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Optimal Spectral Combination of a Hyperspectral Camera for Intraoperative Hemodynamic and Metabolic Brain Mapping

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Received: 24 June 2020; Accepted: 21 July 2020 ; Published: 27 July 2020

Abstract: Intraoperative optical imaging is a localization technique for the functional areas of the human brain cortex during neurosurgical procedures. These areas are assessed by monitoring the oxygenated (HbO₂) and deoxygenated hemoglobin (Hb) concentration changes occurring in the brain. Sometimes, the functional status of the brain is assessed using metabolic biomarkers: the oxidative state of cytochrome-c-oxidase (oxCCO). A setup composed of a white light source and a hyperspectral or a standard RGB camera could be used to identify the functional areas. The choice of the best spectral configuration is still based on an empirical approach. We propose in this study a method to define the optimal spectral combinations of a commercial hyperspectral camera for the computation of hemodynamic and metabolic brain maps. The method is based on a Monte Carlo framework that simulates the acquisition of the intrinsic optical signal following a neuronal activation. The results indicate that the optimal spectral combination of a hyperspectral camera aims to accurately quantify the HbO₂ (0.5% error), Hb (4.4% error), and oxCCO (15% error) responses in the brain following neuronal activation. We also show that RGB imaging is a low cost and accurate solution to compute Hb maps (4% error), but not accurate to compute HbO₂ (48% error) or oxCCO (1036% error) maps.

Keywords: hemodynamic brain mapping; metabolic brain mapping; Monte Carlo simulations; intraoperative imaging; optical imaging; hyperspectral imaging; RGB imaging

1. Introduction

Non-invasive functional brain mapping is an imaging technique used to localize the functional areas of the patient brain. This technique is used during brain tumor resection surgery to indicate to the neurosurgeon the cortical tissues that should not be removed without cognitive impairment. Functional magnetic resonance imaging (fMRI) [1] is the preoperative gold standard for the identification of the patient brain functional areas. However, after patient craniotomy, a brain shift invalidates the relevance of neuro-navigation to intraoperatively localize the functional areas of the patient brain [2]. In order to prevent any localization error, intraoperative MRI has been suggested, but it complicates the surgery gesture, which makes it rarely used. For these reasons, electrical brain stimulation [3] is preferred during neurosurgery. However, this technique suffers from limitations because the measurements could trigger epilepsy seizures. Since optical imaging combined with a quantitative modeling of brain hemodynamic biomarkers could evaluate in real time the functional areas during neurosurgery [4–6], this technique could serve as a tool of choice to complement the electrical brain stimulation.

Hyperspectral imaging allows the in vivo monitoring of the hemodynamic and metabolic status of an exposed cortex. Hyperspectral imaging provides spatially and spectrally resolved images using numerous and contiguous spectral bands [7]. In comparison, a standard color camera (or RGB camera) acquires three colors (red, green, and blue) using broad and overlapping spectral detectors. Both techniques have the ability to measure the oxygenation changes in the tissue using the modified Beer–Lambert law [5,8–12]. In functional brain mapping studies, the concentration changes of oxy- (ΔC_{HbO_2}) and deoxy-hemoglobin (ΔC_{Hb}) can be analyzed to identify the activated cortical areas [5,13–21]. The acquisition of the intrinsic signal in the near-infrared range offers the potential to monitor the brain metabolism with the quantification of the concentration changes of the oxidative state of cytochrome-c-oxidase (ΔC_{oxCCO}) [22–25]. Hyperspectral and color cameras combined with a white light illumination are simple and powerful tools for the computation of intraoperative functional brain maps. The objective is to guide the neurosurgeon during brain surgery to prevent any functional impairments after surgical procedures (tumor resection).

In the literature, all wavelength bands acquired by hyperspectral imaging setups are used to measure the hemodynamic and metabolic changes in the brain [10,24–26]. However, there are some studies in which the choice of the selected spectral bands is discussed. Bale et al. [23] showed that tens to hundreds of spectral bands acquired with a broadband near-infrared spectroscopy setup (780 nm to 900 nm) can be used to measure the oxCCO concentration changes. Arifler et al. [27] showed that eight wavelength combinations between 780 nm and 900 nm give rise to the least possible estimation errors for the deconvolution of ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} when compared to a gold standard (121 wavelengths included between 780 nm and 900 nm). Giannoni et al. [28] proposed a Monte Carlo framework to investigate the performances of broadband spectroscopy to quantify the brain hemodynamic and metabolic responses. The results of this study indicated that eight wavelength between 780 nm and 900 nm should be selected to provide minimal differences in quantification compared to a gold standard of 121 wavelengths (780 nm to 900 nm). Sudakou et al. [29] proposed a method based on the error propagation analysis and Monte Carlo simulations (three layer model: scalp, skull, and brain) allowing the estimation of the cytochrome-c-oxidase uncertainty in data measured with a multispectral time-resolved near-infrared spectroscopy device. The results of this study indicated that 16 wavelengths between 688 and 875 nm could be used to minimize the standard deviation of the cytochrome-c-oxidase concentration changes in the brain layer. Wavelength optimization problems have also been studied for other optical imaging techniques such as near-infrared optical tomography. Chen et al. [30] identified seven laser diodes among 38 commercially available diodes in the range of 633–980 nm to estimate four chromophores (HbO_2 , Hb , water, and lipids) and the scattering prefactor in breast tissue. Chen et al. used the condition number and the residual norm to identify the optimal matrix used for the resolution of a linear system and thus to estimate four chromophores and the scattering prefactor in breast tissue. The optimal wavelengths were identified for a large residual norm and small condition number. The residual norm and the condition number can be interpreted as parameters representing the uniqueness and stability of the solution, respectively.

The commercial hyperspectral cameras have limited choices in the available spectral bands and do not have a spectral resolution as high as the broadband spectroscopy devices used by Bale et al. and Arifler et al. Therefore, the optimal spectral bands identified in these studies may not be available with the commercial cameras. Moreover, the more spectral bands are used, the more time is needed to compute functional brain maps. Since time is the key factor in intraoperative imaging, the smallest number of spectral bands must be acquired while ensuring minimal quantification errors.

First, we propose in this study a method to define the optimal spectral combinations of a commercial hyperspectral camera for intraoperative hemodynamic and metabolic brain mapping. This method could be used with any hyperspectral or standard RGB camera to evaluate its ability to compute accurate hemodynamic (ΔC_{HbO_2} and ΔC_{Hb}) and/or metabolic (ΔC_{oxCCO}) brain maps following neuronal activation. The method is based on the Monte Carlo simulations of the acquisition

of the intrinsic signal acquired by a camera. All spectral combinations of the hyperspectral camera are tested to evaluate the optimal spectral configuration that minimize the quantification errors in ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} . In this work, we also show that a spectral correction [10] of the reflection spectra acquired by a mosaic hyperspectral sensor is mandatory to minimize the chromophores' quantification errors. Finally, we compare standard RGB imaging and hyperspectral imaging for hemodynamic and metabolic brain mapping. We demonstrate that RGB imaging is a low cost, but not an accurate solution to identify the functional areas in a patient brain based on the analysis of the cortical hemodynamics. Hyperspectral imaging is the ideal solution for an accurate computation of hemodynamic and metabolic brain maps.

2. Materials and Methods

We simulated the acquisition of the intrinsic reflection spectra of a patient exposed cortex using hyperspectral imaging to determine the optimal spectral configuration for the computation of hemodynamic and/or metabolic brain maps. We also simulated the acquisition of the intrinsic reflection spectra based on standard RGB imaging to evaluate the potential benefit of using hyperspectral imaging.

