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An integrated measurement system for simultaneous functional magnetic resonance imaging and diffuse optical tomography in human brain mapping

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Abstract

An integrated measurement system is described for performing simultaneous functional magnetic resonance imaging (fMRI) and diffuse optical tomography (DOT) for human brain mapping experiments. The components of this system consist of an MRI-compatible multi-overlapping-channel optical probe, methods for co-registration of optical and fMRI measurements, and DOT reconstruction algorithms with structural and physiological constraints derived from the MRI data. The optical probe is fully MRI-compatible in the sense that it produces negligible MR image distortion and does not require any modification to the MRI scanner or data acquisition protocol. The probe can be attached to any part of the head without posing any limitation on optical data acquisition. Co-registration of images from fMRI and optical measurements was achieved by localizing the positions of the optical fibers using MRI markers. Human studies show successful implementation of the entire system.

INTRODUCTION

Functional magnetic resonance imaging (fMRI) has rapidly become a widely-used imaging method for investigating human brain activity, with numerous applications in medicine and cognitive neuroscience. The majority of such studies use the blood-oxygen-level-dependent (BOLD) effect^{1,2}, with a smaller number using perfusion-based techniques³. In addition to purely applications-driven research, fMRI studies have also been used to study physiological changes associated with neural activity using various system models, most based on the original “balloon model”⁴. Despite the success of this model in qualitatively interpreting BOLD-based phenomena such as the initial post-stimulus signal dip subsequent signal undershoot, the exact relationship between all of the physiological changes induced by neuronal activation and the BOLD signal remains elusive.

Concurrent with the rapid expansion of fMRI applications, significant advances have been made in the past decade in the area of optical imaging of the human brain. An excellent and detailed review has been published recently⁵. Near-infrared (NIR) spectroscopy and imaging, in particular, provide a unique tool to study neurovascular coupling, with the ability to measure changes in the concentration of deoxyhemoglobin [HbR] and oxyhemoglobin [HbO₂] using multiple-wavelengths. These measures can in turn be related

to changes in physiological parameters such as cerebral blood flow (CBF), cerebral blood volume (CBV) and the cerebral metabolic rate of oxygen (CMRO₂).

The major limitations in using NIR methods in studies of human brain activation are the limited penetration, i.e., a rapid fall-off in the signal-to-noise ratio (SNR) deep in the brain, and poor spatial localization of the hemodynamic changes due to the broad photon migration paths between optical sources and detectors resulting from the highly scattering brain tissue. There are two basic methods by which spatial information on hemodynamic changes can be obtained: NIR spectroscopy (NIRS) and diffuse optical tomography (DOT). NIRS assumes that light undergoes scattering through an optically homogeneous medium for a particular measurement channel. Multiple measurement channels can collectively provide spatial resolution of the hemodynamic changes. NIRS methods typically give lateral spatial resolution comparable to the source-detector distance, with considerably poorer resolution in the longitudinal direction, although considerable improvements have been demonstrated by using overlapped measurement channels⁶. Such methodology has been used extensively in both human and animal studies to produce maps of changes in hemoglobin concentrations^{7–9}. In contrast, DOT typically uses more realistic models of photon migration through the skull and brain tissue for all measurement channels simultaneously and subsequently determine the spatial distribution of stimulus-induced changes in optical properties^{8–12}. A limited number of DOT studies have been performed in humans^{6,13,14}.

The first step in DOT is to solve the “forward problem” of photon migration through the head, which is usually based on the diffusion equation¹⁰. The “inverse problem” of image reconstruction is typically underdetermined due to the relatively small number of measurement channels compared with the number of voxels within the region of interest (ROI) and ill-posed due to the highly scattering tissue. As reported in Gibson et al.⁵ a significant recent development in solving the forward problem has been the incorporation of spatial constraints, usually provided by MRI. Both simulation¹⁵ and experimental studies have shown that image quality is improved significantly using this approach. Although the optical and MRI measurements can be made at different times, simultaneous data acquisition minimizes errors from incorrect co-registration and variations of physiological parameters at rest. Anatomical information can also be incorporated into the inverse problem of image reconstruction by constraining the region where activation-induced changes in optical signals can be localized: such an approach has been shown to give improvements for both linear and non-linear reconstruction methods⁶.

