Near Infrared Oxymetry

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Introduction

Near-infrared spectroscopy (NIRS) and near-infrared optical imaging (NIRI) on turbid media such as biological tissue is a rapid growing field of interest. The techniques offer the ability to use light to non-invasive quantify metabolite concentration and to image structure within the human body. In particular methods for monitoring the blood and tissue oxygenation level and blood volume are currently under study. Near infrared light ($\pm$700-900 nm) is used in these applications because of the relative transparency of tissue to light in this wavelength region while the oxygen dependent absorption of hemoglobin is still observable [1-8].

The main goal in oxymetry is to determine the blood oxygen saturation which is defined as the ratio of the concentration c of oxygenated hemoglobin (HbO_2) to the sum of the concentration of HbO_2 and deoxygenated hemoglobin (Hb) of the blood

$$SaO_2 = \frac{c(HbO_2)}{c(HbO_2) + c(Hb)} \qquad (1)$$

The optical techniques are based on differences in spectral absorption coefficients of the two components HbO_2 and Hb. We will first describe the general principles of oxymetry.

Oxymetry

The primary absorber in blood in hemoglobin, an oxygen carrier that exists in two forms, Hb and HbO_2. Its absorption coefficient (μ_a) depends on the wavelength and its oxygenation. The spectral absorption coefficients are depicted in figure 1. The oxygenation level of the blood is determined by the fraction Hb and HbO_2 [eq 1]. The spectral absorption coefficient will in practice be a linear combination of the two extremes in figure 1. Inversely, measurement of the absorption coefficient of blood reveals the oxygenation level.

Because in vivo measurements are used, the absorption of the tissue surrounding the blood e.g. artery wall, fat, muscle etc. also has to be taken into account.

There are a couple of parameters that have to be determined befor the oxygenation level can be calculated from the attenuation of the light. The most important ones are the concentrations of the Hb and HbO_2. Because a ratio (eq. 1) is used, the concentrations can be written as fractions ($f_{hb} = 1 - f_{HbO2}$). Bloodvolume, the pathlength in blood and the absorption of the tissue surrounding the blood are the other parameters to determine. When scattering is neglected, Beer's law for one wavelength can be rewritten as:

$$LN\left(\frac{I}{I_0}\right) = -(P_b \cdot c_{Hbt} \cdot ((f_{HbO2} \cdot \mu_{a,\lambda}^{HbO_2}) + ((1 - f_{HbO_2}) \cdot \mu_a^{Hb}))) - (P_t \cdot \mu_a^{tissue}). \qquad (2)$$

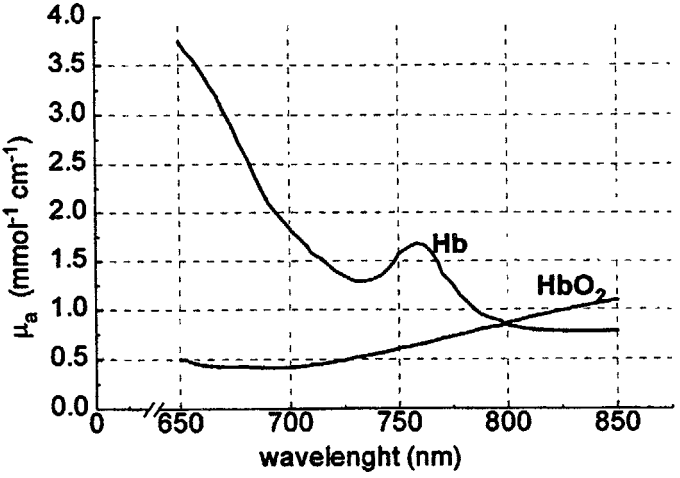

Figure 1:
Spectral absorption coefficients of Hb and HbO_2 in the near infrared region [4].

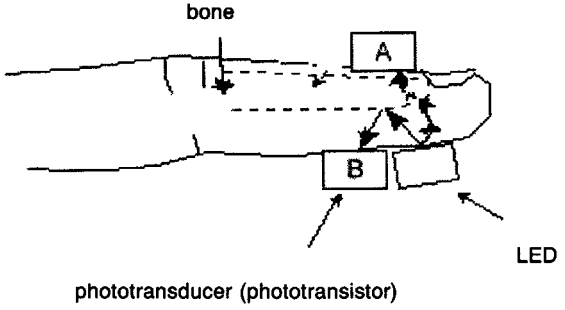

Figure 2:
Transmission mode (A) and remittance mode (B) pulse oxymeter. The black arrows indicate possible lightpaths.

Where P_b pathlength of the photon in blood, P_t: pathlength of the photon in tissue, c: concentration of the absorbing particles in blood or tissue, I_0 intensity of the incident light.

