Non-invasive Functional Brain Mapping Using Registered Transcranial Magnetic Stimulation

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Abstract

We describe a method for mapping the functional regions of the brain using a transcranial magnetic stimulation (TMS) device. This device, when placed on a subject's scalp, stimulates the underlying neurons by generating focused magnetic field pulses. A brain mapping is then generated by measuring responses of different motor and sensory functions to this stimulation. The key process in generating this mapping is the association of the 3D positions and orientations of the TMS probe on the scalp to a 3D brain reconstruction such as is feasible with a magnetic resonance image (MRI). We perform this matching process by (1) registering the subject's head position to an *a priori* MRI scan, (2) tracking the 3D position/orientation of the TMS probe, (3) transforming the TMS probe position/orientation to the MRI coordinate frame, and (4) tracking movements in the subject's head position to factor out any head motion. The resultant process generates a high resolution, accurate brain mapping which supports surgical planning, surgical guidance, neuroanatomy research, and psychiatric therapy. When compared to other functional imaging modalities, this approach exhibits much lower cost, greater portability, and more direct active control over the functional areas being studied.

Categories: Surface Registration, Applications

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Summary Page

1. **What is the original contribution of this work?**

   This paper describes the integration of 3D surface registration and tracking techniques for achieving a new application—non-invasive brain mapping.

2. **Why should this contribution be considered important?**

   By studying the applicability of the 3D registration techniques to new applications, such as brain mapping, we not only open potential new avenues for improving health care, but also learn the benefits and limitations of the technology in this domain. Our brain mapping application also explores an integrated solution for registration and tracking, two problems which are often present in medical applications.

3. **What is the most closely related work by others and how does this work differ?**

   Similar registration techniques have been proposed by Szeliski, Lavallee et al, and by Ayache, et al. This work differs in some of the details of the method, but the primary novelty of the paper is in the application—brain mapping.

4. **How can other researchers make use of the results of this work?**

   While some medical applications of 3D registration and tracking have already been explored, many more are on the horizon. The experience gained by our study of integrated solutions to registration and tracking problems and of the new application of brain mapping may support others as they explore related domains.

1 Introduction

Functional brain mapping, consisting of the association of motor, sensory, and perception functions with different regions of the brain, is currently an active research area with a wide range of potential applications. Sample applications include (1) neuroanatomy research into the structure and functioning of components of the brain, (2) study of neurological disease origination, progression and diagnosis, (3) surgical planning and guidance of biopsy and ablation procedures, (4) treatment monitoring and (5) neurological therapeutic procedures. Current techniques for functional brain mapping utilize 3D medical scanners to image the brain while the subject undergoes an activity aimed at activating the functional area of interest. Scanners currently used for this purpose are single photon emission computed tomography (SPECT), positron emission tomography (PET), and magnetic resonance imaging (MRI). The ability of these scanners to capture brain activity results from their sensitivity to such factors as metabolism rate and blood oxygenation. The benefit of such scanners is their ability to quickly capture 3D snapshots of the complete brain activity. Some of their limitations, however, are:

- High cost limits their use. In addition, the use of radioactive agents in SPECT and PET further limit the frequency of use of those scanners.
- Passive control of functional activation limits the pinpointing of the areas of interest. Ideally, one wants to limit the functional activation of the brain to just the areas of interest and to do so at the same time the image is acquired. Standard methods, such as asking the subject to perform certain activities, or trying to control the environment around the subject, are less than ideal in achieving this since there are many potentially confounding factors that cannot be isolated from the process (for example, it is difficult to ensure that the subject performed only the desired mental activity, and no other related activity, at the time of imaging).

One approach to avoiding these limitations is the use of a transcranial magnetic stimulation device[1] for actively stimulating different parts of the brain. Such devices consist of a circular or figure-8 shaped coil (termed the TMS probe) which can deliver single magnetic field pulse stimuli or pulse trains. In our experiments we have only used a figure-8 coil, which delivers a more sharply focused pulse. The size of the coil is about 5 cm diameter for each circular component of the figure-8. There is no direct electrical contact with the subject—the device

[1] Magstim Company Ltd, England

works by inducing small electrical currents (< 50 mA) in tissue using brief magnetic pulses that are focused in front of the coil. Because of the shape of the field, the stimulation is centered within the head and below the pain receptors, so that no discomfort is imparted to the subject. The peak magnetic fields are similar to those used with MRI scanners, except that magnetic stimulator pulses are very short (< 1 msec). Resulting energy dissipation in tissue is minimal (< 0.25 mJ). The advantages of such a device are:

- Relatively low cost and ease of use—the device is highly portable with little constraints on its applicability.
- Active functional activation—rather than trying to spot brain activity when the subject performs different actions, the TMS attempts to directly stimulate certain brain regions and monitor their impact. In principle, this leads to functional mapping that is highly localized both spatially within the brain and temporally for ease of acquisition.

