



## Basic Neuroscience

# Wireless near-infrared spectroscopy system for determining brain hemoglobin levels in laboratory animals

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## HIGHLIGHTS

- ▶ The concentration changes of HbO<sub>2</sub>, HbR and HbT were significantly related to the traumatic impact strength.
- ▶ The infarction volumes after traumatic brain injury were significantly related to the traumatic impact strength.
- ▶ A wireless and non-invasive near-infrared spectroscopy system is an alternative tool for determining brain hemoglobin levels in laboratory animals after TBI.

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## ABSTRACT

Traumatic brain injury (TBI) is usually caused by brain shaking or impact. It can affect normal brain function and may even lead to disability or death. However, there are very few studies on the associated physiologic changes in humans or animals. In this study, a non-invasive, wireless multi-channel near-infrared spectroscopy (NIRS) was developed to continuously monitor the concentration change of oxyhemoglobin (HbO<sub>2</sub>), deoxyhemoglobin (HbR), and total hemoglobin (HbT) to elucidate changes in the physiological state of the brain during and after different strength impactation. The triphenyltetrazolium chloride (TTC) staining was also used to monitor changes of infarction volume after different strength impactation. The results indicated that the concentration changes of HbO<sub>2</sub> and HbT, and the changes of infarction volumes were significantly related to the impact strength. In conclusion, the status of TBI can be clinically evaluated by detecting HbO<sub>2</sub> and HbT changes. The system proposed here is stable, accurate, non-invasive, and mostly important wireless which can easily be used for TBI study.

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## 1. Introduction

Traumatic brain injury (TBI), often due to brain shaking or impact, affects normal brain function and may lead to disability or even death. In the United States, about 1.5 million people suffer from TBI annually (Thurman, 1999), with a financial burden of more than 50 billion U.S. dollars. The associated increase in intracranial pressure (ICP) after TBI leads to a high risk of brain hypoxemia or edema such that a 30% mortality in the first three days has been reported (Noble, 2010). The lack of timely examination and treatment may also lead to death (Ghajar, 2000).

Intracranial pressure monitoring is usually used to monitor TBI. However, its invasive measurement may cause brain hemorrhage and infection (Heegaard and Biros, 2007). Some non-invasive medical instruments, such as magnetic resonance imaging (MRI), computer tomography (CT), and positron emission tomography (PET), may be used to examine TBI (Belanger et al., 2007, Maas et al., 2008), especially to detect cerebral blood flow and acquire information on oxygen metabolism of cerebral tissue. Their limitations include enormous costs and poor mobility, which restrict their practical use in most clinical settings. Moreover, while MRI, which has no ionizing radiation, is safe, it is also the most expensive and its temporal resolution is poorer than that of CT (Hillman, 2007). Both of PET and CT, which require radioactive substance, are unsuitable for long-term monitoring (Crespi, 2007).

Recently, near-infrared spectroscopy (NIRS) was developed and has since been widely applied for cerebral science. The concept of near-infrared spectroscopy was first proposed by Jobsis in 1977

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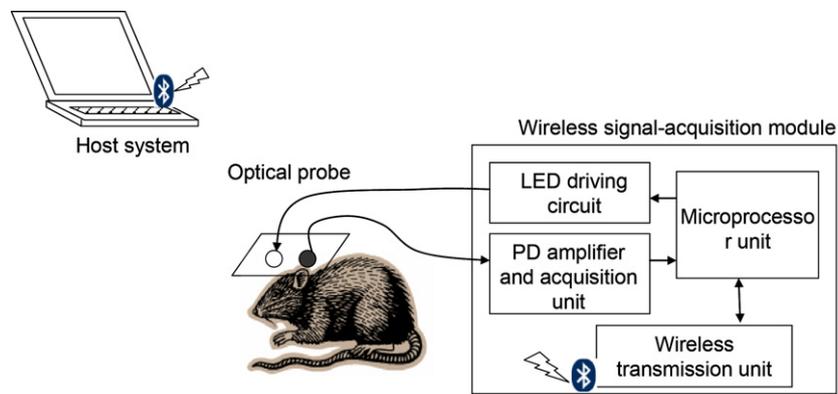


Fig. 1. System architecture of proposed wireless multi-channel NIRS system.

(Jobsis, 1977). For red and near-infrared light, oxyhemoglobin (HbO<sub>2</sub>) and deoxyhemoglobin (HbR) are the most significant absorbers in blood or tissue. Using red and near infrared light to penetrate through the brain to monitor their variation of relative optical transparency, the relative concentration changes of HbO<sub>2</sub> and HbR in relation to cerebral blood flow and oxygen metabolism can be calculated. Therefore, near-infrared spectroscopy may be applied to detect focal cerebral ischemia (Tsuji et al., 1998), hemorrhage (Gopinath et al., 1995), stroke (Bönöczk et al., 2002), newborn infant hypoxia (Wyatt et al., 1990), and post-injury cognitive functions (Merzagora et al., 2011). However, up to now, mostly of the devices is wires dependant.

