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Assessing TD fNIRS capability to detect hemodynamic oscillations in cerebral cortex

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ABSTRACT

We present a simulation study to evaluate the feasibility of using Time Domain fNIRS to monitor hemodynamic oscillations in biological tissues like the cerebral cortex. Two geometries (slab and two-layer medium) were considered to define the optimal acquisition parameters and to assess the ability of the technique to detect and separate oscillations occurring at different depths within the probed medium by exploiting the time-gating of TD fNIRS signals.

Keywords: time domain near-infrared spectroscopy, hemodynamic oscillations, cerebral cortex, numerical simulations

1. INTRODUCTION

Oscillations in signals related to basal cerebral hemodynamics and metabolism have been observed and studied with different techniques. Several studies investigated these fluctuations using functional near-infrared spectroscopy (fNIRS) both in the continuous wave (CW) and frequency domain (FD) modalities, while the use of the time domain (TD) modality was hindered by the lower signal-to-noise ratio (SNR), which limited the measurement acquisition rate below 10 Hz. In a recent publication, the same authors presented a novel TD fNIRS device able to perform *in-vivo* measurements reaching acquisition rates up to 20 Hz[1]. This novel instrument allows filling the technological gap still present with the previous techniques and opening to a proper study of cerebral oscillations via TD fNIRS. However, there is still a lack of knowledge regarding the optimal measurement protocol and data analysis method to be applied for this specific application. In this work, the authors will present the results of some numerical simulations aimed at evaluating the feasibility of using TD fNIRS to detect oscillations in the concentrations of oxy- (O_2Hb) and deoxy- (HHb) hemoglobin in biological tissues, in particular the brain cortex, by exploiting the time-windowing of the TD fNIRS signals.

2. MATERIAL AND METHODS

A dataset of TD fNIRS signals (*i.e.*, photon Distribution of Time of Flight, DTOF) was generated by exploiting the solution of the Diffusion Equation (DE) for two different geometries: a homogeneous slab and a bilayer medium[2]. The time course of the concentrations of O_2Hb and HHb in the medium was defined around the baseline value of 30 μM and 20 μM, respectively. Then, DTOF curves were calculated at two wavelengths (λ = 690 nm, and 830 nm) and for two source-detector distances (ρ = 1 cm, and 4 cm) using a custom-made software. The excitation pulse was considered as an ideal delta shape, and noise following the Poisson distribution was added to the theoretical model.

Slab model. A sinusoidal perturbation of frequency 1 Hz and amplitude of 1% of the baseline value was imposed on the concentrations of both O_2Hb and HHb. Then, the power spectral density (PSD) of the total number of photons counts of the DTOF curve was calculated using a custom-made Matlab script based on the Welch algorithm. Simulations were performed for different values of measurement duration (T_{meas} = 5, 10, 15 min), average total number of counts ($N_{tot} = 10^4$, 10^5, 10^6), and sampling frequency (f_s = 5, 10, 20 Hz) to evaluate the effect of these measurement parameters on the PSD.

Bilayer model. The medium was described using a two-layer model, in which the superficial layer thickness was set to 1 cm as conventionally done to mimic the heterogeneous structure probed during brain monitoring applications, in which the tissue is divided into a superficial extra-cortical layer (scalp, skull and cerebrospinal fluid) and a deep intra-cortical layer (grey and white matter). Simulations were performed considering T_{meas} = 15 min, f_s = 20 Hz and varying N_{tot} (N_{tot} =

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10^4, 10^5, 10^6). The same perturbation as before was imposed on one of the two medium layers at a time. To evaluate the ability of the technique to detect and separate oscillations occurring at different depths, two approaches were applied: first, a time gating[3] (*gating*) of the DTOF was performed using 10 gates of variable width (500, 250, 100 ps). Then, the Mean Partial Pathlength Method (*MPPM*) introduced by *Zucchelli et al.*[4] was used to retrieve the concentrations of O_2Hb and HHb in the two layers of the medium. The PSD of the number of photons counts in each gate (N_g) and of the hemoglobin concentrations were calculated as before. Additional simulations were performed imposing simultaneous perturbations of the same amplitude but with a different frequency: 0.2 Hz in the superficial layer and 1 Hz in the deep one. A random phase shift between the two oscillations was applied.

3. RESULTS

3.1. Slab model

In all the simulations, the PSD presents a significant Fourier component at 1 Hz. The effect of the variation of the three parameters can be summarized as follows: 1) by increasing T_{meas}, the amplitude of the 1 Hz peak increases proportionally, while the noise level remains unchanged; 2) by increasing N_{tot}, the amplitude of the 1 Hz peak increases as N_{tot}^2, while the average noise increases as N_{tot}; 3) by increasing f_s, the amplitude of the 1 Hz peak remains unchanged, while the average noise decreases proportionally. The spectral peak contrast, defined as the difference between the peak value and the average noise level in the PSD, can be therefore increased by increasing all three parameters.

3.2. Bilayer model

Since the previous results for the T_{meas} and f_s parameters are related to the properties of the Fast Fourier Transform, they will apply regardless of the analysed signal, hence the bilayer geometry simulations were performed using the values which gave the best results in terms of contrast: T_{meas} = 15 min and f_s = 20 Hz.