While research is on-going on the biological implications of such a device, the physics of the generated magnetic field, and the development of psychophysical experiments which gauge brain function, we are exploring the technical problems of converting the TMS data, locations of TMS probe and associated muscular/sensory responses, to a 3D functional brain map, similar to ones that are obtained with 3D medical scanners. The heart of our problem is the registration of the subject's MRI scan, the subject position during transcranial magnetic stimulation, and the TMS probe positions/orientations to the same coordinate frame, and the associated tracking problem of maintaining that registration across possible subject movements during the data collection. The following section defines this registration/tracking problem, followed by a description of our registration/tracking system in Section 3. Sample results from the application of our system to a neurosurgery patient are shown in Section 4.

2 Problem Definition

We divide the problem into four parts:

1. Register an MRI scan of the subject's head to the actual subject head position as he is readied for TMS data collection. The goal is to compute a transform from the subject's world coordinate system to the MRI coordinate system to allow us to transform TMS probe points to the MRI scan. The registration should not require any attachment of

fiducials to the patient as the time between the MRI scan and TMS data collection may be large.

2. Track the 3D position/orientation of the TMS probe in the world coordinate system and record those locations when it is stimulated. Also record the muscular/sensory responses of each stimulation.

3. Track the subject's head motion in order to maintain the registration of step 1. Head track avoids the need to fixate the subject.

4. Combine the TMS probe positions/orientations, TMS responses, subject-to-MRI transform, and head motion to generate a functional brain mapping on any 3D surface rendered from the MRI scan, such as cortical or white matter surface.

While the registration does not necessarily need to be real-time, there are advantages to performing all the steps as the TMS data is collected, particularly to show the technician what regions of the head have already been covered, and where maximal responses have been attained. Accuracy requirements are relatively high as many of the active brain centers being studied are on the order of a few mm^3 in volume. Thus the overall accuracy should be within about 1-2 mm, which is generally not much larger than the voxel resolution of the MRI scan.

3 Registration System

The system we have developed to address the problems of Section 2 is shown in Figure 1. We work with three different coordinate systems:

1. MRI: The MRI data is captured in a coordinate frame that is arbitrarily attached to the volume of data. The data itself is segmented into skin surface for registration and internal structures for brain mapping visualization, within this coordinate frame.

2. Laser: The laser scanner provides 3D data of the subject's scalp surface as positioned for transcranial magnetic stimulation. We use a laser striping triangulation system consisting of a laser unit (laser source and cylindrical lens mounted on a stepper motor) and a camera. Here the coordinate frame of the acquired points is centered at a fixed point within the working volume of the laser system.

