Construction and calibration of a diffuse optical hybrid device for brain monitoring

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Abstract

The aim of this project is the development of a new portable, compact and user-friendly device suitable for the intensive care areas in the hospitals. The increasing presence of technical machinery in medical environments claims for bedside devices which are small, compact and easy to manipulate by clinicians. The enabling tool is based on two diffuse optical techniques known as Diffuse Correlation Spectroscopy (DCS) and Continuous Wave (CW) Near Infrared Spectroscopy (CW-NIRS). These two techniques are able to measure hemodynamic parameters in a non-invasive manner even in the brain which can help clinicians in their knowledge of diseases such as ischemic stroke. I have assembled all the elements required for the two techniques, proved their reliability and adapted the existing codes for its control. Finally I have tested the device in a non-hospital environment by measuring the hemodynamics in the arm, in the leg and in the brain.
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1 Introduction

Since the beginnings of the 20th century, scientists used light as a tool in the medical area. The first technique that was employed to establish a diagnostic by means of data extracted from light illumination was called transillumination [1]. It mainly consisted in illuminating tumorous female breast tissue from behind in order to see the shape of the tumor. Despite the poor sensitivity and specificity of the technique, researchers started to notice that the concentration of blood in the tissue was linked with its degree of opacity and that tumors seemed to be opaque.

The development of new technology has pushed the frontiers of photonic sciences beyond unexpected limits. Thanks to sophisticated instrumentation together with the advances reached in the computational field, nowadays hospitals are provided with tools that uses non-ionizing irradiation such as visible or infrared light which give basic parameters for monitoring patients (i.e: the pulsi-oxymeter monitors the heart rate and the saturation of oxygen in blood). Back to the research field, numerous techniques that use light have proved their robustness to contribute to patient diagnostics. Diffuse Correlation Spectroscopy (DCS) and Near-infrared Spectroscopy (NIRS) are two non-invasive techniques that uses diffuse optic physics to provide biomarkers such as the concentration of the two different types of hemoglobin, oxy and deoxy-hemoglobin (Hb and HbO2 respectively) and the blood flow, which have been tested in hospital environments [2, 3]. In particular, both techniques have been used for transcranial monitoring of different brain pathologies such as traumatic brain-injured patients [4], ischemic stroke [6] and obstructive sleep apnea patients [7]. They present similar properties as they both work at wavelengths within the same range (the near-infrared domain which goes approximately from 700 nm to 1300 nm [5]), like the penetration depth (from one to two centimeters) and the temporal resolution (order of hundred of milliseconds). In addition, both techniques appear to be suitable to work with instrumentation that holds in a bedside device.

In a hospital area, and above all in the intensive care unity, a simple property like the size of the device is a key parameter. The bigger the medical device, the more difficult will be its transportation and manipulation. In the Medical Optics group of the Institut de Ciències Fotòniques (ICFO), new applications required the use of diffuse optical techniques in the intensive care unit; therefore there was a must to make new small and user-friendly device.

The aim of my project has been to continue with the design, construction and calibration of this new device, which we called the diffuse optical hybrid (DOH) device. During the pasts months, I have chosen and ordered the missing components, as well as tested and assembled them. Each component of the device needed to fulfilled a specific characteristic. In addition I had adapted the existing Visual Basic 6 codes for its control which allowed me to learn a new programming language. Finally I have made the first measurements in different parts of the human body to compare and contrast the results with the ones of the bibliography, ensuring the expected behavior. In particular, I measured the hemodynamics of an adult arm, an adult calf and an adult brain.

Targeted objectives are specific to each component of the device. For the DCS lasers, the key parameter is to obtain a constant $\beta$ value over time about 0.5 (in sections below we will further discuss the meaning of the $\beta$ parameter). For all NIRS and DCS lasers, a certain
degree of stability in output intensity has to be fulfilled: fluctuations should not exceed the 10\% of the mean intensity. Finally the detector’s dark count should be similar than the one stated in the manufacturer’s datasheet.

In order to prove the validity of the firsts measurements, I have compared the obtained results with the bibliography.
2 Physical basis

2.1 Tissue optics

Light interaction within biological tissues depends on both the properties of the incident beam (wavelength, power and targeted area) and on the optical properties of the tissue [8]. If we consider tissue to be a bulk medium, the primary phenomena of interest are reflection, refraction, absorption and scattering [9], as shown in figure 1a. The majority of incident light will penetrate the tissue while a smaller portion is back reflected due to the refractive index mismatch between the air and the biological sample. This back reflected light will contain information on surface layers. The property of reflectance derived from the Fresnel's equations depends on the incident angle of the light [9], so in order to reduce the effect of reflection, the incident beam must hit the surface perpendicularly. Light interaction within the tissue is affected by both the absorption and scattering, with scattering being the dominate interaction, as tissue is considered a highly turbid media [9].

Light absorption occurs when the energy from a photon is transferred to an electron at a stable level of energy and thus exciting it to another higher energy one [9]. Therefore the total amount of light will be reduced as light travels through the tissue to the point of disappearing after traveling a certain distance. This average distance, which depends on the wavelength, is defined as the absorption length and its reciprocal corresponds to the absorption coefficient denoted by $\mu_a(\lambda)$. The equation that models the absorption phenomena is the Beer-Lambert law [9], shown in equation 1:

$$I(\lambda) = I_0 e^{-\sigma \rho d} = I_0 e^{-\mu_a(\lambda)d},$$

where $\sigma$ is the cross section of the beam, $\rho$ the density of absorbers in the media, and $d$ the optical pathlength. Figure 1b shows us the absorption coefficient as a function of the wavelength for primary chromophores found in tissue. As we can see, the main absorber in the infrared regimen in our body is water, although is not the only one: melanin, hemoglobin in its both forms, oxy-hemoglobin $HbO_2$ and deox-hemoglobin $Hb$, and other proteins also contribute to the absorption process within different ranges of wavelengths. Examining figure 1b it can be seen that there is a significant decrease in the $\mu_a$ from 650nm-950nm. This range is known as the physiological window and enables deeper penetration in tissue [10].

Light scattering occurs when a photon hits a particle and its direction of propagation is deviated. It provides information about micrometer-size objects that scatter light in the sample [11]. Particles that are smaller than the incident wavelength follow the Rayleigh scattering [9]. In this case, the oscillating electric field of the beam interacts with the charges within the particle in such a way that it becomes a radiative dipole. Therefore, the light is scattered mainly at the incident direction, both backwards and forwards. On the contrary, particles that are the same size or bigger than the wavelength tend to scatter light mostly in the forward direction, following the Mie scattering [9]. The larger is the particle as compared with the wavelength, the more light will be scattered in the forward direction. However, tissues do not strictly follow either Rayleigh or Mie scattering, rather there is a combination of the two [9]. The scattering length is defined as the average distance that a photon travels before it scatters, while the transport mean free-path represents the distance
(a) Possible light-tissue interactions with $\Theta_i$ being the incident and reflected angles, $\Theta_r$ the refracted angle and $\Theta_s$ the first scattered angle.

(b) Absorption coefficient of principal chromophores in our tissues: the extra picture corresponds to the physiological window within 650-950 nm.