2.1. Simulated Setup

In this study, the imaging system represented in Figure 1 was simulated. This setup was used in our previous study [5] for the identification of functional areas based on RGB imaging. A continuous wave white light source illuminated the patient exposed cortex. The light source was a halogen bulb (OSRAM Classic 116W 230V) whose spectra was measured with a USB 2000 spectrometer [31]. The intrinsic reflection spectra were acquired by a hyperspectral camera (XIMEA MQ022HG-IM-SM5X5-NIR) and standard RGB camera (BASLER acA2000-165uc). Both RGB and hyperspectral cameras acquire spectrally and spatially resolved images, but these two systems differ in their spectral resolution. The RGB camera acquires three broad and overlapping spectra over 300 nm to 700 nm using a Bayer filter [32] mounted on a CMOS sensor. The hyperspectral camera acquires 25 narrow and contiguous spectral bands in the red in the near-infrared range. A 5×5 mosaic filter (25 Fabry–Perot filters) mounted on a CMOS sensor was used for the acquisition of the 25 spectral bands. Each Fabry–Perot filter has two transmission peaks. The first or the second peak can be selected by mounting an interference filter on the camera lens. In our study, a long pass filter mounted on the hyperspectral camera lens selected the wavelength included between 675 nm and 975 nm.

Figure 1. Schematic of the simulated imaging system.

The intensity R measured by the spectral channel k of the camera ($k \in [1;3]$ for RGB imaging and $k \in [1;25]$ for hyperspectral imaging) is expressed by the following equation:

$$R_k = \int_{\lambda_{min}}^{\lambda_{max}} D_k(\lambda) \cdot \Phi(\lambda) \cdot d\lambda. \quad (1)$$

The integral runs from $\lambda_{min} = 400$ nm to $\lambda_{max} = 700$ nm for RGB imaging and from $\lambda_{min} = 675$ nm to $\lambda_{max} = 975$ nm for hyperspectral imaging. These wavelengths delimit the ranges of the spectral sensitivity profiles provided by the camera manufacturers. D_k is the spectral sensitivity of spectral channel k of the camera, provided by the camera manufacturer. Φ is the diffuse reflection spectra of the illuminated tissue.

2.2. Hyperspectral Correction

In hyperspectral imaging based on mosaic filters, the use of the interference filter does not completely eliminate the crosstalk between the camera spectral sensitivities. To approach the ideal spectral sensitivity D^{ideal} (provided by the camera manufacturer), Pichette et al. [10] proposed to compute a linear combination of the spectral sensitivities:

$$D_m^{Corr}(\lambda) = \sum_{k=1}^{25} X_{m,k} \cdot D_k(\lambda) \quad (2)$$

with D_m^{Corr} the corrected spectral sensibility of the spectral channel m ($m \in [1;25]$) and X the 25×25 correction matrix. This correction matrix X was computed with a linear least squares fitting:

$$\min_X \|D^{ideal} - X \cdot D\|_2^2, \quad (3)$$

The normalized spectral sensitivities ($\int D(\lambda) \cdot d\lambda = 1$) are represented in Figure 2.

Figure 2. Spectral sensitivities of the hyperspectral camera XIMEA MQ022HG-IM-SM5X5-NIR. The uncorrected spectral sensitivities are plotted in solid lines on the left side of the figure and the corrected ones on the right side. The ideal spectral sensitivities are plotted in green dashed lines.

As the normalized spectral sensitivity ($\int D(\lambda) \cdot d\lambda = 1$) represents a probability density function, the Kullback–Leibler divergence can be used to quantify the performance of the spectral correction [33]:

$$KL_k(D_k \| D_k^{ideal}) = \int_{\lambda_{min}}^{\lambda_{max}} D_k(\lambda) \cdot \log \left(\frac{D_k(\lambda)}{D_k^{ideal}(\lambda)} \right) d\lambda. \quad (4)$$

$KL_k(D_k \| D_k^{ideal})$ represents the Kullback–Leibler divergence (KL divergence) computed between the spectral sensitivity of the channel k (corrected or uncorrected) and the ideal spectral sensitivity of the channel k . The KL divergence represents a measure of dissimilarity between D_k and D_k^{ideal} . A value equal to 0 indicates the equality of the two probability density functions. The KL divergence values computed for the corrected and uncorrected spectral sensitivities are represented in Figure 3.

Figure 3. Measure of dissimilarities between the corrected (in orange) or uncorrected (in blue) spectral sensitivities and the ideal spectral sensitivities.

The KL divergence computed between the uncorrected spectral sensitivities and the ideal spectral sensitivities is on average four times higher than those computed between the corrected spectral sensitivities and the ideal spectral sensitivities.

2.3. Sensor Signal-to-Noise Ratio

The signal-to-noise ratios (SNR) of the spectral channel k of the RGB and hyperspectral cameras were measured by acquiring the white light reflected at the surface of a calibration target (plain white sheet of paper) during two minutes with an integration time set to 33 ms:

$$SNR(k) = \frac{\mu_k}{\sigma_k}. \quad (5)$$

μ_k denotes the spectral channel k mean value obtained by computing the mean value of the temporal intensity averaged over the sensor area. σ_k is the spectral channel k standard deviation value obtained by computing the standard deviation value of the temporal intensity averaged over the sensor area. The illumination source power, quantum efficiency and integration time of the cameras directly impact the SNR values. The SNR values of the RGB and hyperspectral cameras we used in this study are represented in Figure 4. The SNR of the red channel of the RGB camera is 1.1 times greater than the one of the green channel and 1.4 times greater than the one of the blue channel. The mean value of the SNR of the hyperspectral is 3.9 times lower than the SNR value of the red channel of the RGB camera. Note that these values are dependent on our experimental configuration and directly impact the amount of noise and the quantification error in the simulated concentration changes.

Figure 4. SNR values of each spectral channel of the RGB and hyperspectral cameras.

2.4. Simulation of the Patient Cortical Activation

Following the patient physiological activity, a hemodynamic change occurs in the activated cortical areas with an increase of the oxygenated hemoglobin concentration (C_{HbO_2}) and a decrease of the deoxygenated hemoglobin concentration changes (C_{Hb}). These hemodynamic changes are not the only ones that occur during a patient physiological activity. The concentration of the oxidative state of cytochrome-c-oxidase (C_{oxCCO}) also varies [22]. Cytochrome-c-oxidase (CCO) is an enzyme in the mitochondria that is involved in the aerobic metabolism of glucose. The total concentration of CCO does not change over a short time period (in the order of hours). However, it is possible to assess the differences between the oxidized and reduced states of CCO to obtain an indicator of the change in the CCO redox state.

The patient cortical activation was simulated by Monte Carlo simulations [34]. A volume of $60 \text{ mm} \times 60 \text{ mm} \times 60 \text{ mm}$ of grey matter was modeled under a homogeneous white light illumination. Each voxel of the modeled tissue included the information of optical parameters (absorption μ_a , scattering μ_s , anisotropy g coefficients, and refractive index n). A white light illumination was simulated by scanning the optical parameters along the entire illumination spectrum (from 400 nm to 1000 nm in steps of 1 nm). The size of the modeled tissues was chosen in accordance with the photon sensitivity profile [5,35] computed for the detector situated at the center of the top face of the volumes. To avoid any photon loss and inexact results due to the boundary conditions (the simulation of the travel of a packet of photon stops when this packet of photon leaves the volume), the size of the models was set to $60 \times 60 \times 60$ voxels with a resolution of 1 mm^3 . The 10^8 packets of photons were homogeneously illuminating the modeled surface. The optical mean path length and the diffuse reflection spectra were measured at the detector position with an integration time set to 33 ms, and the diffuse reflection spectra was normalized to a unitary source.