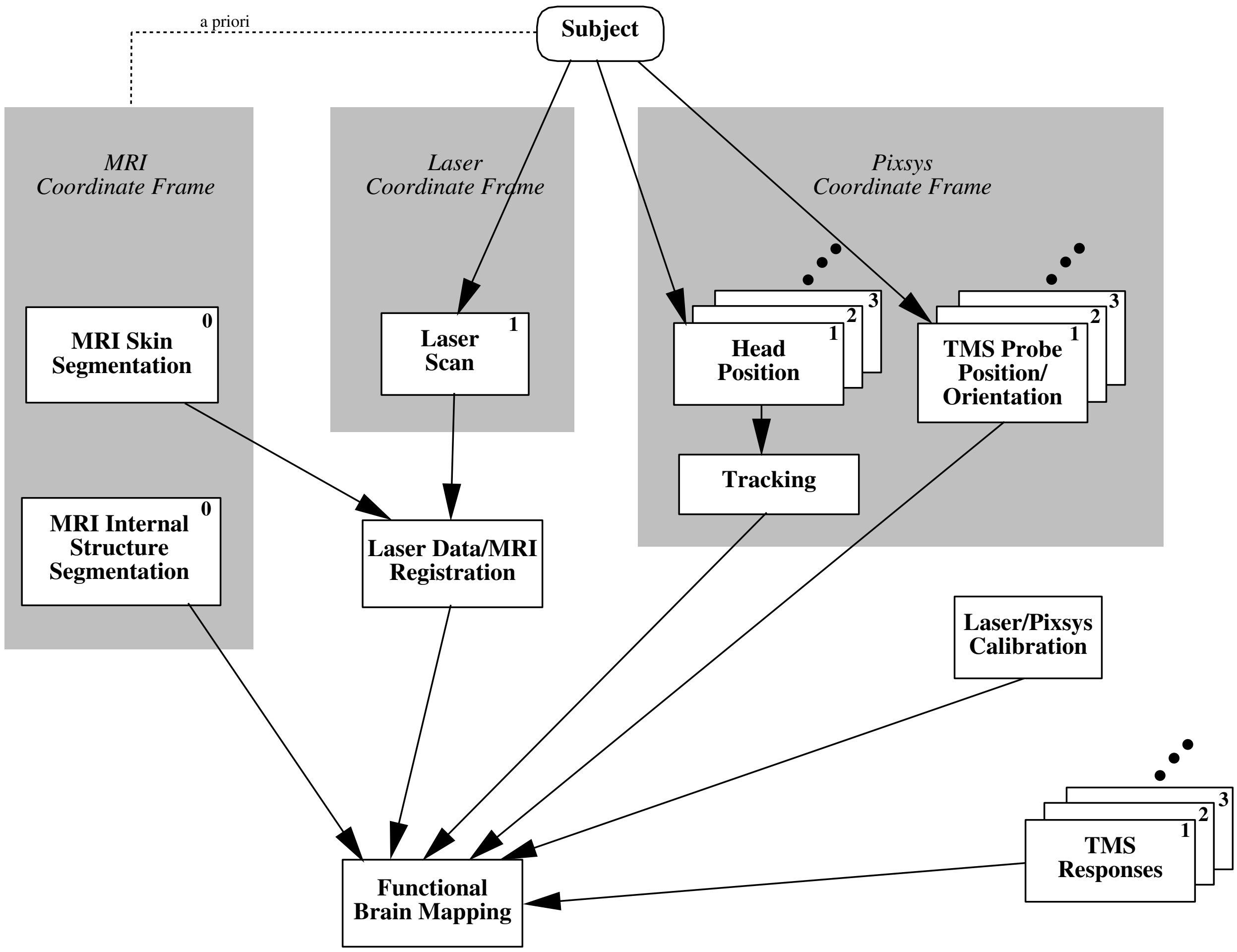

Figure 1: Architecture of functional brain mapping system.

3. Pixsys: This is a 3D tracking system[2] consisting of 3 linear cameras which localize flashing IR LEDs. The system can track a number of LEDs simultaneously. We mount two LEDs on the TMS coil (specifying its 3D position and orientation with twist the only degree of freedom not measured) and tape five LEDs taped on the subject's scalp for tracking head motion. Redundant LEDs are used for tracking head position in case motion is great enough to block up to two of the LEDs. The position and orientation information returned by the system are represented in a coordinate frame centered at a fixed point within the working volume of the cameras.

The goal of the system is to connect all of these coordinate systems together. That is, we need to connect the Pixsys coordinate system to the MRI coordinate system, in order to relate sampled TMS probe points to the corresponding point in the MRI. To do this, we need

[2]IGT Inc., Boulder, Colorado

to connect the patient's current position under the TMS probe to the MRI, which we do by using the laser coordinate system as an intermediary.

The laser scanner (laser and its associated camera) and Pixsys system (three linear cameras) are mounted on the same bar which is attached to a movable arm for ease of placement. Since we fixate the laser and Pixsys systems relative to each other, we perform an off-line calibration to obtain the Pixsys-to-laser transform. This transform is then constant for all subsequent TMS data collections. The transform from laser data to MRI coordinates, though, must be computed for each TMS data collection since the transformation of the TMS probe positions to the MRI scan requires knowledge of the subject's head position during the stimulation session.

A sample data collection procedure, from the perspective of the subject, is:

1. Acquire an MR image of the subject prior to the TMS session. Segment the scan into desired anatomical structures, such as skin, cortical surface, white matter, etc.

2. Prepare for TMS data collection:

   (a) Place subject on a bed.

   (b) For motor cortex mapping, place muscle activity sensors on muscles of interest. Upon appropriate stimulation, the muscles will contract. Visual or speech suppression can be used to map other functional areas.

   (c) Place Pixsys LEDs on the subject's scalp. These LEDs are currently loose LEDs which are taped to the skin such that they will not interfere with the TMS probing, but are spaced widely apart on the head.

3. Laser scan the subject—the laser plane is swept across the subject's head collecting 3D positional data of visible skin surfaces. At the same time the positions of the five LEDs taped to the subject's head are acquired by the Pixsys system.