Nevertheless, the integration of the two imaging modalities, fMRI and DOT, imposes constraints on the design and construction of the optical probe. Furthermore, accurate co-registration of optical and MR images has to be achieved for reproducible experimental results. A number of research groups have published on simultaneous fMRI and optical spectroscopy/imaging^{5,15–20}. Simultaneous methods have also been used for animal studies²¹. In order to extend these studies we have developed a combined DOT and fMRI system¹⁴; a similar device has been reported by Hoge et al.²²

In this paper, we describe in detail the design and construction of an integrated measurement system for simultaneous fMRI and DOT for human brain mapping. The first component is an MRI-compatible optical probe that does not impose any limit on existing MRI and optical data acquisition methods for human brain studies. The optical probe can be attached to virtually any position of the head, fits into a standard MRI birdcage head-coil, and produces negligible MR image distortion. Since the optical and fMRI data are acquired simultaneously, it is possible to determine the positions of optical fibers from the MR images with high accuracy, and register both optical and fMRI results onto the anatomical MR image of the brain. The resulting accuracy of image co-registration is much higher than

that of the traditional digitization method based on polarized 3-D electromagnetic field. By doing so, the chance of introducing error as a result of extra measurements is reduced²³. Furthermore, as the positions of optical sources and detectors, or optodes, are recovered from MRI images *in situ*, the unpredictable deformation of the optical probe within the MR head-coil can be determined.

Optical probe design and testing

Due to the presence of a strong static magnetic (B_0) field, high frequency pulsed electromagnetic (B_1) field, and oscillating magnetic field gradients associated with MRI, the design of the optical probe should ideally be completely metal-free. To comply with this requirement, the optical fibers were “ferruled” using plastic tubing (PEEK semi-flexible tubing) instead of the more conventional stainless steel. From the magnetic susceptibility point of view, any material used for probe construction should produce as little field distortion as possible. From the structural point of view, the optical probe must be robust enough to maintain its structure, yet flexible enough to mould to the shape of the head and provide good contact. We tested different plastic and rubbery materials for field distortion by attaching them to a head phantom filled with saline and acquiring MR images. The material (polyurethane, 70A durometer, McMaster-Carr) that produced the least amount of visible artifact in MR images was selected to construct the frame of the optical probe.

The size of the probe frame and topology of the optodes are designed so that the distribution of source-detector distances spans the optimal range – between approximately 20 and 30 mm. The upper bound of the range is limited by the SNR – if the distance is too large, the SNR of the detected optical signal is too low. The lower bound of the range is determined by the dynamic range of the detector photomultiplier tubes (PMT) – if the distance is too small the PMTs are very likely to be saturated if one needs to maintain an acceptable SNR for distant detectors. Since the source-detector distance is related to the penetration depth of light, it is desirable to have multiple source-detector distances to improve the spatial resolution of the reconstructed image.

The physical structure of the MRI scanner imposes another important constraint on the design of the optical probe, as demonstrated in Figure 1(a). Optical fibers have to be placed in parallel with the long axis of the sixteen-rung birdcage head coil (inner diameter 30 cm). Each of the sixteen pairs of source fibers is fed into heat-treated plastic tubing which has been shaped into a relatively small bend-radius (~5 mm) so that the fibers are bent into a right-angle. Each of the optical fiber pairs is then ferrulized into a piece of short, thinner tubing using opaque adhesive (353ND high-temperature epoxy, Epoxy Technology) and extrudes from the opening of the short arm of the bent tubing to form a source optode. The optode is held by the frame of the optical probe so that its tip is in contact with the scalp. Technical specifications of the source optical fibers indicate the maximum allowed bend radius is 20 mm for short-term and 40 mm for long-term bending. In our experience, the fibers can actually be maintained in a much smaller bend radius for considerable periods of time (months) without degradation in either their physical or optical properties. The height of the optical probe is therefore essentially the length of the short arm of bent plastic tubing, which is kept between 15 and 20 mm. This allows the entire probe to be placed comfortably between the back of the head and the bottom of the birdcage head coil.