The optical parameters were taken from the literature and correspond to a nominal physiological condition [36–41]. The anisotropy, reduced scattering coefficients, and the refractive index used in the Monte Carlo simulations are summarized in Table 1. The scattering coefficient μ_s was calculated from the reduced scattering coefficient (μ'_s) and the anisotropy coefficient (g): $\mu_s = \mu'_s / (1 - g)$. In Table 1, λ denotes the wavelength dependence of the reduced scattering coefficient (in nm).

Table 1. Anisotropy, reduced scattering coefficients, and refractive index used in the Monte Carlo simulations.

Anisotropy Coefficient g	Reduced Scattering Coefficient $\mu'_s \text{ (cm}^{-1}\text{)}$	Refractive Index n
0.85 [42]	$40.8 \cdot \frac{\lambda}{500}^{-3.089}$ [39]	1.36 [38]

The absorption coefficients were calculated using the chemical composition of the chromophores of the simulated tissues, which are summarized in Table 2.

Table 2. Chemical composition of the chromophores of the simulated volumes of grey matter.

	Non-Activated Grey Matter	Activated Grey Matter
Water	73%	73%
C_{Hb} ($\mu\text{mol}\cdot\text{L}^{-1}$)	22.1	18.35
C_{HbO_2} ($\mu\text{mol}\cdot\text{L}^{-1}$)	65.1	70.1
C_{oxCCO} ($\mu\text{mol}\cdot\text{L}^{-1}$)	5.3	5.8

The chemical differences between the activated and non-activated grey matter are represented by a $5 \mu\text{mol}\cdot\text{L}^{-1}$ increase of C_{HbO_2} , a $3.75 \mu\text{mol}\cdot\text{L}^{-1}$ decrease of C_{Hb} , and a $0.5 \mu\text{mol}\cdot\text{L}^{-1}$ increase of C_{oxCCO} . These concentration changes are consistent with those defined in the literature. The reflection spectra and the optical mean path length were measured at the center of the top face of the volume.

2.5. Modified Beer–Lambert Law

The modified Beer–Lambert law is used to convert the acquired intrinsic reflection spectra into concentration changes. Optical functional brain maps are computed by assessing the oxy- and deoxy-generated hemoglobin concentration changes (ΔC_{HbO_2} and ΔC_{Hb}) [9,10,43]. Using the near-infrared range, the oxidative state of cytochrome-c-oxidase concentration changes (ΔC_{oxCCO}) can also be quantified [23]. The modified Beer–Lambert law can be expressed as a linear system [9]:

$$\begin{bmatrix} \Delta A_1 \\ \vdots \\ \Delta A_N \end{bmatrix} = \begin{bmatrix} E_{1,HbO_2} & E_{1,Hb} & E_{1,oxCCO} \\ \vdots & \vdots & \vdots \\ E_{N,HbO_2} & E_{N,Hb} & E_{N,oxCCO} \end{bmatrix} \times \begin{bmatrix} \Delta C_{HbO_2} \\ \Delta C_{Hb} \\ \Delta C_{oxCCO} \end{bmatrix} \quad (6)$$

with

$$E_{k,n} = \int \epsilon_n(\lambda) \cdot D_k(\lambda) \cdot S(\lambda) \cdot L(\lambda) \cdot d\lambda. \quad (7)$$

ΔA_k is the absorbance changes measured by the spectral channel k of the camera ($k \in [1; N]$ with $N \in [3; 25]$ for hyperspectral imaging and $k \in [1; 3]$ for RGB imaging):

$$\Delta A_k = \log_{10} \left(\frac{R_k^{GM_1}}{R_k^{GM_2}} \right). \quad (8)$$

$R_k^{GM_1}$ is the intensity of the non-activated grey matter (see Section 2.4) acquired by the spectral channel k of the camera. $R_k^{GM_2}$ is the intensity of the activated grey matter (see Section 2.4) acquired by the spectral channel k of the camera. The intensities were calculated with Equation (1) using the reflection spectra simulated by Monte Carlo simulations. ΔC_{Hb} is the deoxygenated hemoglobin molar concentration changes (in $\text{mol}\cdot\text{L}^{-1}$). ΔC_{HbO_2} is the oxygenated hemoglobin molar concentration changes (in $\text{mol}\cdot\text{L}^{-1}$) and ΔC_{oxCCO} the oxidative state of cytochrome-c-oxidase concentration changes (in $\text{mol}\cdot\text{L}^{-1}$). ϵ_n is the extinction coefficient of the chromophore n (in $\text{L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$). The spectral sensitivity of the channel k is represented by $D_k(\lambda)$, and $S(\lambda)$ is the normalized intensity spectrum of the light source. $L(\lambda)$ is the wavelength dependent mean optical path length of the photons traveling in tissue estimated by Monte Carlo simulations (in cm); see Section 2.4. The concentration changes were obtained by matrix inversion once the matrix E was calculated.

2.6. Determination of the Optimal Spectral Configuration of the Hyperspectral Camera

The quantification of ΔC_{Hb} , ΔC_{HbO_2} , and ΔC_{oxCCO} can be achieved using at least three wavelengths [44]. With our hyperspectral camera, twenty-five spectral bands were acquired.

Therefore, we can then ask ourselves what is the optimal spectral configuration for the assessment of ΔC_{Hb} , ΔC_{HbO_2} , and ΔC_{oxCCO} ? If N spectral bands were used ($N \in [3;25]$), P combinations may be investigated:

$$\forall N \in [3;25] \quad P = \frac{25!}{(25-N)! \times N!} \quad (9)$$

2.6.1. Noise in Simulations

In order to evaluate the robustness of the chromophores' quantification, zero mean Gaussian noises were added to the simulated quantities. The Monte Carlo noises (noise on diffuse reflection spectra ϕ and mean path length L) were estimated for each simulated wavelength by launching the MCX software 10^3 times using random seeds. The seed is a number used to generate a random number with a pseudorandom number generator. For each wavelength, the standard deviations of the Monte Carlo noises were measured on these 10^3 simulations. The Monte Carlo noise depends on the number of packets of photons used in the simulation. In addition, the noise of the hyperspectral and RGB cameras that were experimentally measured (see Section 2.3) were added to the simulated intensities.

2.6.2. Simulation Based Method

For all the possible P combinations for a group of N spectral bands (see Equation (9)), the quantification errors in ΔC_{Hb} , ΔC_{HbO_2} , or ΔC_{oxCCO} were computed:

$$E_{\Delta C_n}(N, p) = \left| \frac{\Delta C_n^{Expected} - \Delta C_n^{Estimated}(N, p)}{\Delta C_n^{Expected}} \right| \times 100. \quad (10)$$

Note that this quantification error is represented in absolute values. $\Delta C_n^{Expected}$ is the concentration changes of the chromophore n that were expected to be measured in the tissue; see Section 2.4. $\Delta C_n^{Estimated}(N, p)$ is the concentration changes of the chromophore n estimated from the simulated data using the combination p ($p \in [1; P]$) for a group of N spectral bands; see Equation (9). The computation of $\Delta C_n^{Estimated}(N, p)$ and $E_{\Delta C_n}(N, p)$ was repeated 10^3 times to get their mean and the standard deviation values. Different noises were added to the simulated reflection spectra ϕ , mean path length L , and camera intensities R for each iteration. For each group of N spectral bands, the optimal spectral combination among the P possibilities was determined using Equation (11):

$$\min_p \left(\sqrt{m(E_{\Delta C_n}(N, p))^2 + \sigma(E_{\Delta C_n}(N, p))^2} \right). \quad (11)$$

m and σ designate the mean and standard deviation functions, respectively. This metric was chosen to identify the spectral combination of N spectral bands that minimize the average quantification errors while ensuring the reproduction of measurements. Equation (11) leads to the determination of the combination p_n^N , which is the best combination of N spectral bands for the deconvolution of the chromophore n . Finally, the optimal spectral configurations of the hyperspectral camera for the quantification of ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} were obtained using Equation (12):

$$\min_{p_n^N} \left(\sqrt{m(E_{\Delta C_n}(N, p_n^N))^2 + \sigma(E_{\Delta C_n}(N, p_n^N))^2} \right). \quad (12)$$

Note that the spectral configurations determined by Equation (12) are not necessarily the same for the deconvolution of ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} . In other words, this means that three distinct configurations may be used.