Figure 1: Light-tissue interactions

that a photon travels before its direction is randomized. As such, the scattering length is shorter than the transport mean free path [11], denoted by $l_t(\lambda)$, where $\lambda$ is the wavelength of the incident light. The reciprocal of this last parameter is called the reduced scattering coefficient denoted by $\mu'_s(\lambda)$, which is related to the scattering coefficient $\mu_s(\lambda)$ (reciprocal of the scattering length) by $\mu'_s(\lambda) = (1 - g)\mu_s(\lambda)$. The $g$ parameter quantifies the anisotropy of the medium. The equation that models the intensity in function of the traveled distance and which includes both scattering and absorption coefficients [9] is stated in equation 2:

$$I(\lambda) = I_0e^{-(\mu_a(\lambda) + \mu_s(\lambda))d}$$

(2)

Organelles, cell membranes and red blood cells are ones of the main scatterers in our body.

### 2.2 Photon diffusion theory

In the previous section we stated that in tissue the scattering is predominant over the absorption. Typical values for $\mu'_s(\lambda)$ in our tissue are approximately $10cm^{-1}$ and $\mu_a(\lambda)$ about $0.1cm^{-1}$, leading to a ratio of 10 between both coefficients [11]. But in order to obtain the real values for both of them, a model that separates the absorption effects from the ones of the scattering is required. The diffusion model provides a mathematical description for this separation.

Physics of diffuse optics start from the radiative transfer equation (RTE) which mainly provides the balance of the energy of the radiance $L(r,\hat{\Omega},t)$ in tissue [11]. The radiance is defined as the light power per unit area traveling in the $\hat{\Omega}$ direction at position $r$ and time $t$ and can be related with the electric field in a way that $L(r,\hat{\Omega},t) \sim |E(r,\hat{\Omega},t)|^2$. In order to obtain the diffusion equation from the RTE, two main assumptions have to be made: the predominance of the scattering over the absorption which turns the radiance into an
isotropic quantity and the slow variations of the photon flux over time [11]. The remaining photon diffusion equation is then shown in equation 3:

\[ \nabla \cdot (D(\vec{r})\nabla \Phi(\vec{r}, t)) - v\mu_a(\vec{r})\Phi(\vec{r}, t) - \frac{\partial \Phi(\vec{r}, t)}{\partial t} = -vS(\vec{r}, t) \] (3)

where \( D(\vec{r}) \) is the diffusion coefficient approximated by \( D(\vec{r}) = \frac{v^3}{3(\mu'_s + \mu_a)} \approx \frac{v^3}{3\mu'_s} \), \( v \) the velocity of light in the medium, \( \Phi(\vec{r}, t) \) the photon fluence rate \((W/cm^{-2})\) which is related with the radiance [11] and \( S(\vec{r}, t) \) the source term. The detailed explanation to pass from one model to another is developed in [11].

To obtain solutions from the diffusion equation, the boundary conditions and the source term have to be defined. Figure 2b shows the three common type of sources that can be used: continuous wave (CW), intensity modulated (FD) and time-resolved (TR) source. On the one hand, CW is the simplest way of illumination source, though it does not allow \( \mu_a \) and \( D \) be determined simultaneously. In contrast, what can be obtained is the variation of the \( \mu_a \), \( \Delta \mu_a \) (we will discuss this further in section 2.3). FD and TR require more complicated electronics but can provide both absolute parameters simultaneously by incorporating the phase and amplitude of the incident and detected light (in the case of the TR, we get the information from a the Fourier transform thus from a broad band of modulation frequencies) [11]. The isotropic condition is guaranteed as long as the source-detector separation in the reflection configuration \( \rho \) (not to confuse with the previous \( \rho \) defining the density of absorbers) exceeds \( 3l_{tr} \) [13]. In this geometry (see figure 2a), the distribution of the paths that the photons travel before reaching the detector have been studied and have been shown to resemble a banana shape with a width of \( \frac{\rho}{2} \) [14]. Thus, there is a trade-off between the penetration depth of the photons and the intensity detected in the detector: the larger the \( \rho \), the deeper the photons will penetrate, but the intensity read in the detector will decrease.

Regarding the boundary conditions, the sort of geometry that we will study is the planar interface, where the beam crosses from the air to the semi-infinite turbid medium. In this case it is easy to see that the light that escapes from the tissue will never re-enter the medium (unless some optical elements are put in its path). By using the approximations of the diffusion model, reflectance coefficient derived from Fresnel’s equations and the first order Taylor expansion of the photon fluence rate, a relatively simple boundary condition can be derived [15]. This is the extrapolated-zero boundary condition (shown in equation 4) and assumes that the fluence rate \( \Phi \) is zero at the point \(-z_b\):

\[ \Phi(z = -z_b) = 0 \] (4)

where \( z_b = 2l_{tr}(1 + R_{eff})/3(1 - R_{eff}) \), and \( R_{eff} \approx -1.44n^{-2} + 0.710n^{-1} + 0.668 + 0.00636n \), with \( n \) being the ratio of the index of refraction inside and outside the tissue \( n = n_{in}/n_{out} \) [11].

Now that we have defined the source terms and the boundary conditions, the diffusion equation can be solved by using the method of images to find the Green’s function associated with the differential equation. Considering a CW point source and semi-infinite homogeneous media, the Green function in cylindrical coordinates \((r_s = (\rho_s = 0, z_s = l_{tr})\) is:

\[ G_0([\rho, z], [\rho_s = 0, z_s = l_{tr}]) = \frac{1}{4\pi} \left[ \frac{\exp(-kr_1)}{r_1} - \frac{\exp(-kr_b)}{r_b} \right] \] (5)
(a) *Banana pattern* of the photon path in the reflection geometry for homogeneous media.

(b) Types of source: continuous wave (CW), intensity modulated (FD) and time-resolved (TR) sources respectively. Image reproduce with the C. Lindner consent [12].

**Figure 2**

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Figure 3: Extrapolated-zero boundary condition: at point \( l_{tr} \) our laser source becomes a point source shining light in all directions. Some of this light is back scattered to the surface of the tissue, and some of it is transmitted through. At point \(-z_b\) the photon fluence rate \( \Phi \) falls to zero.
where \( r_1 = \sqrt{(z - l_{tr})^2 + \rho^2} \), \( r_b = \sqrt{(z + 2z_b + l_{tr})^2 + \rho^2} \) and \( k = \sqrt{\mu/D} \). We consider \( z = 0 \) (see figure 3).

However, \( \mu_a \) and \( D \) still remain unknowns. As stated before, by using FD and TR sources it is possible to obtain \( \mu_a \) and \( D \) simultaneously as a result of the incorporation of the phase and amplitude variables [11]. In the particular case of the CW source, both coefficients cannot be obtained using the Green’s function solution. The next section provides an alternative method to derive additional parameters from the recorded intensity in CW configuration.

### 2.3 Near-infrared Spectroscopy

The absorption coefficient linearly depends on the concentration of the different chromophores in tissue (see equation 6):

\[
\mu_a(\lambda) = \sum_i \epsilon_i(\lambda)c_i
\]

where \( \epsilon_i(\lambda) \) is the extinction coefficient of a given chromophore and \( c_i \) its concentration in the tissue. The diffusion model has provided us a method to obtain \( \mu_a \) for a given wavelength thus by measuring \( \mu_a \) at different wavelengths we can obtain a system of equations and use this to determine concentrations. The more wavelengths that are employed, the more chromophore concentrations that can be measured. To do so, a selection of the wavelengths is required. To determine the Hb and the HBO\(_2\), two wavelengths are needed at least. In order to avoid light water contribution, the wavelengths had to belong to the region of the physiological window (see figure 1b). Moreover, to minimize the cross-talk between the extinction coefficients, one of the wavelengths should be below the isosbestic point and the other above. The isosbestic point is the wavelength where both coefficient coincide (at ~ 800nm).