4. Collect TMS data—the TMS probe is placed at various points on the subject's scalp. At each point, the TMS generates a brief magnetic pulse and the responses from the muscle sensors (or other responses) are recorded. The position and orientation of the TMS probe is also recorded by the Pixsys system at the same time. 3D renderings of the subject's MRI skin superimposed with TMS points may be generated during the data collection to chart progress and guide continued stimulations.

The processing of the MRI, laser, Pixsys, and TMS data is described in the following sections.

3.1 MRI Segmentation

The MRI data is segmented to extract the skin surface, for use in registration, and the internal structures, for use in visualization. By segmentation, we refer to the process of labeling individual voxels in the MRI scan by tissue type, based on properties of the observed intensities as well as known anatomical information about normal subjects. These labeled voxels are further gathered into connected components, which can be used for graphical manipulation and visualization.

The functional brain mapping is usually overlaid on both the cortical surface and the white matter surface so at least these two structures are segmented. In addition, ventricles, blood vessels, tumors, or other pathologies may also be segmented. Current segmentation techniques used at Brigham and Women's Hospital include an automatic gain artifact suppression technique based on expectation-maximization [16] in association with a cortical volume isolation technique based on image morphology and active contours [9]. These techniques are also complemented by semi-automatic techniques which interactively classify tissue types using high performance rendering algorithms.

3.2 Laser Data / MRI Registration

The MRI segmentation yields a 3D model of the patient's anatomy, which is clearly of utility in visualizing and identifying internal structures. To relate those structures to functional recordings, we need to place the MRI segmentation into correspondence with the actual patient, which we accomplish by registering surface data from the model and the patient. To do this, we need positional information from the patient's skin surface. Here, we have two possibilities available to us. The first uses a laser striping device to acquire positional data from the skin surface of the patient, which we can then register with the segmented skin surface from the MRI. An alternative is to use a Pixsys probe to acquire 3D data of the subject's position by moving the Pixsys probe along the subject's scalp. The laser is preferable due to its high accuracy and avoidance of direct contact with the subject. In either case, laser data or Pixsys data, the registration algorithm is the same. The basis of the registration algorithm have been previously described in [3, 4, 5, 6]. The algorithm is depicted in Figure 2 and is briefly reviewed below.

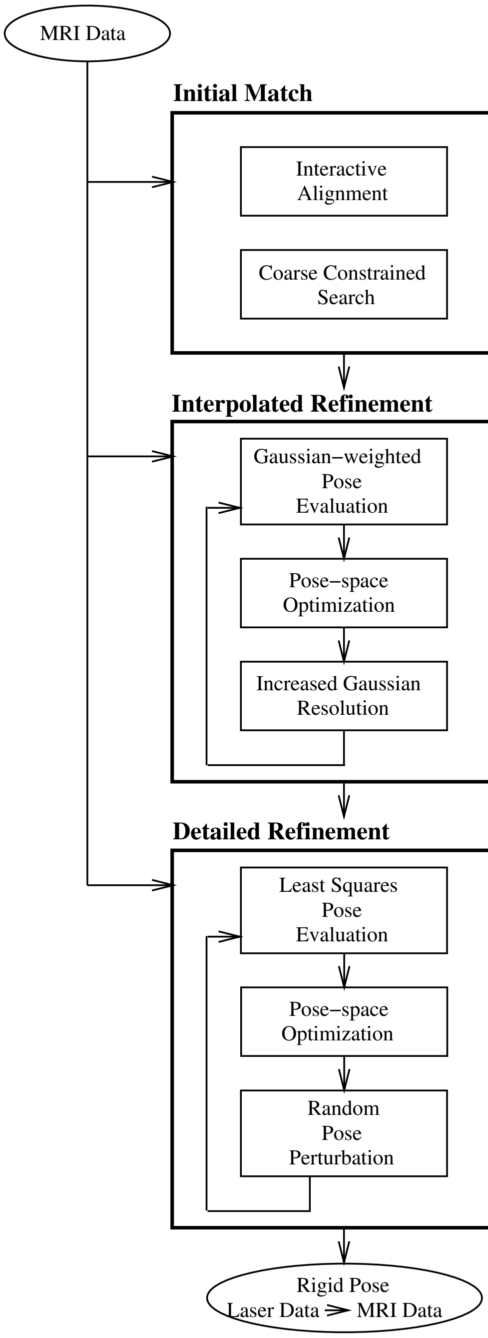

Figure 2: Registration algorithm outline.

3.2.1 Initial Match

Before commencing the matching process we preprocess the laser data to separate data of the subject's head from background data. Currently we do this with a simple user interface in which the view obtained from the video camera used in conjunction with the laser is displayed, with the laser data overlaid two dimensionally on top of that view. The user can thus use a simple mouse interface to block out laser points coming from the skin of the subject. Note that this process need not be perfect—the matching process is designed to deal robustly with outliers.