2.7. Application to a Functional Brain Mapping Study

In functional brain mapping studies, the measured hemodynamic concentration changes' time courses are compared to the patient theoretical hemodynamic responses. These theoretical responses are obtained by convolving the hemodynamic impulse response function to the window function representing the patient physiological stimulus. The functional areas may be identified by testing the Pearson correlation coefficients (computed between the concentration changes' time courses and the theoretical hemodynamic responses) and the concentration changes averaged over the patient activity period with several *T*-tests [5,25]. Another technique derived by BOLD fMRI (blood oxygenation level dependent, functional magnetic resonance imaging) is the NIRS SPM (near-infrared spectroscopy statistical parametric mapping) analyses [13,14] that use a general linear model and random field theory to identify the functional areas in a pixel-wise manner.

We built a simulation of the grey matter hemodynamic and metabolic responses following a patient physiological stimulus based on the Monte Carlo framework described in Section 2.4. The intrinsic signal was acquired during 60 s at 0.5 frames per second with the integration time set to 33 ms. The following paradigm was simulated: 18 s of rest, 20 s of neuronal stimulation, followed by 22 s of rest. We incorporated the temporal hemodynamic response, as well as the temporal oxCCO response following neuronal activation. The hemodynamic responses were obtained by convolving the hemodynamic impulse response function to the window function representing the patient physiological stimulus. The oxCCO response function was introduced by Wobst et al. [45] to describe the metabolic response in the primary and adjacent visual cortex for a stimulus of 6 to 24 s. The theoretical time courses can be roughly represented by the function $h(t) = a \cdot t^2 \cdot e^{-t}$ convolved with the window function representing the patient physiological stimulus. In this function, t represents the time (in s) and a is the characteristic amplitude of ΔC_{oxCCO} . The theoretical temporal variation of the ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} values are represented in Figure 5. Note that these values varied homogeneously in the modeled tissue. During these absorption perturbations, the other optical coefficients were kept constant.

Figure 5. Theoretical ΔC_{HbO_2} (in red), ΔC_{Hb} (in blue), and ΔC_{oxCCO} (in green) responses following the patient physiological activity. ΔC_{HbO_2} and ΔC_{Hb} are expressed by the left vertical axis. ΔC_{oxCCO} is expressed by the right vertical axis. The blue rectangle represent the “patient” physiological stimulus.

With these simulations, we can evaluate the potential benefit from using hyperspectral imaging for the computation of hemodynamic brain maps instead of using a standard RGB camera (see our previous studies [5,11,12]). This approach aims to simulate the quantitative values that are computed in clinical functional brain mapping applications. This makes it possible to test the influence of the optimal spectral band configuration on the quantities measured in clinical applications. For this purpose, the Pearson correlation coefficient is computed. The correlation coefficient was calculated between the

theoretical hemodynamic time courses (see Figure 5) and the hemodynamic time courses simulated with the optimal spectral configuration of the hyperspectral camera (see Section 2.6). The correlation coefficient was also computed with the data simulated with RGB imaging. We can also investigate the ability of hyperspectral imaging to monitor the brain metabolism. For this purpose, the Pearson correlation coefficient values were computed between the theoretical oxCCO time course (see Figure 5) and the ΔC_{oxCCO} time courses simulated with the optimal spectral configuration of the hyperspectral camera (see Section 2.6).

We also compared our results with the measurements computed with the gold standard of 121 wavelengths included between 780 nm and 900 nm [23] and with the 8 wavelengths identified by Arifler et al. [27]. For this purpose, we simulated the hemodynamic and/or metabolic monitoring using two or three chromophore systems that used these wavelengths. Note that we did not incorporate noises in these simulations of references.

3. Results

3.1. Determination of the Optimal Spectral Configuration of the Hyperspectral Camera

In Figure 6, the quantification errors in ΔC_{HbO_2} , ΔC_{Hb} and ΔC_{oxCCO} (see Equation (10)) obtained for the best simulation-based deconvolution systems of N spectral bands ($N \in [3; 25]$) are represented. The solid lines stand for the mean quantification error. The colored areas represent the dispersion range of the quantification errors. The vertical dashed lines indicate the optimal number of spectral bands for the deconvolution of each chromophore. Both corrected (in green) and uncorrected spectral configuration (in red) are represented. Note that these data were obtained using noisy measurements; zeros mean Gaussian noises were added to the camera intensities and to the Monte Carlo quantities (mean path length and reflection spectra); see Section 2.6.1.

Figure 6. Quantification errors (see Equation (10)) in ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} obtained for the best simulation-based deconvolution systems of N spectral bands ($N \in [3; 25]$). The solid lines stand for the mean quantification error. The colored areas represent the dispersion range of the quantification errors. The vertical dashed lines indicate the optimal number of spectral bands for the deconvolution of each chromophore. Both corrected (in green) and uncorrected spectral configuration (in red) are represented.

For the three chromophores, the quantification errors are important when a small number of spectral bands are used, but the quantification errors decrease with a larger number of bands. The quantification errors in ΔC_{HbO_2} are on average 30% lower when the spectral correction is applied than when it is not applied. The quantification errors in ΔC_{Hb} are on average 20% lower when the spectral correction is applied than when it is not applied. The quantification errors in ΔC_{oxCCO} are

equivalent with and without spectral correction. We can notice that the quantification errors reach a plateau when 15 corrected and uncorrected spectral bands are used. These spectral bands are indicated by violet points in Figure 7 and will be named optimal reduced spectral bands in the rest of the paper.

Figure 7. Optimal spectral configuration of the hyperspectral camera XIMEA MQ022HG-IM-SM5X5-NIR obtained with the simulation-based method. The peaks of the selected spectral bands are represented as vertical lines in the molar extinction coefficients of the deconvolved chromophores. The reduced optimal spectral bands are indicated by violet points in the molar extinction coefficients of the deconvolved chromophores.

For each chromophore, different optimal spectral combinations are found. For the quantification of ΔC_{HbO_2} , the best spectral configuration of our hyperspectral camera is composed of 25 spectral bands if the spectral correction is applied and of 16 spectral bands if the spectral correction is not applied. These spectral bands are indicated by black vertical lines in the HbO_2 molar extinction spectra in Figure 7. For these configurations, the quantification error (with Monte Carlo and intensity noise addition) is equal to $28.7\% \pm 21.4\%$ (mean $\pm$ standard deviation of the 10^3 measurements) when the spectral correction is applied and is equal to $38.5\% \pm 26.9\%$ when the spectral correction is not applied.

For the quantification of ΔC_{Hb} , the best spectral configuration of our hyperspectral camera is composed of 24 spectral bands if the spectral correction is applied and of 21 spectral bands if the spectral correction is not applied. These spectral bands are indicated by black vertical lines in the Hb molar extinction spectra in Figure 7. For these configurations, the quantification error (with Monte Carlo and intensity noise addition) is equal to $39\% \pm 29.7\%$ (mean $\pm$ standard deviation of the 10^3 measurements) when the spectral correction is applied and is equal to $49.7\% \pm 36.6\%$ when the spectral correction is not applied.