**The differential pathlength (DPF) approach**

In many cases, we are only interested in measuring the time variations of the hemoglobin concentrations. The differential pathlength approach provides a model in which even with CW laser sources is possible to measure these variations. To do so, we need to recall the Beer-Lambert law (see equation 1) and more precisely the modified Beer-Lambert law (see equation 8) wherein the scattering effect is included. The equation introduces a new parameter, the optical density (OD) which is defined as \( \text{OD}(t) = \ln \frac{I(t, \nu)}{I_0} \) [9], where \( T \) is the transmittance of the medium \( T(t, \nu) = \frac{I(t, \nu)}{I_0} \). The modified Beer-Lambert law is obtained by truncating the Taylor expansion of the optical density at first order:

\[
\text{OD}(\mu_a^{(0)} + \Delta \mu_a, \mu_s^{(0)} + \Delta \mu_s) \approx \text{OD}(\mu_a^{(0)}, \mu_s^{(0)}, \rho) + \frac{\partial \text{OD}(\mu_a^{(0)}, \mu_s^{(0)}, \rho)}{\partial \mu_a} \Delta \mu_a + \frac{\partial \text{OD}(\mu_a^{(0)}, \mu_s^{(0)}, \rho)}{\partial \mu_s} \Delta \mu_s
\]

Then if we consider \( \Delta \text{OD}(\lambda, t, \rho) = \text{OD}(\mu_a^{(0)} + \Delta \mu_a, \mu_s^{(0)} + \Delta \mu_s) - \text{OD}(\mu_a^{(0)}, \mu_s^{(0)}, \rho) \) and replace the value of \( \Delta \mu_a \) by equation 6, we obtain the modified Beer-Lambert law:

\[
\Delta \text{OD}(\lambda, t) \approx \sum_i (\epsilon_i(\lambda) \Delta c_i(t))d_a(\rho, \lambda) + \Delta \mu_s'(\lambda, t)d_s(\rho, \lambda) \sim \sum_i (\epsilon_i(\lambda) \Delta c_i(t)) \text{DPF}(\lambda) \rho
\]
where \( d_a = \frac{\partial \text{OD}(\mu_a(0), \mu'_s(0), \rho)}{\partial \mu_a} \) and \( d_s = \frac{\partial \text{OD}(\mu_a(0), \mu'_s(0), \rho)}{\partial \mu_s} \). In tissue optics the reduced scattering coefficient is generally assumed constant thus \( \Delta \mu'_s = 0 \) and \( d_a(\rho, \lambda) = DPF(\lambda) \rho \), where DPF is the differential pathlength factor obtained from the literature specific for each type of tissue [16]. Therefore, by measuring the intensity over time at different wavelengths, we can relate it to the \( \Delta \text{OD} \) and thus with the concentration of the tissue chromophores. We will study Hb and HbO\(_2\) concentrations assuming that the effect of the rest of the relevant chromophores (such as water and lipids) will remain constant in our near-infrared range of study (690 nm-830 nm).

### 2.4 Diffuse Correlation Spectroscopy

**Concept of Speckle**

Coherent light such as that of a CW laser generates some granular pattern when shined on most surfaces [17]. A surface is typically rough in the wavelength scale and thus when coherent light strikes it, it scatters at different points and generates a visible interference pattern called speckle pattern (see figure 4). In a similar vein, when laser light travels through diffuse media composed by particles in suspension like biological tissues, light will be scattered by the different particles at random directions and will interfere constructively and destructively creating the speckle pattern [18]. Therefore, if the particles in suspension were not in movement, the interference created at a certain point A in the surface of the tissue would be approximately constant (vibrations of the particles would still affect). On the contrary, if some of the scattering particles were in movement, the scattered electrical wave would arrive with a different optical phase to point A, modifying the interference pattern. In tissue the main moving scatterers are the red blood cells. The diffuse correlation spectroscopy (DCS) technique records the variation over time of a single speckle attributed to red blood cells motion and by means of some statistical functions further introduced, provides the relative cerebral blood flow (rCBF).

![Speckle pattern](image)

Figure 4: Speckle pattern formed when coherent laser light illuminates a rough surface such as paper.
Diffuse Correlation Spectroscopy technique

DCS analysis uses the optical properties of the tissue to fit an effective Brownian diffusion coefficient (i.e., blood flow index) to the decay of the electric field autocorrelation $G_{1}(\tau)$ function of a single speckle. The most important physical effect that enables blood flow measurements is the fact that $G_{1}(\tau)$ diffuses through tissue in the vein of that of the light fluence rate [11]. Therefore $G_{1}(\tau)$ follows the dynamics of the so-called diffusion correlation equation, which is similar to the diffusion equation except from an extra term related to the absorption of the dynamic scatterers (we recall that in tissue the main moving scatterers are the red blood cells). The diffuse correlation equation is then:

$$\left[\nabla \cdot (D(\vec{r})\nabla) - v\mu_{a}(\vec{r}) - \frac{\alpha}{3}v\mu'_{s}k_{0}^{2}\langle \Delta r^{2}(\tau) \rangle \right]G_{1}(\vec{r},\tau) = -vS(\vec{r},t)$$

(9)

where $G_{1}(\vec{r},\tau)$ together with its normalized function are:

$$G_{1}(\vec{r},\tau) = \langle E^{*}(\vec{r},t)E(\vec{r},t+\tau) \rangle \quad \text{&} \quad g_{1}(\vec{r},\tau) = \frac{\langle E^{*}(\vec{r},t)E(\vec{r},t+\tau) \rangle}{\langle |E(\vec{r},t)|^{2} \rangle}$$

(10)

$\tau$ is the delay time, $k_{0} = 2\pi/\lambda$ is the wavenumber of the CW light traveling through the tissue, the brackets $\langle \rangle$ represent time-averages for experiments and ensemble averages for calculations, $\alpha$ is the fraction of photon scattering events that occur from moving particle in the medium, $\langle \Delta r^{2}(\tau) \rangle$ is the mean-square displacement in time $\tau$ of the scattering particles and $D$, $\mu_{a}$, $\mu'_{s}$ and $v$ are the parameters that appeared in the photon diffusion equation. It has been proven that $\langle \Delta r^{2}(\tau) \rangle$ follows a Brownian motion rather than a random velocity one [11]. Thus $\langle \Delta r^{2}(\tau) \rangle = 6Db\tau$, where $Db$ is the diffusion coefficient of the moving scatterers expressed in $(cm^{2}/s)$ and which differs from the documented Einstein parameter of particles of the same size. Like both photon diffuse equation and diffusion correlation equation are similar, by following the mathematical path derived in section 2.2 (including the assumptions of the zero-extrapolated boundary condition (see equation 4) and Green’s function analysis), we can obtain an analytic solution from the diffuse correlation equation. For instance, by considering a semi-infinite homogeneous media, the solution to equation 9 is (the position vector is expressed in cylindrical coordinates):

$$G_{1}([\rho, z, t], [\rho_{s} = 0, z_{s} = l_{tr}]) = \frac{1}{4\pi D} \left[ \frac{\exp(-K(\tau)r_{1})}{r_{1}} - \frac{\exp(-K(\tau)r_{b})}{r_{b}} \right]$$

(11)

