Published in final edited form as:

Proc SPIE Int Soc Opt Eng. 2005 March 29; 5696: 117–124. doi:10.1117/12.593345.

Signal and image processing techniques for functional near-infrared imaging of the human brain

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Abstract

Near-infrared spectro-imaging (NIRSI) is a quickly developing method for the in-vivo imaging of biological tissues. In particular, it is now extensively employed for imaging the human brain. In this non-invasive technique, the information about the brain is obtained from the analysis of spatial light bundles formed by the photons traveling from light sources to detectors placed on the surface of the head. Most significant problems in the functional brain NIRSI are the separation of the brain information from the physiological noise in non-cerebral tissues, and the localization of functional signals. In this paper we describe signal and image processing techniques we developed in order to measure two types of functional cerebral signals: the hemodynamic responses, and neuronal responses.

Keywords

brain; MRI; near-infrared; functional imaging

1. INTRODUCTION

There is a series of outstanding questions regarding the detection of brain activity in measurements made on the surface of the head and about the origin of the observed changes in the optical parameters of tissues. Originally, the question was: Can changes be observed through the skull? Only recently, non-invasive observations of fast changes in optical parameters were reported¹⁻⁴. In these pioneering experiments, near-infrared light was brought to the external surface of the head using a source optical fiber and the reflected light was measured at a distance of about 3-4 cm using a collection optical fiber. In this configuration, the light must travel deep (1 to 1.5 cm) into the head to reach the detector fiber. There was shown with experiments on phantoms and with simulations that changes in the optical properties of a small region, at a depth of about 1.5 cm from the head surface can affect the amount of light collected. These experiments showed that, in principle, it is possible to measure changes in optical parameters occurring in a deep region. The question remains whether we have sufficient sensitivity to measure changes due to neuronal activity.

Another topical application of the optical techniques to brain studies is the near-infrared spectroimaging (NIRSI) of metabolic processes. The main advantage of NIRSI over other techniques used in this area is its outstanding biochemical specificity, which is based on the classical optical spectroscopic methods. In recent years, many studies have demonstrated that cerebral hemodynamic changes associated with functional brain activity can be assessed non-invasively not only in infants, but also in adult human subjects. Several types of brain activity have been accessed, including motor⁵⁻⁸, visual^{9,10}, auditory¹¹, and cognitive^{12,13} activities. Apart from purely spectroscopic measurements aimed at local detection of functional cerebral hemodynamic changes, several groups have performed imaging-type studies aiming at localization of cerebral hemodynamics^{14,15}. Most significant problems in the functional brain NIRSI are the separation of the brain information from the physiological noise in non-cerebral tissues, and localization of functional signals. In this paper we describe signal and image processing techniques we developed in order to measure two types of functional cerebral signals: the hemodynamic responses, and neuronal responses. Our methodology is based on the integrated NIRSI-MRI approach, which allows utilizing structural information from high resolution MR images in modeling light transport in the realistic head model. Besides, we use the functional MRI data to test the accuracy of our results.

2. HEMODYNAMIC RESPONSES

Near-infrared instruments we use record AC, DC, and phase time series corresponding to multiple source-detector pairs. We extract physiological information from the AC and phase time series, because the DC signals are compromised by the ambient light. Fig. 1 (a) shows a typical AC trace. Its power spectrum is presented in Fig. 1 (b). The spectrum shows prominent peaks at the heart rate and its harmonics, and below 0.3 Hz. The latter corresponds to systemic and local low frequency fluctuations in blood volume and oxygenation. Since the brain activation paradigms used in functional neuroimaging experiments typically include activation blocks of 10-30 s long, the hemodynamic response to such activation blocks falls into the spectral band below 0.1 Hz. Therefore, when analyzing the hemodynamic response, signal processing techniques such as detrending, low pass filtering (to filter out the heart beat), and the block averaging are used to preprocess the signal. Fig. 2 shows the preprocessed AC signal from a single source-detector channel in the visual cortex area corresponding to one visual activation block.

The next step is the reconstruction of the spatially resolved changes in the oxy- and deoxyhemoglobin concentrations. The 3-D anatomical full-head MR image (Fig. 3) is segmented into 4 types of tissues, namely scalp-skull, cerebrospinal fluid (CSF), white matter, and gray matter. The segmented head phantom is used to produce the head model. Based on the positions of optodes and the structure of the head model, the forward problem of optical image reconstruction under baseline condition (without activation) is solved using Monte Carlo simulations, which in turn determine the integral kernel of the perturbation (Born approximation) equation (See Fig. 4). The inverse problem is solved using SIRT from the optical signal.