The assembly of the optical probe, as shown in Figures 1(b)–(d), has thirty-two 400- μ m-diameter plastic clad multimode silica source fibers (FT-400-EMT, Thorlabs, Newton, NJ) and 4 detector fiber bundles (3 mm diameter, 650 cm length, 0.55 numerical aperture, Sunoptic Technologies, Jacksonville, FL). The frame of the probe consists of a polyurethane annulus of 45-mm inner diameter, 55-mm outer diameter, and 8-mm thickness. The thirty-two source optical fibers are paired and distributed in an even radial pattern into sixteen

positions between the inner and outer edges of the rubber ring. The cross-sectional area of the source optodes is chosen so that it is small enough to minimize interference of the patient's hair on the measurements, yet large enough to ensure reasonable conformability for adult patients.

Each of the detector fiber bundles is attached to a glass total-internal-reflection right-angle prism ($5 \times 5 \text{ mm}^2$, Melles Griot Photonics, Rochester NY) using optical adhesive (M-62, Sumner Optical) so that the fiber bundles can be placed parallel to the scalp. The reflection layers on the hypotenuses of the prisms are made from dielectric material (MAXBRite® for diode lasers) instead of conventional aluminum or silver coatings to reduce artifacts due to induced eddy currents during MRI data acquisition. The four-detector fiber bundles are fixed to the rubber so that the prisms are positioned around the center of the probe yet still allow limited flexibility. An MRI visible "marker" is attached onto the frame adjacent to each of the sixteen source optodes. A pair of markers is used to identify one particular position number so that it can be easily recognized from the MR images, and subsequently the rotation of the optical probe determined. These cylindrical markers are made from sealed plastic tubes filled with fully hydrogenated vegetable oil (shortening), which gives a bright signal in T_1 -weighted MR images.

MRI and optical data acquisition

Non-magnetic LCD goggles (Resonance Technology, Northridge, CA) were placed in front of the patient's eyes inside the birdcage head coil, as shown in Figure 1(a). The visual stimulation paradigm comprised four blocks, each consisting of a 28.8-second fixation followed by a 19.2-second black-and-white checkerboard pattern, at reversal frequencies of 1, 2, 4, or 6 Hz.

The optical signals were recorded by a multi-source, multi-detector NIR spectrometer (Imagent, ISS), which was synchronized with the visual stimulation and the fMRI study by a TTL trigger-pulse from the MRI scanner. The optical sources were laser diodes (690 and 830 nm, 15 mW optical power output) which were amplitude modulated at 150 MHz and time-multiplexed. Photons reaching the optical detectors were amplified by the PMTs (side on, 1 in., Hamamatsu Photonics) and subsequently converted into AC, DC, and phase signals for each of the source-detector combinations, or measurement channels, at each laser wavelength. The data sampling rate was 52 Hz.

MRI was performed using a 3-T head-only scanner (Allegra, Siemens) equipped with a birdcage coil. In this particular study, the optical probe was attached to the back of the head and aligned with the primary visual cortex of the patient. The BOLD fMRI signal was measured using a gradient-echo echo-planar imaging (EPI) pulse sequence (field-of-view (FOV) $240 \times 240 \text{ mm}^2$, data acquisition matrix 64×64 voxels, slice thickness 4 mm, slice gap 0.4 mm, tip angle 60° , echo-time 25 ms, repetition time 2000 ms). A T_1 -weighted 3-D anatomical MR image of the same volume using spin-echo pulse sequence, with the same FOV, slice orientation, and number of slices, but higher in-plane resolution (data matrix 512×512 voxels, slice thickness 4 mm, slice gap 4 mm, tip angle 90° , echo-time 7 ms, repetition time 425 ms) was acquired for intermediate co-registration of the EPI images. Finally, another T_1 -weighted high-resolution 3-D full-head anatomical image (MPRAGE) (data matrix 512×512 voxels, 144 sagittal slices, voxel size $0.94 \times 0.94 \times 1.2 \text{ mm}^3$, tip angle 8° , echo-time 4 ms, repetition time 1800 ms) was acquired for optical image reconstruction and served as the basis of co-registration of results from BOLD fMRI and optical measurements.