Here, $r_{b}$ and $r_{1}$ are the same than for the photon diffusion equation, but now the exponent is also dependent on $\tau$ through the constant $K(\tau) = \sqrt{(\mu_{a} + \alpha\mu'_{s}k_{0}^{2} < \Delta r^{2}(\tau)>/3)v/D}$. Nevertheless, what it is typically measured in an experiment is the intensity auto-correlation function $G_{2}(\tau) = \langle I^{*}(t)I(t+\tau) \rangle$, where intensity $I(t) = |E(t)|^{2}$. By means of the Siegert relation, one can link the normalized intensity auto-correlation function $g_{2}(\tau) = \langle I^{*}(t)I(t+\tau) \rangle/\langle |I(t)|^{2} \rangle$ with $g_{1}(\tau)$:

$$g_{2}(\tau) = 1 + \beta|g_{1}(\tau)|^{2}$$

(12)

where $\beta$ is a constant parameter related to the optical employed system. Thus, $G_{1}(\tau)$ is derived from the experimental $G_{2}(\tau)$ data, and $K(\tau)$ from the fitting of the temporal decay of the analytic solution of $G_{1}(\tau)$ for a given source-detection distance $\rho$. By combining this
information with the optical parameters of the tissue, one can obtain the $\alpha Db$ parameter contained in $K(\tau)$, the remaining unknown in our equations, which is redefined as the blow flow index (BFI). Equation 13 finally relates the processed data with relative changes in the cerebral blood flow [20]:

$$rCBF(\%) = \left( \frac{BFI(t)}{BFI_0} - 1 \right) \times 100$$  \hspace{1cm} (13)

Figure 5: Example of fitted $g_1(\tau)$ from a human arm with a source-detector distance of $\rho=2.5$cm. Pink dots correspond to the experimental data and solid black line is a brownian motion fit ($\langle \Delta r^2(\tau) \rangle \sim \tau$). The accuracy of the fit depends on the delay time ($\tau$). The longer the delay time, the more deviated is the fit due to higher contributions of the superficial photons. Note also that the experimental data never reaches the zero value, it is a characteristic of the arm measurements
3 Diffuse Optical Hybrid Device

The previous section described the techniques that are implemented in the DOH device as well as the physics behind them. While with the DCS technique the goal is to monitor changes in the cerebral blood flow, with the NIRS technique we want to obtain the variation of the concentration of both oxy and deoxy-hemoglobin. The particularity of this device is that data from both hemispheres of the brain can be recorded simultaneously. Figure 6 shows the setup to acquire the required data from one hemisphere. In this section, which constitutes the major part of my project, I will describe the device that I helped to design and construct at ICFO to achieve the desired objectives stated in the Introduction. The device is referred as the Diffuse Optical Hybrid (DOH) device due to the incorporation of the two diffuse optical techniques.

3.1 Block Diagram

The diagram shown in figure 7 describe the basic connections between the different elements of the DOH device. As we can see, the device is divided in two separated structures which are an enclosure on top of a stand (the computer is placed on the enclosure).

DOH device contains six CW laser of three different wavelengths: 785 nm for the DCS technique and 690 nm and 830 nm for the NIRS technique. All six lasers are computer controlled by means of a data acquisition card (a USB-6341 National Instrument DAQ with 24 digital Inputs/Outputs, 16 analog inputs and 2 analog outputs) together with a Visual Basic 6 code run by the computer. In addition, the DAQ reads the photodiode signal from the NIRS lasers which is stored in a file (the meaning of this signal will be developed in section 3.2.1). In parallel, the counted pulses sensed from the detectors are sent to the correlator which provides the normalized intensity auto-correlation function \( g_2(\tau) \) and the number of counts. Just as with the photodiode signal, the information extracted from the correlator is saved in the same file. Two fans are the responsible of ventilate the enclosure. Further information of the electronic connections of the DOH device is detailed in figure 8. The new green blocks next to the detectors are their power board and they will be explained in section 3.2.3.

Apart from being the holder of the enclosure, the stand contains the different devices to power supply all the elements of the enclosure, including the computer. The devices that directly required 230 V are plugged in the isolation transformer, while the rest of them are plugged in the power box which provides voltages of 5.5 V and 12.0 V. The Mechanical Workshop at ICFO constructed all the fixations of the different elements in the enclosure, drilled the holes for the ventilation system and built the stand.
Figure 6: Setup for measuring one hemisphere with the DOH device. Laser 1 corresponds to the 785 nm (for the DCS technique) and laser 2 and 3 correspond to 690 nm and 830 respectively (for the NIRS technique). During a certain interval (let us say 3 seconds although it varies depending on the character of the experiment), one of the lasers shines CW light into one side of the forehead through a multi-mode (MM) fiber. Every three seconds the on laser is switched. The back scattered light is guided through a single-mode (SM) fiber to a four independent channel APD detector which translates the intensity registered into a train of pulses. Finally the pulses are sent to a correlator which gives the correlation function $g_2(\tau)$ and the intensity registered over time and, after some data processing, we obtain the variation in concentration of both oxy and deoxy-hemoglobin ($\Delta HbO_2$ and $\Delta Hb$) and the relative cerebral blood flow (rCBF).
Figure 7: General diagram of the electronic connections in the DOH device
Figure 8: Complete diagram of the electronic connections in the DOH device. UPS stands for Uninterrupted Power Supply.
3.2 Description of the elements

3.2.1 NIRS Lasers

The Electronic Workshop at ICFO designed and built under our supervision the electronics behind the four diode laser bought from the company OZ optics. Two of them have a wavelength of 690 nm and the other two of 830 nm. The four of them are calibrated in such a way that at the state of non-emitting light, wherein the working current is at its threshold, the lasers emit around 30 $\mu$W of power while at the ON state, they emit around 50 mW (the working power stated according to the datasheet).

Each of the lasers contains two different boards whose functions are to activate the laser and to control the temperature at which it works by maintaining constant the working current (see figure 9b). The driver laser board incorporates a transimpedance amplifier to filter, amplify and transform to voltage the photocurrent sensed by the photodiode included in the laser. This voltage is an additional parameter read in the data acquisition card to monitor the state of the laser. The temperature controller board implements a proportional integral control which controls the Peltier by having as a reference the temperature sensed by an Negative Temperature Coefficient (NTC) thermistor incorporated in the laser. In addition, the laser contains an extra thermistor to directly check the temperature of the atmosphere. The Peltier is a thermoelectrical cooler (TEC) which cools or warms the atmosphere depending on the direction of the current that it receives. An H bridge is in charge of guiding the direction of the current driven into the Peltier.

(a) One of the four NIRS lasers. (b) Laser driver board (left) and temperature controller board (right).

Figure 9

3.2.2 DCS Lasers

The lasers employed for the DCS technique are solid state laser made by CrystaLaser (see figure 10, Stabilized Compact Red CrystaLaser©) shining light at 785 nm with a maximal optical power of 100 mW (lasers include a potentiometer to regulate the output power). Apart from being within the physiological window, this wavelength is close to the isosbestic point (see figure 1b), thus we are less sensitive to the differences in the variation of both Hb and
HbO₂ concentration. In addition, the availability of this wavelength in the market is higher than others [20].

The main requirement that a laser needs to fulfill to be used in the DCS technique is to emit light with a narrow-bandwith $\Delta \lambda$. Lasers with narrow-bandwith, also called single longitudinal mode, have a long coherence length $L_c$ because $L_c \sim \lambda^2/\Delta \lambda$. The condition to have constructive interference in the detector point is derived from the basic interferometry theory which states that the differential pathlength of all the photons has to be smaller than the coherence length of the laser [21]. Therefore, a safe value for the coherence length is larger than 3 m [20]. According to the CrystaLaser’s datasheet, our lasers have a coherent length larger than 10m ($\Delta \lambda < 0.01\text{pm}$) and also emit with TEM₀₀, thus single transverse mode too.