In the present study, a wireless multi-channel NIRS system was designed to monitor changes in HbO<sub>2</sub>, HbR, and total-hemoglobin (HbT) concentrations during and after TBI. A TTC staining was also used to monitor changes of infarction volume after different strength impaction. These aimed to clarify the state of brain injury under different impact conditions.

## 2. Materials and methods

### 2.1. Design of wireless multi-channel near-infrared spectroscopy system

A wireless multi-channel near-infrared spectroscopy system was designed to monitor changes in the relative HbO<sub>2</sub> and HbR concentrations under TBI. The entire system architecture mainly consisted of a wireless signal acquisition module, an optical probe, and a host system (Fig. 1). The optical probe contained light-emitting diodes (LED) and photodiodes (PD), and was firmly fixed on the subjects. The LED and PD were used to supply the red and infrared light sources, and to transfer the intensity of diffusely reflective light into current or voltage, respectively. The wireless signal acquisition module was designed to drive the red and infrared light sources and to acquire signals obtained from photodiodes. When light was emitted by biological tissue, very little light would penetrate through the tissue due to the scattering and absorbing properties of the different structures. The brain contains five layers (scalp skin, skull, cerebrospinal fluid layer, gray matter, and white matter), and for the wavelength of near-infrared, their scattering coefficients are about 1.9, 1.6, 0.24, 2.2, and 9.1 mm<sup>-1</sup>, respectively. And the absorption coefficients of the five tissues for near-infrared are about 0.018, 0.016, 0.004, 0.036, and 0.014 mm<sup>-1</sup>, respectively (Okada and Delpy, 2003). As such, the penetrating light usually carried physiologic information regarding the tissue (Payne et al., 2011). For the wavelength of near-infrared, the absorptions of the five tissues are far less than those of HbO<sub>2</sub> and HbR. Therefore, the absorptions of HbO<sub>2</sub> and HbR are mainly considered in the absorption model.

In general, the penetrating depth of the red and infrared light was about a half of the distance between the light source and the detector (Crespi et al., 2005). The specific area for monitoring HbO<sub>2</sub> and HbR changes could be determined by using this rule. Intensity changes of penetrating red and infrared lights measured by the photodiode was delivered into the wireless signal acquisition module, and then amplified and digitalized. The microprocessor unit in the wireless signal acquisition module calculated the changes of HbO<sub>2</sub> and HbR by using a modified Beer-Lambert law (MBLL). The differential path-length factor (DPF) used in MBLL is a scaling factor relating to the light source-detector distance to the true optical path-length traveled by the scattered light (Boas et al., 2001, van der Zee et al., 1992), and can be expressed by,

$$B = \frac{1}{2} \left( \frac{3\mu'_s}{\mu_a^{initial}} \right)^{1/2} \left[ 1 - \frac{1}{(1 + L(3\mu'_s^{initial}\mu_a^{initial})^{1/2})} \right] \quad (1)$$

where  $\mu'_s$  is the transport scattering coefficient,  $\mu_a$  is the absorption coefficient, and  $L$  denotes the light source-detector distance. And the relative change  $\Delta[\text{HbT}]$  of total-hemoglobin from its baseline can then be calculated by using the formula:

$$\Delta[\text{HbT}] = \Delta[\text{HbO}_2] + \Delta[\text{HbR}] \quad (2)$$

where  $\Delta[\text{HbO}_2]$  and  $\Delta[\text{HbR}]$  represented the relative concentration changes of HbO<sub>2</sub> and HbR from their baseline, respectively. These data were then transmitted into a computer or wireless handheld device.

#### 2.1.1. Optical probe

Most near-infrared spectroscopy systems used laser diodes and avalanche photodiodes combined with a fiber-optic module as the optical probe (Culver et al., 2003). Instead of laser diodes and avalanche photodiodes, surface mounted device (SMD) LED (SMT735/850, EPITEX, Japan) and silicon-pin PD (PD15-22C/TR8, EVERLIGHT, Taiwan), which were low-cost, safe and small-volume, were used as the light source and the detector, respectively. These were embedded in the optical probe to effectively maintain contact with the head of subject (Fig. 2). Through the module design of the probe, the number of LEDs and PDs were easily selected for different applications.

#### 2.1.2. Wireless signal acquisition module

The wireless signal acquisition module mainly consisted of a microprocessor unit, a LED driving circuit, a PD amplifier and acquisition unit, and a wireless transmission unit. Texas Instruments MSP430, with the advantage of ultra-low power consumption and high operation performance, was used as the microprocessor unit. The wireless transmission unit consisted of a Bluetooth module, with Bluetooth v2.0 compliant specification, and an antenna on

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