For the quantification of ΔC_{oxCCO} , the best spectral configuration of our hyperspectral camera is composed of 21 spectral bands if the spectral correction is applied and of 25 spectral bands if the spectral correction is not applied. These spectral bands are indicated by black vertical lines in the $oxCCO$ molar extinction spectra in Figure 7. For these configurations, the quantification error (with Monte Carlo and intensity noise addition) is equal to $251.1\% \pm 195.4\%$ (mean $\pm$ standard deviation of the 10^3 measurements) when the spectral correction is applied and is equal to $237.6\% \pm 183.1\%$ when the spectral correction is not applied.

Quantification Performances of Deconvolution Systems

When using the optimal or the reduced optimal spectral configurations of the hyperspectral camera (see Figure 7), three linear systems have to be defined to independently quantify ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} . In the rest of the paper, these systems will be named multiple deconvolution

systems. When inspecting the spectral band used in the optimal reduced multiple systems, twenty-one different spectral bands are used with and without spectral correction. Thus, a single system can be designed using these spectral bands to quantify ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} in a single measurement. In the same way, when inspecting the spectral variables used in the optimal multiple systems, all spectral bands of the hyperspectral camera are used. The accuracy of the quantification of the chromophore n can be measured using the mean and the standard deviation of the quantification error (see Equation (10)). According to ISO 5725-1 standards, the term “accuracy” stands for the trueness of the measurement (mean quantification errors close to 0%) and the repeatability of the measurement (standard deviation of quantification errors close to 0%). The mean and standard deviation values were calculated on 10^3 noisy measurements. These metrics were calculated using the multiple and single deconvolution systems of the hyperspectral camera; see Table 3.

Table 3. Quantification performances of the multiple and single deconvolution systems of the hyperspectral camera.

		Multiple Deconvolution Systems		Single Deconvolution Systems	
		Optimal	Optimal Reduced	Optimal Reduced	All Spectral Bands
Spectral correction	$m(E_{\Delta C_{HbO_2}})$	28.7	29.7	29.1	28.7
	$\sigma(E_{\Delta C_{HbO_2}})$	21.4	23.1	21.9	21.4
	$m(E_{\Delta C_{Hb}})$	39	39.7	39.4	39
	$\sigma(E_{\Delta C_{Hb}})$	29.7	31.1	29.8	29.7
	$m(E_{\Delta C_{oxCCO}})$	251.1	252.1	250.1	250.1
	$\sigma(E_{\Delta C_{oxCCO}})$	195.4	198.9	194	195.2
No spectral correction	$m(E_{\Delta C_{HbO_2}})$	38.5	38.7	40.6	40.6
	$\sigma(E_{\Delta C_{HbO_2}})$	26.9	27.8	28.1	27.3
	$m(E_{\Delta C_{Hb}})$	49.7	50.9	50.5	50.1
	$\sigma(E_{\Delta C_{Hb}})$	36.6	37.5	36.8	36.6
	$m(E_{\Delta C_{oxCCO}})$	237.6	244.3	239.1	237.6
	$\sigma(E_{\Delta C_{oxCCO}})$	183.1	186.5	183.9	183.1

For each chromophore, the lowest values of the mean and standard deviation of the quantification errors in ΔC_{HbO_2} and ΔC_{Hb} are obtained with the optimal multiple deconvolution system using corrected spectral bands. When the spectral bands are not corrected, the mean and standard deviation values of the quantification errors in ΔC_{HbO_2} and ΔC_{Hb} are higher than the values obtained with corrected spectral bands. However, we can notice that the mean and standard deviation values of the quantification errors in ΔC_{oxCCO} computed without spectral correction are lower than the values obtained with corrected spectral bands. The quantification errors computed with the optimal multiple system are similar to those obtained with the single system composed of all the spectral bands of the hyperspectral camera. The quantification errors computed with the optimal reduced multiple system are similar to those obtained with the single optimal reduced system.

3.2. Impact of the Signal-to-Noise Ratio in the Measurements

As mentioned in Section 2.3, the SNR values of the imaging system directly impact the amount of noise and the accuracy of the simulated quantities. To illustrate the effect of SNR on the measurements, the mean and standard deviation of the quantification errors in ΔC_{HbO_2} , ΔC_{Hb} and ΔC_{oxCCO} (see Equation (10)) obtained for the optimal spectral configuration of the hyperspectral camera (see Figure 7) and the RGB camera are represented as a function of SNR; see Figures 8 and 9. For each chromophore system, the mean and standard deviation values of the quantification errors are high for low SNR values and decrease with increasing SNR values.

Figure 8. Mean quantification errors in ΔC_{HbO_2} (b), ΔC_{Hb} (blue curves), and ΔC_{oxCCO} (green curves) (see Equation (10)) obtained for the optimal spectral configuration of the hyperspectral camera (see Figure 7) and the RGB camera as a function of SNR. The solid lines were computed using the RGB camera; the curves with circles and with triangles were computed using the hyperspectral camera with and without spectral correction, respectively. Red, green, and blue vertical lines indicate the SNR values of the R, G, and B channels of the RGB camera and black vertical lines the SNR values of the spectral channels of the hyperspectral camera.

Figure 9. Standard deviation of the quantification errors in ΔC_{HbO_2} (red curves), ΔC_{Hb} (blue curves), and ΔC_{oxCCO} (green curves) (see Equation (10)) obtained for the optimal spectral configuration of the hyperspectral camera (see Figure 7) and the RGB camera as a function of SNR. The solid lines were computed using the RGB camera; the curves with circles and with triangles were computed using the hyperspectral camera with and without spectral correction, respectively. Red, green, and blue vertical lines indicate the SNR values of the R, G, and B channels of the RGB camera and black vertical lines the SNR values of the spectral channels of the hyperspectral camera.

When a two-chromophore system is considered with the RGB camera ($SNR = 10$), the quantification errors in ΔC_{HbO_2} and ΔC_{Hb} are equal to $236\% \pm 187\%$ and $226\% \pm 179\%$, respectively. When the SNR value is equal to 1000, the quantification errors in ΔC_{HbO_2} and ΔC_{Hb} are equal to $52\% \pm 3\%$ and $6\% \pm 3\%$, respectively. For high SNR values, it is interesting to note that the

quantification of ΔC_{HbO_2} is not accurate (low $\sigma(E_{HbO_2})$ values and high $m(E_{HbO_2})$ values) and the quantification of ΔC_{Hb} is accurate. Moreover, the mean quantification errors in ΔC_{HbO_2} reach a plateau for an SNR value equal to 110. For the hyperspectral camera with an SNR value equal to 10, the quantification errors in ΔC_{HbO_2} are equal to $232\% \pm 173\%$ when the spectral correction is applied and $259\% \pm 193\%$ when it is not applied. The quantification errors in ΔC_{Hb} are equal to $235\% \pm 176\%$ when the spectral correction is applied and $267\% \pm 201\%$ when it is not applied. When the SNR value is equal to 1000, the quantification errors in ΔC_{HbO_2} are equal to $8\% \pm 6\%$ when the spectral correction is applied and $28\% \pm 6\%$ when it is not applied. The quantification errors in ΔC_{Hb} are equal to $8\% \pm 6\%$ when the spectral correction is applied and $52\% \pm 5\%$ when it is not applied. For high SNR values, the quantification of ΔC_{HbO_2} and ΔC_{Hb} is accurate when the spectral correction is applied and not accurate when the spectral correction is not applied (low $\sigma(E_n)$ values and high $m(E_n)$ values). When the spectral correction is not applied, the mean quantification errors in ΔC_{HbO_2} and ΔC_{Hb} reach a plateau for an SNR value equal to 200 and 110, respectively.