![Figure 10: Crystalaser of single longitudinal and transverse mode, 785 nm](image)

### 3.2.3 Detectors

To sense the back scattered light from the forehead, a bundle of four single-mode optic fibers is placed at the probe at a certain distance $\rho$ of the source point (the distance between each fiber of the bundle is neglected so as to consider a unique $\rho$). In section 2, we have seen that for the DCS technique it is necessary to detect changes in a single speckle. Although we are using single longitudinal and transverse mode lasers, light scatters within the tissue creating the interference pattern seen in section 2.4; thus the incoming signal at the detector does not longer have a single mode. For that reason, by using a single-mode optic fiber for 785 nm (the wavelength of our DCS laser) in the detection path we ensure having a single recorded speckle. Each fiber is then guided to one of the four channels of the single photon counting module (SPCM-AQ4C) showed in Figure 11a from ©Excelitas. The channels are independent from one to another. As our goal is to measure both hemispheres of the
brain at the same time, we will have two modules which four detectors each with the same characteristics.

![Four channel detector SCPM-AQ4C from Excelitas](image1)

(a) Four channel detector SCPM-AQ4C from Excelitas

![Tester Board to test the power board from HemoPhotonics](image2)

(b) Tester Board to test the power board from HemoPhotonics

![Front of the power Board to supply the detector transforming 12V into 2V, 5V and 30V](image3)

(c) Front of the power Board to supply the detector transforming 12V into 2V, 5V and 30V HemoPhotonics

![Back of the power Board to supply the detector transforming 12V into 2V, 5V and 30V](image4)

(d) Back of the power Board to supply the detector transforming 12V into 2V, 5V and 30V HemoPhotonics

Figure 11: Components of the detection system.

The sort of experiments that we are dealing with implies to expose human tissues directly to the light of a laser. As a consequence, the power of the light has to be limited in order not to damage the tissues (the maximal power that can be emitted to a subject is 35 mW). Moreover some light is lost while it is carried by the optical fibers so we are really interested in the contribution of every single photon. In addition, our goal is to obtain a digital pulsed signal to drive it to the correlator. For these reasons we use a single photon counting avalanche diode (SPAD) in the detection system, which is an avalanche photodiode (APD) that works in the Geiger Mode and which incorporates some electronics to transform the photocurrent in digital pulses. Our APD are solid semiconductor detectors made of silicon working in the reverse bias voltage configuration so as to be able to start the avalanche process [22]. Generally in an APD, two different working modes are available: the linear and the Geiger mode. On the one hand, in the linear mode, the intensity of the avalanche current is directly proportional to the amount of light that targets the sensing area. On the other hand, in the Geiger mode, a single photon can fire the avalanche process inducing a high intensity current. Therefore with the same amount of light, the photocurrent intensity
of the Geiger mode will be higher than in the linear mode. Further description of the working process of an APD in linear and Geiger mode is developed in [22].

However, the fact of working in the Geiger mode also increases the electronic noise of the detector. In every APD, thermal effects can induce the recombination of an electron-hole pair in the depletion zone and then fire the avalanche effect, leading to the so-called dark current [22]. In the Geiger mode, this dark current is intensified. Table 1 contains the value in counts per second (Hz) of the dark current of every channel of both SPCM-AQ4C detectors. According to the datasheet, they should not exceed the 500Hz.

<table>
<thead>
<tr>
<th>Serial number of the SPCM-AQ4C</th>
<th>Channel 0</th>
<th>Channel 1</th>
<th>Channel 2</th>
<th>Channel 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detector 1 (#457)</td>
<td>266 Hz</td>
<td>341 Hz</td>
<td>295 Hz</td>
<td>439 Hz</td>
</tr>
<tr>
<td>Detector 2 (#458)</td>
<td>356 Hz</td>
<td>424 Hz</td>
<td>333 Hz</td>
<td>319 Hz</td>
</tr>
</tbody>
</table>

Table 1: Dark counts of the SPCM-AQ4C detectors according to the manufacturer’s datasheet.

The detectors require a particular set of voltages to be powered up as different actions need to be undertaken. As we commented previously, the SPAD are working in the Geiger mode, so a high reverse voltage is needed to create the wide space charge region and to work over the breakdown voltage. In our case this voltage is 30.00V. In addition, in order to reduce the dark current to the minimal threshold, the detectors incorporate a temperature controller that also needs to be supplied. For this action a voltage of 2.00 V is required. Finally, as an APD gives the signal as an intensity, another 5.00 V extra volts are required to supply all the electronics to transform the photocurrent into digital pulses or digital counts. Table 2 lists the previous voltages by providing their minimal and maximal values as stated in the datasheet.

<table>
<thead>
<tr>
<th>Voltage</th>
<th>Minimum</th>
<th>Typical</th>
<th>Maximum</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.00 V</td>
<td>1.95 V</td>
<td>2.00 V</td>
<td>2.05 V</td>
<td>Supply for the termo-electrical cooler (TEC).</td>
</tr>
<tr>
<td>5.00 V</td>
<td>4.75 V</td>
<td>5.00 V</td>
<td>5.25 V</td>
<td>Supply for the digital part.</td>
</tr>
<tr>
<td>30.00 V</td>
<td>29.00 V</td>
<td>30.00 V</td>
<td>31.00 V</td>
<td>Reverse bias voltage applied to create the space charge zone.</td>
</tr>
</tbody>
</table>

Table 2: Supplied voltages for the SPCM-AQ4C according to the manufacturer’s datasheet.

Therefore, in order to avoid buying three different power supplies for a single detector, a PCB was designed to transform a single input of 12.00 V into 2.00 V, 5.00 V and 30.00 V. Moreover, the power board includes four independent connectors which deliver the pulsed signal obtained from the SPCM-AQ4C. This PCB is property of the spin-off related to the Medical Optics group @HemoPhotonics. It is called AQ4C driver, but we will refer to it as the power board (see figure 11c and 11d). To avoid damaging the detectors, before plugging the power board into the detectors, the power board has to be tested with another board shown in 11b which we call the tester board.
3.2.4 Correlator

The correlator incorporated in the DOH device is a 8 channel correlator, with 256 bins per channel (Flex05-8 ch, see figure 13a). By means of some data processing, the correlator provides the normalized intensity auto-correlation function $g_2(\tau)$ and the number of counts sensed in each channel within a certain duration. The particularity of this correlator is the acquisition mode of the samples: instead of using the simple linear method to construct the auto-correlation function, it works according to the multi-$\tau$ scheme (see figure 12). The main difference is the distribution of the acquired samples: in the linear case, the bin width of every register is the same (we define a register as the time during which the correlator is counting the number of received pulses and a bin a space in the memory of the correlator) while in the multi-$\tau$ case, the first 16 registers have a bin width of $\tau = 200\,\text{ns}$, the next 8 registers a width of $2\tau$, and from now on every 8 registers the bin width doubles with respect to the previous one. Further information of how a multi-$\tau$ works and constructs the $g_2(\tau)$ function is developed in [23]. The advantage of this technique is the efficient use of the memory: the number of bins required to record data during a certain duration is smaller in the case of the multi-$\tau$ method than in the linear one.