In addition, optode localization requires acquisition of another two MRI data sets. The first is a calibration that needs to be done only once for a given optical probe, and does not

require the presence of the subject. The optical probe is laid flat on a surface containing an MRI-visible material (fully hydrogenated vegetable oil). The optodes are pressed lightly into this material, before the acquisition of MR images to determine the relative positions of the optodes (dark areas on a bright background) with respect to the MRI-visible markers. The second additional scan involves the acquisition of a high-resolution 3-D image over a limited FOV encompassing just the optical probe on the subject's head to localize the MRI-visible markers with respect to the brain. This scan, termed "probe localizer", comprised a high-resolution 3-D spin-echo image (data matrix 256×256 voxels, 30 slices, voxel size 0.50 × 0.50 × 1.0 mm³, tip angle 90°, echo-time 8 ms, repetition time 820 ms). Analysis of these two scans allows estimation of the local positions of the optical fibers on the surface of the subject's head with high precision. A sample image of the "probe localizer" is shown in Figure 2.

Simple image processing algorithms were written to extract automatically features from MR images. Markers were identified and extracted from the "probe-localizer" using a combined clustering and thresholding analysis: the MR markers have a relatively well-defined size in contiguous images, and signal intensity well above the noise level. Since each optode corresponds to one cylindrical marker, its orientation in 3-D could then be calculated. By combining this information with the 3-D MPRAGE scan these local fiber positions are converted into global positions with respect to the full head. The optode localization process had been fully automated using image processing routines in Matlab (R14, MathWorks, Natick, MA). It should be noted that the frame of the optical probe was considered "locally rigid"; i.e., the deformation between a marker and its corresponding optode-position was negligible. Details of the co-ordinate transformation process can be found in the Appendix. Figure 3 shows the reconstructed source- and detector-positions (bright dots) superimposed on the anatomical MR image. The error of localization was estimated to be within 2 mm. The above localization result has been compared with the one obtained using the traditional digitization method using a polarized EM field and was believed to be much more accurate by inspecting the structural MR image for the marks on the scalp produced by the optodes.

Optical image reconstruction

The mathematical characteristics of light transport are described by the radiative transport equation (RTE). For a highly scattering medium, such as brain tissue, the RTE can be simplified to the diffusion equation:

$$-\nabla \cdot \kappa(r) \nabla \Phi(r, t) + \mu_a \Phi(r, t) + \frac{1}{c} \frac{\partial \Phi(r, t)}{\partial t} = q_0(r, t) \quad (1)$$

The detected signal can be expressed in terms of the summation of frequency-independent (DC) and frequency-dependent terms ($AC \sin(2\pi ft + \text{phase})$, where is the modulation frequency). The general solution to the first-order perturbative approximation of the above equation in the frequency-domain is given by

$$\delta \Phi(r_s, r_d) = - \int_{\Omega} \left[\delta \mu_a(r) \Phi_0(r_s, r) G(r, r_d) + \frac{\delta D(r)}{c} \nabla \Phi_0(r_s, r) \bullet \nabla G(r, r_d) \right] d^3 r \quad (2)$$

For purely absorbing inhomogeneities, solving only the first term of the integrand of the above equation is necessary, while for purely scattering inhomogeneities, solving the second term of the integrand suffices. In measuring the hemodynamic response to functional stimulation it is widely assumed that only changes in the absorption coefficient need to be

considered, and that, since these changes are small, a perturbative approach to solving the diffusion equation can be utilized using the Born approximation. This results in:

$$\delta\Phi(r_s, r_d) = - \int_V \delta\mu_a(r) \Phi_0(r_s, r) G(r, r_d) d^3r \quad (3)$$

where $\Phi_0(r_s, r)$, the photon density at r due to a light source at position r_s , and the Green's function $G(r, r_d)$, the photon density at detector position r_d due to a hypothetical infinitesimal light source at r , are determined in the frequency domain using the baseline optical properties. The Jacobian $\Phi_0(r_s, r)G(r, r_d)$ of Equation (3) dictates the sensitivity function, i.e., the contribution of a given voxel to the detected optical signal. In traditional NIRS methods the sensitivity function is alternatively referred to as the “effective pathlength” since it can also be considered as an indication of the pathlength that light travels within a given sample volume.