When a three-chromophore system is considered with the RGB camera (SNR = 10), the quantification errors in ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} are equal to $712\% \pm 531\%$, $822\% \pm 617\%$, and $9427\% \pm 7011\%$, respectively. When the SNR value is equal to 1000, the quantification errors in ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} are equal to $164\% \pm 10\%$, $138\% \pm 12\%$, and $1431\% \pm 138\%$, respectively. The mean quantification errors in ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} reach a plateau for an SNR value equal to 110, 130, and 130, respectively. For high SNR values, the quantification of ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} is not accurate (low $\sigma(E_n)$ values and high $m(E_n)$ values). For the hyperspectral camera with an SNR value equal to 10, the quantification errors in ΔC_{HbO_2} are equal to $345\% \pm 267\%$ when the spectral correction is applied and $328\% \pm 248\%$ when it is not applied. The quantification errors in ΔC_{Hb} are equal to $486\% \pm 379\%$ when the spectral correction is applied and $496\% \pm 382\%$ when it is not applied. The quantification errors in ΔC_{oxCCO} are equal to $2908\% \pm 2190\%$ when the spectral correction is applied and $2951\% \pm 2201\%$ when it is not applied. When the SNR value is equal to 1000, the quantification errors in ΔC_{HbO_2} are equal to $10\% \pm 8\%$ when the spectral correction is applied and $33\% \pm 8\%$ when it is not applied. The quantification errors in ΔC_{Hb} are equal to $14\% \pm 11\%$ when the spectral correction is applied and $41\% \pm 11\%$ when it is not applied. The quantification errors in ΔC_{oxCCO} are equal to $90\% \pm 68\%$ when the spectral correction is applied and $91\% \pm 70\%$ when it is not applied. For high SNR values, the quantification of ΔC_{HbO_2} and ΔC_{Hb} is accurate when the spectral correction is applied and not accurate (low $\sigma(E_n)$ values and high $m(E_n)$ values) when the spectral correction is not applied. The quantification of ΔC_{oxCCO} is not accurate with and without spectral correction (low $\sigma(E_{oxCCO})$ values and high $m(E_{oxCCO})$ values). We can notice that the measurement uncertainty of ΔC_{oxCCO} is similar for all SNR values with and without spectral correction. When the spectral correction is not applied, the mean quantification errors in ΔC_{HbO_2} and ΔC_{Hb} reach a plateau for an SNR value equal to 200.

3.3. Hemodynamic Monitoring

The hemodynamic monitoring (ΔC_{HbO_2} and ΔC_{Hb} measurements) following a simulated patient neuronal stimulation (see Section 2.7) is represented in Figures 10 and 11. In Figure 10, the ΔC_{HbO_2} and ΔC_{Hb} values were computed with the optimal spectral combination of the hyperspectral camera; see Figure 7. In Figure 11, the ΔC_{HbO_2} and ΔC_{Hb} values were computed with the RGB camera. In these figures, the modified Beer–Lambert law was computed 10^3 times, using different Monte Carlo and intensity noise occurrences for each time iteration. When using the 121 wavelengths included between 780 nm and 900 nm [23] to quantify the concentration changes during the stimulation period (from $t = 18$ s to $t = 38$ s), there is a 12% overestimation of the ΔC_{HbO_2} values and a 34% underestimation of the ΔC_{Hb} values compared to the theoretical measurements. When using the eight wavelengths identified by Arifler et al. [27] to quantify the concentration changes during the stimulation period, there is a 13% overestimation of the ΔC_{HbO_2} values and a 31% underestimation of the ΔC_{Hb} values compared to the theoretical measurements.

Figure 10. Hemodynamic monitoring following neuronal activation computed with the spectral configuration of the hyperspectral camera obtained with the simulation-based method (see Figure 7). The dashed lines represent the theoretical hemodynamic responses following the neuronal stimulation. The dispersion ranges of the measurements are represented by colored areas. The concentration changes averaged over the 10^3 noisy measurements are represented in solid lines. The concentration changes' time courses computed with the 121 wavelengths included between 780 nm and 900 nm [23] are represented with yellow points. The ones computed with Arifler et al.'s wavelengths [27] are represented with black triangles. The blue rectangle represents the “patient” physiological stimulus.

In Figure 10, the hemodynamic monitoring following a simulated neuronal stimulation was computed using hyperspectral imaging. The optimal corrected and uncorrected spectral configurations of the hyperspectral camera were used to quantify the ΔC_{HbO_2} and ΔC_{Hb} values. The quantification dispersion ranges of the corrected and uncorrected spectral configurations have approximately the same range of magnitude. The standard deviation averaged over all time measurements for ΔC_{HbO_2} and ΔC_{Hb} are equal to $0.9 \mu\text{mol}\cdot\text{L}^{-1}$ and $0.7 \mu\text{mol}\cdot\text{L}^{-1}$, respectively. When the spectral bands are corrected, the ΔC_{HbO_2} and ΔC_{Hb} values averaged over the 10^3 noisy measurements have a good match with the theoretical hemodynamic responses. During the stimulation period, there is on average a 14% overestimation of the ΔC_{HbO_2} values and a 18% underestimation of the ΔC_{Hb} values compared to the theoretical measurements. When the spectral bands are not corrected, there is on average a 17% underestimation of the ΔC_{HbO_2} values and a 58% underestimation of the ΔC_{Hb} values compared to the theoretical measurements. The correlation coefficients computed between the theoretical HbO_2 response and the ΔC_{HbO_2} time courses are higher when the spectral bands are corrected ($r = 0.951 \pm 0.013$) than when they are not ($r = 0.904 \pm 0.026$). In the same way, the correlation coefficients computed between the theoretical Hb response and the ΔC_{Hb} time courses are higher when the spectral bands are corrected ($r = 0.932 \pm 0.018$) than when they are not ($r = 0.783 \pm 0.059$). The correlation coefficient values are summarized in Table 4.

In Figure 11, the hemodynamic monitoring following a simulated neuronal stimulation was computed using RGB imaging. The standard deviation averaged over all time measurements is equal to $0.35 \mu\text{mol}\cdot\text{L}^{-1}$ and $0.20 \mu\text{mol}\cdot\text{L}^{-1}$ for ΔC_{HbO_2} and ΔC_{Hb} , respectively. The ΔC_{HbO_2} values averaged over the 10^3 noisy measurements do not have a good match with the theoretical HbO_2 response; however, the match is rather good between the ΔC_{Hb} values and the theoretical Hb response. During the stimulation period, there is on average a 48% underestimation of the ΔC_{HbO_2} values and a 4% underestimation of the ΔC_{Hb} values compared to the theoretical measurements. The correlation coefficients computed between the theoretical HbO_2 response and the ΔC_{HbO_2} time courses are equal to

$r = 0.949 \pm 0.013$. The correlation coefficients computed between the theoretical Hb response and the ΔC_{Hb} time courses are equal to $r = 0.989 \pm 0.002$. The correlation coefficient values are summarized in Table 4.

Figure 11. Hemodynamic monitoring following neuronal activation computed with RGB imaging. The dashed lines represent the theoretical hemodynamic responses following the neuronal stimulation. The dispersion ranges of the measurements are represented by colored areas. The concentration changes averaged over the 10^3 noisy measurements are represented in solid lines. The concentration changes' time courses computed with the 121 wavelengths included between 780 nm and 900 nm [23] are represented with yellow points. The ones computed with Arifler et al.'s wavelengths [27] are represented with black triangles. The blue rectangle represents the “patient” physiological stimulus.