Most clinically used oxymeters use two wavelengths. For the next example we take 750 and 800 nm, and determine the *ratio* of their intensities. When we assume the isobestic point of hemoglobin to be around 800nm (figure 1) we can make the assumption:
When we further assume that the absorption coefficient for the surrounding tissue is equal for both wavelengths, equation 2 can be rewritten to:

$$LN\left(\frac{I_{760}}{I_{800}} \cdot \frac{I_{0,760}}{I_{0,800}}\right) = -(P_b \cdot (f_{HbO2} \cdot (\mu_{a,760}^{Hb} - \mu_{a,760}^{HbO_2})) + P_b \cdot (\mu_{a,800} \cdot \mu_{a,760}^{Hb})) \qquad (3)$$

The effects of scattering are now included in the pathlength factors P_b and P_t As we can see in equation 3 the oxygenation level can still not be calculated without knowledge of the optical pathlength.

Pathlength
We assume that the intensity of the light along the scattered path is exponentially attenuated, independent of direction of propagation, which is reasonable when tissue is considered a homogeneous medium. Beer's law in this form can be used in different geometries when source and detector are nog aligned.

Figure 2 shows two typical geometries in oxymetry. Configuration A shows the light source and the detector on opposite sides on the issue (transmission mode). This is the most common clinical configuration. Configuration B shows the light source and the detector both on the same side of the issue (remittance mode).

The optical pathlength and therefore the attenuation of the light will directly depend on the structure of the tissue and the source-detector geometry. When, in remittance mode, the source fibre and the detection fibre are placed to close to each other it is to be expected that the detected signal will contain relatively little information of the deeper lying tissues. A larger distance between source- and detector fibre geometry will result in a measured signal that contains information of deeper lying layers in the tissue but that will be less strong and therefore has a worse signal to noise ratio.

Measurement methods
In practice there are three measurement techniques that are used clinically. Each uses different ways to extract pathlength information from the transmitted or remitted light.

– Time resolved measurements:
short incident light pulses are used and the distribution of the time of flight of the light pulse contains information about the pathlength distribution

– Frequency domain measurements:
Phase differences between high frequency modulated incident light and light that escapes the tissue contains information about the pathlength distribution

– Continuous light measurements:
A continuous light source is used and the spectral attenuation is measured. This signal contains no data about the pathlength. Knowledge of the pathlength is needed for the interpretation and quantification of the data. Using the optical properties of the issue, the pathlength distribution can be estimated using the **diffusion theory** or **Monte Carlo** modeling.

Diffusion theory
The net propagation of energy carrying particles in a scattering and absorbing medium can be described as a diffusion process. There are some requirements for the approximate validity of the theory. The optical mean free path has to be smaller than the dimensions of the problem considered. That is, the distance to the boundaries or the sources. In this theory a homogeneous medium that is (semi) infinite in thickness is assumed. Furthermore, the photon should be scattered many times before it is absorbed or, in our case, escapes from the medium. The photon flux results from a gradient in photon density, and, consequently the energy flux results from a gradient in flunk rate. These relationships result in Ficks law. From this we can derive the diffusion equation. Analytic solutions to the diffusion equation can be found for simple geometries such as an infinite slab, a cylinder and a sphere. The time resolved solution may be used to calculate possible pathlength distributions.

Monte Carlo
An approach often used in tissue optics is to apply 'brute force' to the problem and

simulate the propagation of photons one by one in a computer model. A set of rules is applied every step and every scattering or absorption event. The two key parameters are the mean free path for scattering and absorption and the scattering angle. Events of interest are scored in a volume matrix from which an estimation of the quantity of interest is possible. e.g. number of photons reaching a detector.

The Monte Carlo program uses an input file with a set of parameters defining the medium (optical properties (g, μ_a, μ_s, n)) of the layers, the source detector geometry and the number of photons that have to be launched.

From the output we can extract

- The average depth of the photon paths: in each 'cell'' of the matrix, the number of absorption events is scored. The depth of the cell is used as a weight in the averaging process. This is done for the whole matrix, which results in an average monitored depth. This quantity gives an indication of the area in the tissue in which the system is most sensitive to changes in optical properties.
- Pathlength of each individual photon
- The shape of the photon paths: The presence of different layers or blood vessels has its influence on the monitored area. Visualization of the paths as described before, can give more insights in the effects of these irregularities in the medium.

Figure 3: An example of Monte Carlo output. A remittance measurement was simulated. The arrow on the left indicates a light source and the areas in the 'medium'