A Monte Carlo method was used to determine the Jacobian in Equation (3). The particular implementation represents a frequency-domain formulation of the time-domain method described in detail by Boas et al.²⁴. The frequency-domain formulation can be made computationally-efficient by using the fact that the photon density at a voxel r that contributes to the photon density at detector r_d from a source at r_s is proportional to the sensitivity function which, after normalization, can also be considered as a “complex probability function” of light for voxel r . It is worth noting that since the perturbative approach is adopted, both terms in the Jacobian are determined using the baseline optical properties. The Green's function can be regarded as the “impulse-response” of the transfer function of the system: in other words, for the diffusion equation, which is a linear differential equation, its Green's function $G(r, r_d)$ is the photon density present at detector r_d due to an infinitesimal unit source at r . The photon density is defined as the radiant energy of light (or number of photons) per unit volume. Therefore, for a particular measurement channel, the Jacobian is the photon density at detector r_d from source r_s that has passed through voxel r . Its value in the frequency-domain is related to the result from the Monte Carlo simulations in the time-domain by:

$$\Phi = \frac{\sum_n \Phi_n}{N_{photons}} = \frac{\sum_n \exp\left(\sum_m K_m L_{n,m}\right)}{N_{photons}} \quad (4)$$

where Φ_n represents individual photon densities, $L_{n,m}$ is the path length of photon n in medium m , and $N_{photons}$ is the total number of photons. The value of K_m , the complex wave vector of medium m , is given by:

$$K_m = i \frac{2\pi n_m f}{c_0} - \mu_{a(m)} \quad (5)$$

where f , n_m , c_0 , and $\mu_{a(m)}$ are the modulation frequency, index of refraction in medium m , the speed of light in vacuum, and the absorption coefficient of medium m , respectively. A large number of simulations, typically $>10^7$, have to be performed in order for the “photons” to behave collectively in a similar fashion to the true nature of light propagation. These simulation produce a 3-D “light bundle”, with the spatially-dependent intensity of the bundle proportional to the desired Jacobian for a given measurement channel.

For quantitative image reconstruction, it is necessary to obtain absolute values of the Jacobian. This requires two generally unknown constants: one relating the photon density to the recorded optical signal, and the other representing the total number of photons used in the experiment. Nonetheless, these two unknown constants can be eliminated by applying the following two normalization factors. The first is given by

$$\sum_r \sum_n \Phi_{n,r} \quad (6)$$

where n is the index of the detected photons. The second normalization factor is

$$\frac{\sum_n \Phi_{n,r}}{N_s} \quad (7)$$

where N_s is the total number of simulations (one photon per simulation). Incorporation of the two normalization factors results in the final closed-form equation for the forward problem

$$\frac{\Delta S(r_s, r_d)}{S_0(r_s, r_d)} = - \frac{N_s}{\sum_n \Phi_n} \frac{\sum_r \Delta \mu_a(r) \sum_p \Phi_{p,r}}{\sum_{r'} \sum_n \Phi_{n,r'}} \quad (8)$$

where S is the measured optical signal and Φ is the photon density given by Equation (4).

Using the above method, the “light bundle” (normalized amplitude) of a particular optical measurement channel with a modulation frequency of 150 MHz in a realistic head model of a patient is shown in Figure 4. The head model was generated by segmenting the 3-D MPRAGE MR data set of the patient into four types of tissue (scalp/skull, cerebrospinal fluid, gray matter, and white matter) and assigning each type of tissue with optical properties from the literature, shown in Table 1.