Table 4. Pearson correlation coefficients computed between the theoretical hemodynamic responses and the simulated concentration changes' time courses; see Figures 10 and 11. $\mu(r_n)$ and $\sigma(r_n)$ designate the mean and standard deviation, respectively, of the Pearson correlation coefficients computed with the 10^3 noisy time courses of the chromophore n .

	RGB Imaging	Hyperspectral Imaging	
		Spectral Correction	No Spectral Correction
$\mu(r_{HbO_2})$	0.949	0.951	0.904
$\sigma(r_{HbO_2})$	0.013	0.013	0.026
$\mu(r_{Hb})$	0.989	0.932	0.783
$\sigma(r_{Hb})$	0.002	0.018	0.059

3.4. Hemodynamic and Metabolic Monitoring

The hemodynamic and metabolic monitoring (ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} measurements) following a simulated patient neuronal stimulation (see Section 2.7) are represented in Figures 12 and 13. In Figure 12, the ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} values were computed with the optimal spectral combination of the hyperspectral camera; see Figure 7. In Figure 13, the ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} values were computed with the RGB camera. In these figures, the modified Beer–Lambert law was computed 10^3 times, using different Monte Carlo and intensity noise occurrences for each time iteration. When using the 121 wavelengths included between 780 nm and 900 nm [23] to quantify the concentration changes during the stimulation period (from $t = 18$ s to $t = 38$ s), there is a 1.2% underestimation of the ΔC_{HbO_2} values, a 0.4% overestimation of the ΔC_{Hb} values, and a 1.3% overestimation of the ΔC_{oxCCO} values compared to the theoretical measurements.

When using the eight wavelengths identified by Arifler et al. [27] to quantify the concentration changes during the stimulation period, there is a 1.7% underestimation of the ΔC_{HbO_2} values, a 1.91% overestimation of the ΔC_{Hb} values, and a 6% overestimation of the ΔC_{oxCCO} values compared to the theoretical measurements.

Hemodynamic and metabolic monitoring using the best deconvolution system obtained with the simulation-based method

Figure 12. Hemodynamic and metabolic monitoring following neuronal activation computed with the optimal spectral configuration obtained with the simulation-based method (see Figure 7). The dashed lines represent the theoretical hemodynamic and metabolic responses following the neuronal stimulation. The dispersion ranges of the measurements are represented by colored areas. The concentration changes averaged over the 10^3 noisy measurements are represented in solid lines. The concentration changes' time courses computed with the 121 wavelengths included between 780 nm and 900 nm [23] are represented with yellow points. The ones computed with Arifler et al.'s wavelengths [27] are represented with black triangles. The blue rectangle represents the “patient” physiological stimulus.

In Figure 12, the hemodynamic and metabolic monitoring following a simulated neuronal stimulation was computed using hyperspectral imaging. The optimal corrected and uncorrected spectral configurations of the hyperspectral camera were used to quantify the ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} values. The quantification dispersion ranges of the corrected and uncorrected spectral configurations have approximately the same range of magnitude. The standard deviation averaged over all time measurements for ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} are equal to $1.23 \mu\text{mol}\cdot\text{L}^{-1}$, $1.27 \mu\text{mol}\cdot\text{L}^{-1}$, and $1.07 \mu\text{mol}\cdot\text{L}^{-1}$, respectively. When the spectral bands are corrected, the ΔC_{HbO_2} and ΔC_{Hb} values averaged over the 10^3 noisy measurements have a good match with the theoretical hemodynamic responses. The ΔC_{oxCCO} values averaged over the 10^3 noisy measurements have a good match with the theoretical metabolic response with and without spectral correction. When the spectral bands are corrected, there is on average a 0.5% underestimation of the ΔC_{HbO_2} values, a 4.4% overestimation of the ΔC_{Hb} values, and a 15% overestimation of the ΔC_{oxCCO} values compared to the theoretical measurements. When the spectral bands are not corrected, there is on average a 25% underestimation of the ΔC_{HbO_2} values, a 42% underestimation of the ΔC_{Hb} values, and a 19% underestimation of the ΔC_{oxCCO} values compared to the theoretical measurements. The correlation coefficients computed between the theoretical HbO_2 response and the ΔC_{HbO_2} time courses are higher when the spectral bands are corrected ($r = 0.843 \pm 0.043$) than when they are not ($r = 0.749 \pm 0.068$). The correlation coefficients computed between the theoretical Hb response and the ΔC_{Hb} time courses are higher when the spectral bands are corrected ($r = 0.780 \pm 0.063$) than when they are not ($r = 0.577 \pm 0.112$). The correlation coefficients computed between the theoretical $oxCCO$ response and the ΔC_{oxCCO} time

courses are higher when the spectral bands are corrected ($r = 0.256 \pm 0.177$) than when they are not ($r = 0.177 \pm 0.175$). The correlation coefficient values are summarized in Table 5.

Figure 13. Hemodynamic and metabolic monitoring following neuronal activation computed with RGB imaging. The dashed lines represent the theoretical hemodynamic and metabolic responses following the neuronal stimulation. The dispersion ranges of the measurements are represented by colored areas. The concentration changes averaged over the 10^3 noisy measurements are represented in solid lines. The concentration changes' time courses computed with the 121 wavelengths included between 780 nm and 900 nm [23] are represented with yellow points. The ones computed with Arifler et al.'s wavelengths [27] are represented with black triangles. The blue rectangle represents the “patient” physiological stimulus.

In Figure 13, the hemodynamic and metabolic monitoring following a simulated neuronal stimulation was computed using RGB imaging. The standard deviation averaged over all time measurements is equal to $1.24 \mu\text{mol}\cdot\text{L}^{-1}$, $1.04 \mu\text{mol}\cdot\text{L}^{-1}$, and $1.54 \mu\text{mol}\cdot\text{L}^{-1}$ for ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} , respectively. The computed ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} values do not have a good match with the theoretical hemodynamic and metabolic responses. During the stimulation period, there is on average a 169% underestimation of the ΔC_{HbO_2} values, a 147% underestimation of the ΔC_{Hb} values, and a 1036% overestimation of the ΔC_{oxCCO} values compared to the theoretical measurements. We can notice that there is an important crosstalk between the chromophores. The ΔC_{HbO_2} values were mainly interpreted as Hb variations, the ΔC_{Hb} values as oxCCO variations, and the ΔC_{oxCCO} as HbO₂ variations.

Table 5. Pearson correlation coefficients computed between the theoretical hemodynamic and metabolic responses and the simulated concentration changes' time courses; see Figures 12 and 13. $\mu(r_n)$ and $\sigma(r_n)$ designate the mean and standard deviation, respectively, of the Pearson correlation coefficients computed with the 10^3 noisy time courses of the chromophore n .

	RGB Imaging	Hyperspectral Imaging	
		Spectral Correction	No Spectral Correction
$\mu(r_{HbO_2})$	−0.727	0.843	0.749
$\sigma(r_{HbO_2})$	0.072	0.043	0.068
$\mu(r_{Hb})$	−0.499	0.780	0.577
$\sigma(r_{Hb})$	0.126	0.063	0.112
$\mu(r_{oxCCO})$	0.880	0.256	0.177
$\sigma(r_{oxCCO})$	0.030	0.177	0.175

4. Discussion

Matcher et al. [46] showed that the performance of spectroscopic analysis can be improved by increasing the number of wavelengths of illumination. The results of our study are consistent with Matcher et al.'s results; see Figure 6. The simulation-based method presented in this paper aimed to identify the optimal spectral combination of our hyperspectral camera for the brain hemodynamic and metabolic monitoring. When the spectral bands are corrected, the optimal spectral configuration is composed of 21 and 22 spectral bands; see Figure 7. This configuration could be however reduced from 10 to 12 spectral bands while keeping fairly constant performances. We can observe a plateau in the quantification errors of ΔC_{HbO_2} when 10 or more spectral bands are used. We also can observe a plateau in the quantification errors in ΔC_{Hb} and ΔC_{oxCCO} when 12 or more spectral bands are used; see Figure 6. This reduction of the number of the spectral bands could be interesting for the real-time computation of hemodynamic and metabolic brain maps in the operative room using commercial hyperspectral cameras and for the conception of dedicated cameras used in functional brain mapping studies.

