (BLL) [16–19]. Change in deoxyhemoglobin (ΔHb) and change in oxyhemoglobin (ΔHbO) concentrations can generally be determined from NIRS measurements based on measuring reflected light at two or more wavelengths. These wavelengths should be located on both sides of the isosbestic point of the absorption spectrum of oxyhemoglobin (HbO) and deoxyhemoglobin (Hb), i.e. at 800 nm, where the extinction coefficient of oxygenated and deoxygenated hemoglobin is the same, see Fig. 3. Commonly used wavelengths in blood oxygenation measurements lie between 670–710 nm and 850–890 nm, when aiming at maximum signal sensitivity [17]. If, however, the photon path length needs to be as close to both wavelengths as possible, then the wavelengths of 735 nm and 890 nm are suggested to be chosen [20]. Furthermore, Strangman et al. determined in 2003 that all wavelengths in the 770–800 nm range, when used in combination with 830 nm, provide poor data on oxygenation. Nowadays, maybe the most common combination of wavelengths is red (660–695 nm) and infrared (830–850 nm) which is used also for example in Hitachi's ETG-4000 Optical Topography System [21–23]. Different NIRS measurement methods and their key features and parameters have been reviewed in detail, for example, in the following publications [7,24,25] and handbooks [8,26]. Moreover, different combinations of wavelengths have been studied for example by Silva et al. 2003 [27].

2. Measurement and analysis methods

2.1. Hardware and software based lock-in amplification

In our first measurement, we validated the measurement method and setup both with hardware and software based implementation of lock-in amplification. Shown in the following presentation are our experimental results, obtained using a sinusoidal carrier wave. Light was used to illuminate a person's forehead at 660 nm (red) and 830 nm (infra-red). At 660 nm, the modulation frequency was 8 kHz, while that for 830 nm was 6 kHz. Because of limited bandwidth of HPLEDs selected modulation frequencies are lower than commonly is the case with LDs in FD based NIRS techniques. Hardware-based lock-in amplification was realised by an AD630 high-precision balanced modulator [9], while software-based lock-in amplification was accomplished using LabVIEW. For comparison, both methods used the same setup, which included a light source-detector pair, modulators, amplifiers, filters and a data acquisition card to save captured data on a hard disk. Hardware-based lock-in amplification can be implemented in several other ways as well, for example, by using field-programmable gate array circuits (FPGA) [28].

Fig. 1 shows that both lock-in methods allow detection of pulses from the forehead using an optical source-detector distance of 3 cm. Additionally, Fig. 1 demonstrates that there is a potential risk of cross talk in methods based on modulation techniques - in this experiment, the hardware method suffers from strong crosstalk between the two different wavelengths, indicated by the similar curve shapes. This occurred because band-pass filtering prior to the inputs of the demodulators was too expanded. Crosstalk of this type can be avoided by modifying the filters or changing the modulation frequencies. Naturally, this kind