Optical images were reconstructed using the simultaneous iterative reconstruction technique (SIRT)^{25,26}. *A priori* physiological and spatial constraints can be used to reduce the number of unknowns in the linear equations by reducing the size of the sensitivity function. Specifically, the following two criteria were used as constraints: (a) the hemodynamic response can occur only within brain tissue, and (b) any activation far away from the optical probe is essentially undetectable due to the very low SNR of the measurement. The first constraint was implemented by forcing the values of sensitivity function within the skull and scalp to be zero. The second constraint was enforced by assuming a maximum value of the hemodynamic “activation”, i.e., a maximum percentage change in the tissue absorption coefficient from its baseline value, and comparing this maximum “signal” with the normalized noise levels of a given measurement channel. The normalized noise level was determined by the standard deviation of the raw optical signal divided by its mean value. A voxel was considered “potentially visible” in a particular channel if the hypothetical signal was larger than the calculated noise level. A voxel was considered “sensitive” if it was visible to at least half of the channels. By applying the above two constraints to the Jacobian

matrix, the underdetermined nature of the sensitivity function for the forward problem has been reduced significantly.

The raw optical signal was low-pass filtered and resampled at 1 Hz to reduce the data size. From the processed optical signal, image reconstruction produced a 4-D (3-D maps in the time-series) matrix of changes in absorption coefficient at each of the two laser wavelengths (690 and 830 nm). Using Beer-Lambert's law and given the values of the extinction coefficients at the two wavelengths ($\epsilon_{\text{Hb}}^{830} = 0.1797$, $\epsilon_{\text{Hb}}^{690} = 0.7923$, $\epsilon_{\text{HbO}_2}^{830} = 0.2419$, $\epsilon_{\text{HbO}_2}^{690} = 0.0719 \text{ mm}^{-1}\text{mM}^{-1}$) the changes in absorption coefficients were converted into the changes in oxy- and deoxyhemoglobin concentration.

For each voxel, a linear "baseline" was estimated and subtracted from the corresponding time-series signal to compensate for any drift in laser power and low frequency changes in physiological parameters. The correlation coefficient between the resulting time-series hemodynamic signals (changes in oxy- and deoxyhemoglobin concentration) and the pattern of visual stimulation, delayed by 6 s, were calculated as the criteria for identifying physiological activation. Voxels that had correlation coefficient higher than the threshold (± 0.5 in this study) were considered as activated.

Human studies

The overall data acquisition and processing structure used in human studies is summarized in Figure 5.

Figures 6 and 7 show the experimental result from an individual patient, in which the spatial and temporal responses, respectively, of oxy- and deoxyhemoglobin concentrations are compared with the BOLD fMRI data. All structural images have been transformed into Talairach space²⁷. The result was averaged over 4 measurements at a visual stimulation frequency of 2 Hz. The spatial hemodynamic response, i.e., correlation maps of $\Delta[\text{HbR}]$ and $\Delta[\text{HbO}_2]$, corresponds to the fMRI result very well. The spatial changes in oxy- and deoxyhemoglobin concentration are very similar but not identical.

The temporal hemodynamic response shows the expected activation patterns: a decrease in deoxyhemoglobin concentration, an increase in oxyhemoglobin concentration, and an increase in their sum, i.e., the total hemoglobin concentration. This result is consistent with the commonly-held assumption that the BOLD signal arises primarily from changes in blood oxygenation level and CBV, caused by the discrepancy between the relative values of the changes in CMRO_2 and CBF.

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Appendix - Co-ordinate transformation

The 3-D MPRAGE data set was acquired with the frequency encoding direction parallel to, and the two phase-encoding directions perpendicular to the B_0 axis. For optimal detection of the MR marker positions, the probe localizer scan was acquired at an oblique angle, roughly parallel with the optical probe. Since the two images were taken with different orientations, the first step was to transform the coordinates from the local system (defined by the “probe localizer,” or the local image) to the global system (defined by the MPRAGE, or the global image). Several markers were identified in the global image so that the translation and rotation of the local image with respect to the globe image was recovered. The coordinates of the markers in the local system were subsequently mapped to the global system. In other words, the overall positions of the optical probe had been determined. The second step was to determine the rotation of the optical probe with respect to its “standard” position in the reference MR image. This was achieved by identifying one closely positioned pair of markers. The next step, determination of the deformation of the optical probe, was very crucial to the accuracy of localization because the frame of the probe could deform considerably depending on the shape of the head and how the probe was attached to the head. Such deformation was determined by finding the orientations of the markers, which

had been identified and labeled previously. After multiple coordinate system transformations, the coordinates of optodes in the “microscopic coordinate systems” in the reference MR image, which described the relative positions of the optodes with respect to their corresponding markers, transformed to the global system. As the last step, the optode positions were reconstructed by translating these coordinates onto those of the markers in the global image. The resulting coordinates can be mapped onto the stereotactic Talairach space²⁷ for cross-subject image co-registration and various data analysis methods.