![Linear vs Multi-\(\tau\) correlator](image)

Figure 12: Linear VS Multi-\(\tau\) correlator

3.2.5 Power box

The power box designed and mounted by the Electronic Workshop at ICFO (see figure 13b) is a smart solution to encapsulate the commuted power supplies required by the elements which need different voltages than 230 V to work. It contains five different sources, each one in charge of supplying a specific component in the enclosure. The front panel includes a switch for every single source as well as a general switch. Additionally, each power source is protected with a fuse.

As we saw in section 3.2.1, each NIRS laser has two different boards that need 5.5 V at 1 A to work: the laser driver board and the temperature controller board. The Peltier used to regulate the temperature together with its electronics typically induces important quantities of noise in the circuit. For this reason, we decided to separate the laser driver power supply from the one of the temperature controller. The sources used are the TXM 035-105 power...
supply from ©Tracopower, which provide 5.0 V at 6.0 A, and can be regulated at 5.5 V. The criteria followed to choose the sources, apart from the fact that they provide enough power to supply the fourth lasers, is that they do not need any minimal charge to work.

Two identical 12.0 V power supplies working at 4.2 A are used to supply each one of the detectors. Once again we bought them from ©Tracopower (model TXM 050-112) as they do not need a minimal charge to work. According to the datasheet, the maximal current required by one of the detectors is 4.0 A. For that reason we choose the 50 W power supplies.

![Correlator](image1.png)  ![Power Box](image2.png)

(a) Correlator  (b) Power Box

Figure 13

Finally another source of 12.0 V at 1.3 A (TXL 015-12S model from ©Tracopower) is used to supply the fans. Just as the Peltiers, the fans introduce a lot of noise in the circuit [24], thus we separate them from the detector sources.

### 3.2.6 Fans

Two ©BISONIC fans are placed inside the right side of the enclosure, just behind the detectors and the NIRS lasers. I decided this localization because I noticed that the boards of the detectors warmed up a little and because the opened side of the box that encloses each NIRS faces the fans. Like this, we ensure that both devices receive a proper general cooling. Apart from that, by means of holes in the left side of the enclosure, we ensure that the delivered air from the fans circulates within all the elements and that the hot air is extracted.
3.2.7 Isolation Transformer

The main function of an isolation transformer is to provide electrical power to the powered devices while isolating them from the power source. According to the datasheet, the REO-MED transformer 230 V/230 V from ©REO inductive components, provides a galvanic separation \textsuperscript{[25]} between primary and secondary circuit. Thus the isolation transformer belongs to the safety system of the device. It contains 9 outlets which deliver 230 V each and 1000 VA of power.

3.2.8 Battery

The Uninterruptible Power Supply (UPS) from ©Protec-Sai (K-LCD 1200 model) is placed between the isolation transformer and the current plug of the building. Its main function is to provide near-instantaneous extra power supply to the isolation transformer and thus the whole device in case of failure of the general electrical system of the building. Like this we avoid causing damage to all the electrical equipment that could suffer from an unexpected power disruption and ensure the data collection. According to the datasheet, the UPS unity can supply the device during 10 minutes at 1200 VA.

3.2.9 Safety keys

The device incorporates in the front panel four independent key switches of two positions to control the state of the six laser. On the one hand, position one corresponds to the open switch state where the laser cannot emit light (OFF mode). On the other hand, position two corresponds to the closed switch state where the laser emits a few microwatts of power (ON mode). As we commented in the previous section, the laser are fully computer controlled, thus to emit the required light they need to receive the TTL signal from the NI DAQ.

Regarding the DCS laser, each of them already came with its own key, so no further action was required. However, for the NIRS lasers, we had to buy the keys and design the circuit. My goal was to reduce the number of keys in the front panel in order to minimize the actions that a non-qualified person had to do to properly operated with the DOH device. Therefore, the four NIRS laser are controlled with only two keys, one for each pair of lasers with the same wavelength.

3.3 Picture of the device

The final result of the device is shown in figure 14. The stand includes free-rotating wheels to allow the total mobility of the entire device, each one with its corresponding brake. The height was set in order to have the suitable distance at which to work with the computer.

3.4 Validation of the components

3.4.1 Lasers

The first characteristic that needs to be verified for every laser is the stability in power over the time. The setup designed to check the stability consists in shining CW light through
Figure 14: Diffuse Optical Hybrid device. The enclosure contains the six lasers, the two modules with the eight detectors, the correlator, the data acquisition card and the fans. The stand contains the isolation transformer, the power box and the UPS.
a multi-mode fiber which ends in a probe placed on the surface of a lipofundin phantom. Another single-mode fiber is placed in the probe at a distance $\rho$ and connected to the detection system made of one APD detector and the correlator (the detectors and correlator used to sense the signal are not the ones incorporated in the DOH device). The whole setup is covered with a black plastic blanket to minimize the contributions from the ambient light. Finally, the optical characteristics of the phantom try to mimic the ones of the tissue: $\mu_a = 0.1 \text{ cm}^{-1}$ and $\mu'_s = 10 \text{ cm}^{-1}$. Figure 15 shows a picture of the setup.

![Figure 15: Setup for measuring the laser stability. Laser light is guided to the probe placed on the surface of the lipofundin phantom through a multi-mode fiber, and collected at a distance $\rho$ with a single-mode fiber attached to the detectors (all detectors and correlator are not the ones included in the DOH device).](image)

**NIRS Laser**

The stability test for the left hemisphere NIRS lasers was set during a whole night ($\sim 16$ hours). By looking to figure 16, we can see that the test was successful. The top figure shows the variation over time of the number of counts sensed on the surface of the phantom (pink for the 690 nm laser and blue for the 830 nm) and in both cases, the maximal amplitude is within the range of 5-10 counts, which does not imply any relevant change in the concentration of Hb and HbO$_2$ (further results in section 4.3 will confirm it). The plots of the photodiode signal also prove the stability of the lasers: despite the little observed peaks, both voltages vary in a range of 10-20 mV, which in power is equal to 0.3-0.6 mW. We obtain this equivalence by means of a simple experiment: every NIRS laser incorporates a potentiometer to tune both threshold and on current, thus, by plugging the photodiode voltage into an oscilloscope and...
the fiber optic into a power-meter, we observed that approximately, a variation of 15mW in power corresponded to a variation of 500mV in voltage.

**DCS Laser**

Regarding the DCS lasers, from the beginning I saw clearly that they were not working as we wanted (see figure 17): $\beta$ presents unexpected peaks regularly. In order to obtain reliable data using the DCS technique, the $\beta$ parameter should be constant over time. Recall that the $\beta$ parameter was the one which allowed the passage from $g_2(\tau)$ to $g_1(\tau)$ by the Siegert equation and which depended on the optical system employed. There was a fabrication issue which delayed considerably my project, because without the final elements, the Mechanic Workshop was not able to start the fabrication of the fixations inside the enclosure, nor the final assembly. It also took time to receive the new alternative laser. In the end I was able to test it and learn how to work with it (although results are not shown in this thesis).

The fixed laser were tested again under the new conditions specified by the manufacturer. After the repetition of the same experiment we observe that now the fixed lasers were working as we expected (see figure 18). The $\beta$ parameter was finally stable around a 0.5 value and the same for the intensity sensed over time (note than in figure 19, the fluctuations in the BF do not exceed the 10%). In order to work with the new fixated lasers, an attenuator has to be placed to achieve the 35 mW (we recall that this is the maximal power that can be sent to a subject).