Structural and physiological *a priori* knowledge is applied to reduce the number of unknowns in image reconstruction and for image registration. From the anatomical MR image (MPRAGE), the brain tissue can be used as a spatial constraint to the solution. Another spatial constraint to the solution is via the estimation of the optical sensitivity region, which consists of voxels with significant contributions to the optical signal. Two different methods were used to estimate such a sensitivity region. The first method is to threshold the integral kernel of the perturbation equation, i.e. to threshold the probability that photons pass through voxels. A value of 0.01 was used in this paper. In addition, for each voxel, its time-series values are compared with the paradigm of the visual stimulation with a 6 s delay. Voxels that have a correlation coefficient higher than a threshold value (± 0.5 used in this paper) are considered as being activated. This also allows the possibility that voxels have negative activation. The other method is to find voxels that produce signal with magnitudes greater than the noise level of the optical signal of all channels/measurements. In other words, the forward problem is solved for each voxel (an activation of 5% from the baseline value was used in this paper); the result (estimated optical signal due to the activation from that particular voxel) is compared with the normalized noise level to determine if this channel/measurement is sensitive to that particular voxel. Finally, the magnitude of activation in both methods is determined by averaging over the whole time period of visual stimulation, but delayed by 6 seconds to represent the hemodynamic response.

The above procedure of image reconstruction is applied to the optical signals obtained at 830 and 690 nm and produces the changes in absorption coefficient at both wavelengths. These changes are consequently converted into changes in the oxy- and deoxyhemoglobin concentrations, i.e. $[\text{HbO}_2]$ and $[\text{Hb}]$, respectively.

In our experiments, the optical probe (Fig. 5 a) was attached to the back of the head and aligned with the primary visual cortex, as shown in Fig. 5 b. Nonmagnetic goggles for producing the visual stimulus were fixed in front of the subject's eyes inside the birdcage MR coil. The paradigm of visual stimulation consisted of 4 blocks, each of which is a 28.8-second fixation followed by a 19.2-second reversing black-and-white checkerboard pattern (Fig. 5 c).

The hemodynamic response (changes in oxy- and deoxyhemoglobin concentration, i.e., $[\text{HbO}_2]$ and $[\text{Hb}]$) of activated voxels identified using the first method (thresholding the integral kernel and correlation coefficient) is shown in Figure 6. The activation patterns of $[\text{Hb}]$ shown in Figure 6(b) are consistent with the pattern of the BOLD signal (Fig. 6 a). As shown in Figure 6(c), the images of $[\text{HbO}_2]$ demonstrate similar yet slightly different patterns. Note that the dark spots represent regions with large changes of hemoglobin concentration changes.

3. NEURONAL RESPONSES

Event-related optical signals (EROS) are related to changes in the optical properties of the neuronal tissue of the brain in response to relatively fast events, such as checkerboard reversing. Since the duration of neuronal response is about 100 ms, and the changes are very

small, in order to increase the sensitivity, experimenters use series of events, in which events occur at frequencies higher than 1 Hz. In this frequency range the signal due to harmonics of the heart beat can be quite significant (see Fig. 1). Pulsation may produce substantial artifacts that are difficult to eliminate with simple band-pass filtering approaches. It is therefore important to separate the changes in intensity due to hemodynamics from the changes due to neuronal activity. An algorithm was developed for the estimation of the pulsation artifact¹⁶ based on regression procedures in which the effect of systolic pulsation is estimated from the data. Summarizing, the algorithm extracts a mean shape of the pulsation by screening each trace separately for pulses. The period of each pulse is adjusted before averaging. This mean shape corresponds to the best estimate of each pulse and is used to remove each pulse from the data. This requires adjusting the period of the mean shape to the one of each pulse and scaling the shape by linear regression. Figure 7 shows the cross-subject averaged result of EROS analysis.

4. CONCLUSION

A remarkable biochemical specificity of the optical method allows researchers to understand physiological mechanisms of complex metabolic processes, such as functional cerebral hemodynamics. Using NIRS we have compared spatial distribution of hemodynamic changes with those imaged by fMRI during motor activation. A good collocation of the fMRI and NIRS signals suggested a good accuracy of our method. Using the optical method we were able to measure neuronal signals simultaneously with fMRI data acquisition. Further integration of NIRS and MRI techniques promises a significant mutual enhancement of both by combining a remarkable spatial resolution of MRI with outstanding temporal and spectral resolutions of NIRS.

ACKNOWLEDGEMENT

This work is supported by the grant number 1R01MH065429-01A2 awarded by National Institutes of Health.

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Fig. 1.
A typical AC NIR optical signal recorded on the human head (a), and its power spectrum (b).

Fig. 2.
Optical AC signal after low-pass filtering and block averaging.

Fig. 3.
Structure of the human head

Monte Carlo Simulation

Structural MR image
is segmented in
four tissue types:

- Scalp
- Skull
- CSF
- Brain

1,000,000 “photons”

Fig.4.

Light bundle for a single source-detector pair computed using the Monte Carlo simulation for one million photons

EXPERIMENT

Fig. 5. Experimental setup: (a) Optical probe for imaging human visual cortex; (b) positioning probe on the head; (c) presentation “checkerboard” pattern

Fig. 6.
Functional maps of: (a) fMRI BOLD signal; (b) optical deoxyhemoglobin; (c) optical oxyhemoglobin

Fig. 7.
Event-related optical signal.