The first step used coordinate system transformation. If a given point P has coordinates i_B , j_B , k_B with respect to an origin at O_B in coordinate system B, then its position in coordinate system A with origin O_A can be represented by:

$$P^{(A)} = R_{(A)}^{(B)} P^{(B)} + {}^{(B)}O_{(A)}$$

where ${}^{(B)}O_{(A)}$ is the translation from $O^{(B)}$ to $O^{(A)}$ and $R_{(A)}^{(B)}$ can be written as a matrix of dot products of the axis vectors of the two coordinate systems

$$R_{(A)}^{(B)} = \begin{bmatrix} i_A \cdot i_B & j_A \cdot i_B & k_A \cdot i_B \\ i_A \cdot j_B & j_A \cdot j_B & k_A \cdot j_B \\ i_A \cdot k_B & j_A \cdot k_B & k_A \cdot k_B \end{bmatrix}$$

The second step uses vector rotation and translation. Transforming from coordinate system A to system B is accomplished by first applying the rotation matrix R, and then translation t.

If the two frames are known, $R_{(A)}^{(B)}$ is uniquely determined, while

$$R = \prod_m R_m$$

is dependent on the order of rotation, where $m = x, y$, or z , each of which represents rotation of an angle θ about the x -, y -, or z -axis and

$$R_x(\theta) = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\theta & \sin\theta \\ 0 & -\sin\theta & \cos\theta \end{bmatrix}, R_y(\theta) = \begin{bmatrix} \cos\theta & 0 & -\sin\theta \\ 0 & 1 & 0 \\ \sin\theta & 0 & \cos\theta \end{bmatrix}, R_z(\theta) = \begin{bmatrix} \cos\theta & \sin\theta & 0 \\ -\sin\theta & \cos\theta & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

Figure 1.

(a) Placement of the optical probe on the head inside the birdcage head coil of the MRI scanner. (b) Photograph of the optical probe, (c) and (d) top- and side-view schematics of the optical probe.

Figure 2.

(a), (b) and (c), three orthogonal oblique-axis views from the three-dimensional MRI data set used to determine the position of the MRI-visible markers on the human head.

Figure 3. (left) Three dimensional surface reconstruction of a subject's head with the MRI-visible markers. (right) Reconstructed positions of the sixteen source optodes and four detectors with respect to the cortical surface of the subject's brain.

Figure 4. Sagittal and axial views of the normalized amplitude of the sensitivity function, or the "light bundle," for a particular measurement channel at 150 MHz modulation frequency using a realistic head model.

Figure 5.
A flowchart of the data acquisition and processing procedures used for simultaneous fMRI and DOT.

Figure 6.

The correlation coefficient maps of (a) the BOLD signal, (b) deoxy-, and (c) oxyhemoglobin concentrations. The maps shown in (a)–(c) are thresholded at a correlation coefficient of 0.5. The slice thickness is 0.94 mm, and the interslice distance is 2 mm. All images are shown in the Talairach space.

Figure 7. Time-series plots of the changes in deoxy- and oxyhemoglobin concentration averaged over activated voxels.

Table 1

Optical properties used for Monte Carlo simulations

Tissue	μ_a (mm ⁻¹)	μ_s (mm ⁻¹)	g	n
Scalp and skull	0.014	0.860	0	1.4
Cerebrospinal Fluid	0.004	0.100	0	1.4
Gray Matter	0.010	1.110	0	1.4
White Matter	0.010	1.110	0	1.4
Activation	0.011	1.110	0	1.4