**3.4.2 Detectors**

The procedure for testing the detection system consists in two parts (each of them repeated twice as we have two detectors). Firstly, the power boards (see figure 11c and 11d) for the detector have to be tested with another tester board which simulates the detector to confirm that the delivered voltages are within the acceptable ranges of table 2. Secondly, the number dark counts of the detectors have to be compared with the ones provided by the manufacturers. This last step is very important because it will define the level of noise of our detector.

**Testing the power board**

The testing part of the power board is split in two steps. The first one consists in measuring the voltages directly on the testing points of the board while the second one consists in measuring them at the testing points of the tester board (see figure 11b), which simulates the detectors.

Initially, with the version 2.3 (2.3v) of the boards, I followed the steps stated in the report of an ancient engineer of the Electronic Workshop who designed and built the power boards two years ago. My goal was to compare his values with mine, trying to set the same measuring conditions. I used the linear power supply TTI EL302RT to deliver the 12.0 V and two different detection systems, a Fluke 87v multimeter and an Agilent Mixed Signal Oscilloscope (MSO7104B), as it was not specified in the report. Figure 20 shows the results for one of the 2.3v boards.
Figure 16: Stability test for the left NIRS laser during a whole night (pink for the 690nm and blue for the 830nm): the top plot shows the intensity (in number of counts) sensed on the surface on the phantom over time; the bottom plot shows the voltage of the photodiode of each laser together with its normalized value.
Figure 17: Intensity and beta stability for the DCS lasers shining light at 35mW before being repaired. All night experiment. Clearly the results are not the expected ones because of the $\beta$ oscillations. These lasers were returned to be fixated.
Figure 18: These are the repaired lasers. Intensity and $\beta$ stability for the DCS lasers shining light at 100mW are shown. All day experiment. The top plot in each subfigure represents the value of $\beta$ over the time; the histogram gives precise view of the most repeated values for $\beta$ and the bottom plot shows the variation of the intensity of the DCS laser in counts over the time.
Figure 19: $\alpha Db$ variation over time of both DCS lasers measuring over lipofundin phantoms. The supposed relative blood flow is plotted in order to quantificate the degree of background noise.
Figure 20: Results from single power board 2.3v. Values in gray correspond to initial document reported measurements. The Oscilloscope delivers some statistics where: $V_{AC RMS}$ is the standard deviation value of the root mean square and $V_{AC PP}$ is the mean value of the peak-to-peak value. Additional information about the different symbols in the table: (*) Addition of the 5.0 V to activate the enable of the boards; (†) Measuring between the corresponding test points of the power board ; (‡) Measuring between the corresponding test points of the tester board ; (’) The first and second values correspond to the ‘No test board’ and ‘Test board connected’ setup. Fluke is multimeter used and Agilent MSO is the oscilloscope.
Extra debugging following the schematics of the board was required to manage to turn it on: the 2.3v, needed an extra 5.0 V to set up the enable. The results that we obtained were very similar to the engineer’s values (even better because most of the values of \(V_{AC_{RMS}}\) and \(V_{AC_{PP}}\) are lower than what he measured, meaning that the noise is reduced). However it is remarkable that in the 'Test board connected' configuration, the values for the 2.0 V did not reach the minimal voltage of 1.95 V stated in 2. Following the engineer’s path we considered that the tests had been successful, taking into account that possibly the dark count of the detectors could be higher as the TEC was not supplied in the desired conditions.

Nevertheless, v2.3 was discarded due to two main reasons: on the one hand, we wanted to avoid the extra 5.0 V to enable the board; on the other hand, when we tried one of the power boards with a detector, the measured dark count of one of the channels was giving unexpected data: 300 kHz (300 000 counts per second) were measured instead of the expected 500 Hz. We changed the board to ensure that the photodiode was not broken and in this case all four channels had reasonable dark counts. Therefore and taking profit from the new 2.4v board that had been built, we decided to change the power boards. In this case too I had to spend time to make them work because, by following the signal thanks to a multimeter and the schematics, I found out that the signal was lost in one of the components. So I brought them back to the Electronics Workshop and they confirmed me that the soldering at that pin was not precise enough. The particularity of the 2.4 version is that the extra 5.0 V are no longer required, and the defective components of the v2.3 were replaced. Thus, the new boards had to be tested with the protocol described above.

\[
\begin{array}{|c|c|c|}
\hline
 & \text{Without} & \text{With the} \\
 & \text{the tester} & \text{tester} \\
 & \text{board} & \text{board} \\
\hline
\text{2.0 V TP of the PB} & 2.001 V & 1.917 V \\
\text{5.0 V TP of the PB} & 4.971 V & 4.941 V \\
\text{30.0 V TP of the PB} & 30.21 V & 30.210 V \\
\text{2.0 V TP of the TB} & - & 1.907 V \\
\text{5.0 V TP of the TB} & - & 4.889 V \\
\text{30.0 V TP of the TB} & - & 30.170 V \\
\hline
\end{array}
\]

Table 3: Results from single power board 2.4v. "TP" means test point, "TB" means tester board and "PB" means power board.

Just as with the 2.3v, 30.0 V and 5.0 V are within the expected range while the value of the 2.0V when the tester board is plugged is slightly below the manufacturer’s limits.

**Testing the Dark current**

The key parameter of the SCPM-AQ4C that has to be tested is the dark current of each of its APD. The setup implemented to achieve this purpose is shown in figure 21, whose principal goal is to isolate the detectors from every photon of light. As we can see in the picture, the detectors were enclosed into a black box (with some slits to allow the placement of the cables), covered with a black plastic blanket to reinforce the isolation. In addition,
some cardboards were placed to stop the light from the oscilloscope. The output pulsed signal from each APD detector is read by the Agilent MSO oscilloscope in order to count the pulses with the counter function. Figure 22 shows an example of the data obtained in the screen of the oscilloscope. Finally, table 1 summarizes the measured values: the numbers were obtained by making an average of ten recorded values using the segmented mode of the oscilloscope over 30 different segments of 2 µs (the pulse width is 25 ns ). Note that in the 458 module, values for channel 0 and channel 2 exceed the maximal range.

Figure 21: Setup to sense the dark current of the SPCM-AQ4C. The detector together with the power board are placed inside the black covered box in order to isolate them from any light contribution. The pulsed signal from single APD is guided to the oscilloscope wherein the number of pulses will be measured. An anti-static bracelet is required to manipulate the detectors.

<table>
<thead>
<tr>
<th>Detector</th>
<th>Channel 0</th>
<th>Channel 1</th>
<th>Channel 2</th>
<th>Channel 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected values #457</td>
<td>266 Hz</td>
<td>341 Hz</td>
<td>295 Hz</td>
<td>439 Hz</td>
</tr>
<tr>
<td>Obtained values #457</td>
<td>268 Hz</td>
<td>496 Hz</td>
<td>311 Hz</td>
<td>453 Hz</td>
</tr>
<tr>
<td>Expected values #458</td>
<td>356 Hz</td>
<td>424 Hz</td>
<td>333 Hz</td>
<td>319 Hz</td>
</tr>
<tr>
<td>Obtained values #458</td>
<td>576 Hz</td>
<td>374 Hz</td>
<td>619 Hz</td>
<td>305 Hz</td>
</tr>
</tbody>
</table>

Table 4: Detector’s dark count

In average the results are convenient. Note that the measurements that we will undertake are in a range between 20-50 kHz. Therefore a dark count of 500 Hz only implies 1-2.5% of extra noise. In addition, in the case of the NIRS technique, the vector of the detected count rates (thus the intensity recorded over time) used to obtain the variation of both hemoglobin concentrations is normalized to a baseline during the data process. Thus, by assuming a constant coupling between all the optical elements, this normalization suppresses all constant background noise (including the electronic noise of the detectors).
Figure 22: Screen-shot of the oscilloscope showing the pulsed signals emitted by channel 1 of the SPCM-AQ4C #457. The measured value (333 Hz) is within the expected ranges of the detector (see table 4).
4 First Measurements

There are many experiments in the bibliography that ensure the robustness of the DCS and NIRS technique. In order to prove the proper behavior of the DOH device, some of them have been replicated in a non-hospital environment. However each experiment has only been tested once, thus to ensure the repeatability, more tests have to be undertaken.