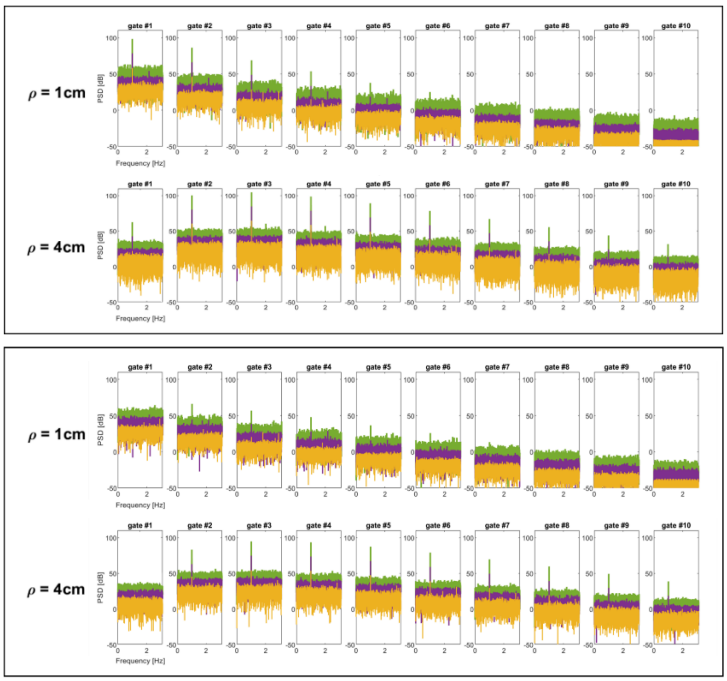

Figure 1. PSD of N_g when the perturbation is imposed on the superficial (top panel) or deep (bottom panel) layer only. Results are shown for all values of ρ (1 cm and 4 cm) and N_{tot} (10^4 in yellow, 10^5 in purple and 10^6 in green), and for λ = 690 nm.

Gating. Figure 1 represents the retrieved PSDs for N_g in the case of a time gating of the DTOF curves using 10 windows of 500 ps, covering the 0-5 ns time range after the medium excitation. In particular, in the top and bottom panels are reported the results obtained when imposing the perturbation in the superficial and deep layer, respectively. The most important difference between the two cases concerns the first time window, which is sensitive only to oscillations occurring

in the superficial layer. As also confirmed using time windows of lower width, for both source-detector distances, photons detected within the first 500 ps are only sensitive to the hemoglobin behavior in the superficial layer. Another important observation is that the 1 Hz peak was visible also in time windows in which the average value of N_g was very low, in some cases even lower than 1. This suggests that studying the medium hemodynamics by observing the properties of the raw signal could increase the technique sensitivity.

MPPM. When the PSDs of the hemoglobin concentrations are calculated using the MPPM, the effect of the variation of N_{tot} is different from the one seen above: by increasing N_{tot}, the noise level decreases, while the 1 Hz peak amplitude remains unchanged, since it only depends on the imposed perturbation amplitude. To increase the spectral peak contrast, it will be therefore necessary to maximize N_{tot}. In real acquisitions, N_{tot} and f_s are inversely related since a doubling of f_s implies halving the maximum reachable N_{tot}. However, by comparing the effect of N_{tot} and f_s on the PSD, results show that the contrast improvement obtained by doubling f_s is much higher with respect to the one obtained by doubling N_{tot}. Comparing results obtained for the two source-detector distances, important differences were found. At 1 cm, the small ratio between late and early photons generates a signal relative to the deep layer with a very high variance. The obtained PSDs in this case have a too low SNR, and the periodicity in this layer is never detected, even for the maximum value of N_{tot}. At 4 cm, instead, the increase in the relative number of late photons reduces the signal variability, generating a PSD in which the 1 Hz peak is visible for all N_{tot} values. The signal relative to the upper layer is always correctly reconstructed for both source-detector distances. When simultaneous perturbations are imposed on the two layers of the medium, the hemoglobin behavior of the two layers is always correctly reconstructed at 4 cm, while, as seen before, the poor SNR at 1 cm allows detecting oscillations occurring in the superficial layer only. No cross-talk between the two layers was observed.

4. CONCLUSIONS

In this work, numerical simulations were used to evaluate the feasibility of using TD fNIRS to monitor cerebral hemodynamic oscillations. The presented results demonstrated that the proposed technique has the potential to be used in this field, since it allows the detection and depth-localization of periodical fluctuation occurring in the concentrations of O_2Hb and HHb within the probed medium, at least when the system geometry is correctly modeled. The two methods proposed to study the phenomenon revealed different and interesting features. The use of the *gating* approach demonstrated great ability in detecting the presence of oscillatory components in the signal even in presence of very low count rates, together with the ability to isolate the behavior of the more superficial layer of the medium. Therefore, the implementation of a method that make use of the first 500 ps of the DTOF to correct the information encoded in the late photons could allow obtaining a depth-selective description of the Fourier domain of the probed tissue hemodynamics even with very low photon count rates. The *MPPM* used to retrieve the O_2Hb and HHb concentrations was able to correctly reconstruct the signals coming from the two layers, with good sensitivity and no cross-talk.

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