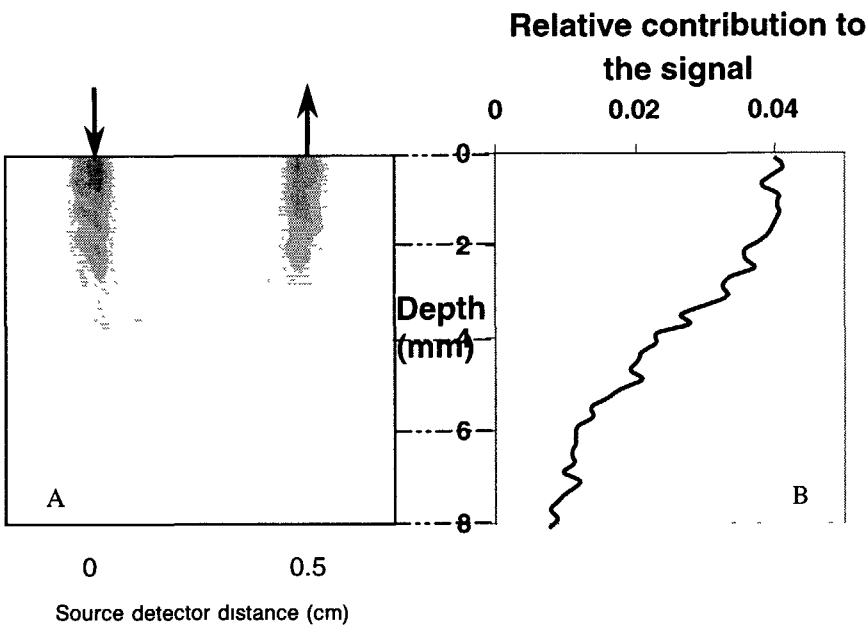

Figure 3:
An example of Monte Carlo output. A remittance measurement was simulated.

give an indication of the amount of photons that are absorbed or have past through that volume element. Figure 3B gives the relative contribution to the measured signal as a function of depth. From this Monte Carlo we can see that the optical properties of a small volume directly under the fibers primarily infuences the signal.

Application of the theories

A combination of the presented theories can be used to get a complete insight in the complex behavior of light in tissue. The time derived diffusion equation enables calculation of the distribution of photon pathlengths when the optical properties of the tissue are all known. This information can also be obtained by Monte Carlo calculations but the calculations are very time-consuming. The possibility to calculate the depth of the photons is an advantage of the MC calculations of the diffusion equation.

A practical example

We built a simple remittance setup using two frequency modulated diode lasers (758, 805 nm). Optical fibers were used to guide the excitation light to the tissue and collect the fluorescence light from the tissue to a Photomultiplier. An A/D converter and a fourier transform algorithm were used to extract the remitted power from the separate wavelengths.

Measurements were performed on the forearm of a volunteer. Figure 4 shows the Changes in remitted light intensity in response of total arterial occlusion

The ratio graph shows an immediate

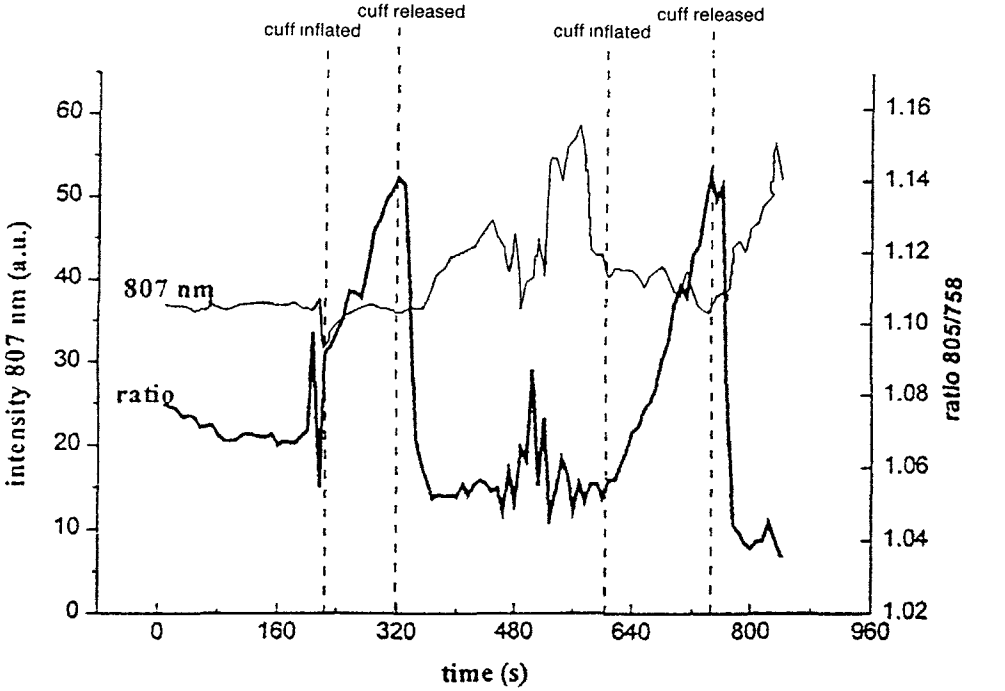

Figure 4:
Measurements on human forearm.

response to the occlusion while the 805 nm curve remains fairly stable during the oxygen consumption. The noise between the occlusions is due to repositioning of the probe. Using optical properties from literature[9], a calculated pathlength and figure 1, the change in oxygenation was estimated to be approximately 20%.

Conclusions

Although near infrared is already used clinically for a long time there is a lot to be improved. Especially real time determination of the pathlength and monitored volume are important. Furthermore, the amount of wavelengths has to be equal to or exceed the number of chromofores that contribute to the signal.

A disadvantage is the difficulty to monitor only arterial or venous blood. In practice, on skin under normal conditions, a mixture of highly oxygenated arterial blood (±99%) and less oxygenated venous (±60%) will be monitored.

Near infrared **imaging** is currently under development but there is still no clinical device available.

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