In this study, the optimal spectral configurations were obtained by searching the three chromophores deconvolution systems that minimize the quantification errors in ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} . Therefore, three different spectral configurations were obtained for the deconvolution of the three chromophores. These spectral configurations, as well as the reference configuration identified by Bale et al. [23] and Arifler et al. [27] are represented in Figure 14.

Figure 14. Peaks of spectral bands that minimize the quantification errors in ΔC_{HbO_2} , ΔC_{Hb} and ΔC_{oxCCO} . The spectral configuration identified by Bale et al. [23] and Arifler et al. [27] are also indicated.

The comparison between the spectral configuration identified by Arifler and al. and ours is not trivial since our hyperspectral camera does not acquire exactly the same wavelengths; see Figure 2. There are some similarities between the wavelengths used in our system and in the system of Arifler et al. Indeed, between 780 nm and 900 nm, some wavelengths correspond. Our system also used others wavelengths inferior to 780 nm (703, 754, and 767 nm) and superior to 900 nm (916, 929, 937, 947, 953, and 958 nm). The quantification of ΔC_{HbO_2} , ΔC_{Hb} , and ΔC_{oxCCO} computed with the optimal spectral bands of our hyperspectral camera are consistent with those computed with 121 wavelengths included between 780 nm and 900 nm [23] and with those computed with the eight wavelengths identified by Arifler et al. [27]. For a two-chromophore deconvolution system, the quantification error in ΔC_{HbO_2} measured with our system is equivalent to those measured with 121 wavelengths. However, the choice of our spectral bands aims to reduce the quantification error in ΔC_{Hb} ; see Figure 10. For a three-chromophore deconvolution system, the quantification errors measured with our system are a little higher than those measured with 121 wavelengths or with Arifler et al.'s wavelengths; see

Figure 12. This difference may be explained because the illumination and the acquisition of the 121 wavelengths of reference, as well as the eight wavelengths identified by Arifler et al. were simulated as ideal sources and detectors. This means that for these simulations, the term $D \times S$ in Equation (7) is equal to one. To efficiently compare our spectral configuration with these spectral configurations of reference, the spectral sensitivities of the detectors and the illumination sources have to be considered. However, the acquisition condition is different since we acquired the intrinsic signal of an exposed cortex, whereas the wavelengths identified in Bale et al.'s and Arifler et al.'s studies were identified for functional near-infrared spectroscopy devices.

We showed that a spectral correction (see Section 2.2) is required when a hyperspectral mosaic sensor is used [10]. The spectral correction aims to reduce the quantification errors in the measurements and allows a better follow-up of the temporal hemodynamic and metabolic variations; see Table 5.

We also compared hyperspectral imaging to RGB imaging for the computation of hemodynamic and metabolic brain maps. Hyperspectral imaging is the suitable solution to compute hemodynamic maps and metabolic maps thanks to its ability to acquire the intrinsic signal in the near-infrared range [23]. A very important crosstalk between HbO_2 , Hb, and oxCCO can be observed when the RGB camera is used for the computation of hemodynamic and metabolic brain maps; see Figure 13. Therefore, RGB imaging is not a suitable solution to compute metabolic brain maps. An RGB camera could be however a low-cost solution to compute hemodynamic maps; see Figure 11. This solution is not accurate to quantify ΔC_{HbO_2} , but is very accurate for the quantification of ΔC_{Hb} . This original result is interesting because most surgical microscopes used in the operating room are equipped with standard RGB cameras. It is known that the BOLD signal used in fMRI studies is predominately due to the paramagnetic properties of deoxygenated hemoglobin [47]. This result indicates that the ΔC_{Hb} quantified with RGB imaging can be used in a robust way for intraoperative functional mapping based on SPM analyses.

We incorporated the camera noises in our simulation to find the most robust and reliable spectral configuration. In Figures 8 and 9, we show that the SNR of the imaging system has a drastic impact on quantification performances. An accurate quantification could be obtained with a high SNR value. Therefore, the light source and the camera specifications and settings have to be carefully chosen in order to guarantee an optimal SNR. This simulation framework could be a great tool for industry or researchers working on intraoperative functional brain mapping solutions to help them in the choice of commercial camera. However, our simulation framework needs to be improved. For the moment, a homogeneous volume of grey matter was considered. A realistic mapping of the exposed cortex could be simulated as suggested by Giannoni et al. [28]. This will be considered in future studies. Moreover, the hemodynamic and metabolic changes following neuronal activation were homogeneously simulated in the volume of grey matter. These events are obviously not consistent with those appearing in a real cortical tissue. This modeling also has to be taken into account to improve our method of identification of the optimal spectral bands of a hyperspectral camera for brain hemodynamic and metabolic monitoring.

5. Conclusions

We present in this paper a method for the identification of the optimal spectral bands of a commercial camera for the intraoperative monitoring of the brain hemodynamic and metabolic responses following neuronal activation. The method described in the report is based on Monte Carlo simulations of the light propagation in a volume of grey matter and incorporates a realistic modeling of the camera acquisition with the addition of Gaussian noises (experimentally measured with the cameras). We identified that an optimal spectral combination of our hyperspectral camera composed of 21 to 22 spectral bands can be used to compute accurate hemodynamic and metabolic brain maps. This configuration could be however reduced from 10 to 12 spectral bands while keeping fairly constant performances, which is consistent with the spectral configurations proposed in the literature. We also showed that RGB imaging is not a suitable technique to compute metabolic brain

maps, but is very accurate to compute hemodynamic maps with the quantification of deoxygenated hemoglobin concentration changes. Our Monte Carlo framework needs to be improved, namely with the consideration of the perfusion of grey matter by blood capillaries.

Author Contributions: Conceptualization: C.C., L.M.-W., and B.M. Methodology: C.C., L.M.-W., R.S., M.S., and B.M. Software: C.C., L.M.-W., and M.S. Writing, original draft: C.C. Writing, review and editing: C.C., L.M.-W., R.S., M.S., J.G., and B.M. Supervision: R.S. and B.M. Funding acquisition: R.S. and B.M. Investigation: J.G. Resources: J.G. Project administration: B.M. All authors have read and agreed to the published version of the manuscript.

Funding: These works were funded by LABEX PRIMES (ANR-11-LABX-0063) of Université de Lyon, within the program “Investissements d’Avenir” (ANR-11-IDEX-0007), operated by the French National Research Agency (ANR); Cancéropôle Lyon Auvergne Rhône Alpes (CLARA) within the program “OncoStarter”; Infrastructures d’Avenir en Biologie Santé (ANR-11-INBS-000), within the program “Investissements d’Avenir” operated by the French National Research Agency (ANR) and France Life Imaging.

Acknowledgments: We want to acknowledge the PILoT facility for the support provided for the image acquisition.

Conflicts of Interest: No conflicts of interest, financial or otherwise, are declared by the authors.

Abbreviations

The following abbreviations are used in this manuscript:

HbO ₂	Oxygenated hemoglobin
Hb	Deoxygenated hemoglobin
oxCCO	Oxidative state of cytochrome-c-oxidase
BOLD	Blood oxygenation level dependent
fMRI	functional magnetic resonance imaging
NIRS	Near infrared spectroscopy
SPM	Statistical parametric mapping
SNR	Signal-to-noise ratio

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