4.1 Arm cuff experiment

One of the simplest experiments that can be displayed is an arm cuff experiment. An air pressure band is placed in the arm simulating a tourniquet and the probe is fixed in the muscle of the forearm (see figure 23a). The source-detector distance for all three lasers was $\rho=2.5$ cm. During the first three minutes we recorded data for the baseline and then the challenge started: the air bracelet applied 180 mmHg of pressure for five minutes and then we quickly loosed it. Another five minutes were set for the recovery period (the complete protocol is shown in figure 23b). Results are totally in agreement with the expected ones [26]. Regarding the blood flow, in the left plot of figure 26, we clearly see the drop during the cuffed period and the rising peak just at the beginning of the recovery period. In accordance to it, the HbO$_2$ in the right plot decreases during the cuffed period while the Hb increases. Finally when we release the pressure HbO$_2$ rises and Hb decreases.

![Figure 23: Left figure shows the setup for the arm cuff experiment. Two different probes have been used, one for the NIRS lasers and other for the DCS laser. In both cases the source-detector distance was $\rho=2.5$ cm. Right figure explains the complete protocol of the experiment. Lasers shined light sequentially every three seconds: first the DCS, then the NIRS 690 nm and finally the NIRS 830 nm. The challenge was divided in three different parts including 3 minutes for the baseline, 5 minutes with the arm cuffed at a pressure of 180 mmHg, and 5 final minutes for the recovery period.](image)
Figure 24: Results from the arm cuff experiment. The different marks delimit the different parts of the experiment: baseline, beginning of the addition of pressure, stabilization at 180 mmHg, release of the pressure leading to the recovery period. Left figure shows in the top the variation of the $\alpha Db$ parameter and in the bottom the subsequent relative blood flow. Right figure shows the variation in concentration of Hb and HbO$_2$ with time. During the cuffed period, the blood flow and the HbO$_2$ decreased while the Hb increased. When we remove the pressure, both blood flow and HbO$_2$ show a peak and the Hb decreases.
4.2 Calf experiment

In this case only the DCS technique has been tested. In addition, settings have been adjusted so as to have a data file every 5 seconds instead of the previous 3 seconds. The source-detector separation once again is $\rho=2.5$ cm. After the three minutes of baseline, the subject was asked to raise his left leg holding a weight of 6 kg during 1 minute. After that, we have another three minutes recovery period. It is expected that the blood flow increases as the muscle is doing some exercise. The results showed in picture are in agreement with this hypothesis [27]: the blood flow does increase within the exercise period. Previous peak might correspond to motion artifacts of the subject.

![Setup for the calf experiment](image)

Figure 25: Setup for the calf experiment. Fiber optics were omitted in the draw, but a multimode fiber is placed in the source (S) position and at a distance $\rho=2.5$ cm, a single-mode fiber is placed in the detector (D) position.

4.3 Breath-Hold test

A breath-hold test consists in measuring the effects in the hemodynamics of the brain while you stop breathing during a few seconds. We recall that both DCS and NIRS techniques appear to be able to measure hemodynamics through intact skull, although the amount of light sensed is considerably reduced compared with the previous tests due precisely to the presence of the skull and other layers which absorb part of the emitted and back scattered light (see figure 27a) [28, 29].

The protocol followed in this experiment consists in recording a baseline for two and a half minutes, holding the breath during thirty seconds and finally measuring the recovery period for another two and a half minutes. In this case the temporal resolution is lowered to 1 second as the length of the challenge is lower than the previous tests and we expect to see changes in a lower scale. The probe is placed in the left side of the forehead with source-detector distances of $\rho=2.5$ cm for all NIRS lasers and DCS laser (see figure 27b). By comparing the obtained results with [29], we can confirm that the test was successful: during the breath-hold exercise, the rCBF shows a drop and immediately after high peak,
Figure 26: Results from the calf experiment. The fit $\alpha Db$ parameter and so the rBF present a peak during the period of exercise. The previous peak in the baseline period belongs to a slight movement of the subject.

(a) Brain layers. Note that before reaching the brain, light should travel within different layers.

(b) Setup for the breath-hold test. The probe is placed in the left side of the forehead with source-detector distances of $\rho = 2.5$ cm for both NIRS lasers DCS laser. All laser fiber optics are multi-mode (MM) while the detector senses light with a single-mode fiber (SM).
just as the behavior of the HbO₂ curve (see figure 28). Although bibliography does not give a clear argument to explain this behavior because there are many hypothesis that play with different variables such as the vasoreactivity of the veins, one explanation could be that when the brain notices that the levels of O₂ have decreased, the blood flow increases to compensate the loss.

Figure 28: Results from the breath-hold (BH) test.
5 Future outlook and conclusions

During these five months I have learnt the basic theoretical concepts of a brand new branch of physics, diffuse optics, together with two techniques that are based on it: Diffuse correlation spectroscopy and Near-Infrared spectroscopy. In addition, I was able to deep into different courses that I took in the degree, specifically Biomedical Photonics, Electronics Physics and Electromagnetic waves since elements such as lasers, fiber optics and the avalanche photodiodes detectors requires the background given in these subjects to understand their functioning. Furthermore, I acquire brand new knowledge about electronics since I actively participated in debugging the power board to supply the detectors.

Main objectives have been achieved. I have made a first check of the stability in intensity for all the available lasers and the stability in the $\beta$ parameter in case of the DCS lasers. The results showed in the previous sections prove that the intensity of every kind of laser is within the expected parameters (fluctuations of less than the 10%) and that the $\beta$ parameter is almost 0.5. To do so, I measured phantoms having similar optical properties than human tissue at different source-detector distances. Further tests need to be accomplished following a specific routine to really ensure the repeatability of the device (i.e: make at least ten day measurements for each laser on phantoms). In addition I tested the specifications of the detectors which appear to work in the desired conditions as they are within the ranges stated by the manufacturers. Finally, after selecting the remaining components, I was able to assembly all the elements inside the specific designed enclosure and its correspondent stand, accomplishing the objective of making a compact and portable device suitable for intensive care units areas of the hospitals. Additional work has to be undertaken regarding the safety of the device by testing the isolation transformer with the recently acquired electrical safety analyzer (Rigel 288 from ©Rigel Medical). In addition, some temperature tests need to be done to ensure that the ventilation holes in the stand are enough to guarantee the proper functioning of the device. The lack of one of the 830 nm laser prevent us for testing the efficiency of the simultaneous measurement of both hemispheres in the brain in the breath-hold test.

Regarding the control code, I adapted the existing versions to the new requirements of the device, learning a new programming language. Additional buttons can be added to the interface to expand the control of non-technician user over the protocol of the device.

First measurements with the device appear to be in agreement with the bibliography. For future expansions of the device, additional outlets are available in the isolation transformer.
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7 References


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