To initiate the matching, we have several options. First, we have developed a simple graphical interface that can be used to roughly align the laser data with the 3D MRI skin model. This is done by selecting one of a small number of standard views, then roughly estimating the orientation of the subject's nose in the view. This is used to compute a very rough rotation of the laser data, which is then displayed on a series of three orthogonal 2D views, together with the MRI data. The user can further refine the initial transformation by rotating and translating the data in any of the three orthogonal views. This initial alignment does not need to be very accurate: rotational errors on the order of 20 degrees, and translational errors on the order of centimeters are permissible, since the subsequent matching stage is quite reliable at removing these misalignments.

If we do not want to rely on operator intervention, we can instead use an automated procedure to find the initial alignment. In this method, we first select a pair of widely separated laser points, and at each point, we estimate the surface normal, by a local least squares fit. We then search over all possible pairs of MRI surface points, at some subsampling, and use those pairs whose distance roughly agrees with the distance between the chosen laser points. For each pair of MRI points and the pair of laser points, we solve for the transformation that aligns the points and the surface normals at the two points, provided such a transformation exists. For those pairings of points with legal transformations, we apply the transformation to all of the laser points, and measure the least squares distance between the transformed laser data and the MRI skin model. We use this measure to rank order the possible alignments. For efficiency purposes, we hash the pairings of MRI points by distance, in a coarse-to-fine manner, thereby saving considerably on the computation required. We keep the n best transformations for use at the next stage. Note that we can accomplish the same constrained search by using triples of points without normal information, if desired.

For each selected alignment transformation, we execute the refinement processes described below.

3.2.2 Interpolated Refinement

We first refine the alignment of the two data sets by minimizing an evaluation function that measures the amount of mismatch between the two data sets. In particular, we sum, for all transformed laser points, a term that is a sum of the distances from the transformed laser point to all nearby MRI points, where the distance is weighted by a Gaussian distribution [17]. This Gaussian weighting roughly interpolates between the sampled MRI points to estimate the nearest point on the underlying surface to the transformed laser point. More precisely, if vector ℓ_i is a laser point, vector m_j is an MRI point, and $\mathcal{T}$ is a coordinate frame transformation, then the evaluation function for a particular transformation is

$$E_1(\mathcal{T}) = -\sum_i \sum_j e^{-\frac{|\mathcal{T}\ell_i - m_j|^2}{2\sigma^2}}. \tag{1}$$

Because of its formulation, the objective function is quite smooth, and thus facilitates "pulling in" solutions from moderately removed locations in parameter space.

In order to minimize this evaluation function we use the Davidon-Fletcher-Powell (DFP) quasi-Newton method [12]. This method requires an estimate of the gradient of the objective function, which is easily obtained in closed form. Solving this minimization problem yields an estimate for the pose of the laser points in MRI coordinates.

We execute this minimization stage with a multiresolution set of Gaussians. A broad Gaussian is used to allow influence over large areas, resulting in a coarse initial alignment, which can be reached from a wide range of starting positions. Then, narrower Gaussian distributions are used to focus on only nearby MRI points to derive the pose.

3.2.3 Detailed Refinement

Starting from the pose obtained with the interpolated refinement stage, we repeat the evaluation process, using a rectified least squares distance measure. We again use the DFP method to minimize the evaluation function:

$$E_2(\mathcal{T}) = \sum_i \min \left\{ d_{\max}^2, \min_j |\mathcal{T}\ell_i - m_j|^2 \right\} \tag{2}$$

where $d_{\max}$ is some preset maximum distance used to limit the impact of outliers. This objective function acts much like a robust chamfer matching scheme (e.g. [8]). The expectation is that this second objective function is more accurate locally, since it is composed of saturated quadratic forms.

We observe that while this refinement method gets very close to the best solution, it can get trapped into local minima in the minimization of E_2. To improve upon this problem, we take the pose returned by the above step and perturb it randomly, then repeat the minimization. We continue to do this, keeping the new pose if its associated RMS error is better than our current best. We terminate this process when the number of such trials that have passed since the RMS value was last improved becomes larger than some threshold. The final result is a pose, and a measure of the residual deviation of the fit to the MRI surface.

3.3 Pixsys Data Processing

The Pixsys 3D tracking system is a self-contained system which can be used to generate 3D coordinates of LEDs in the system's field of view. The system is based on a straightforward triangulation process, in which a point is observed in three cameras, whose positions and orientations are known with respect to one another. By identifying the image projection of the same point in each camera, one can back out the projection geometry to determine the position of the point in scene coordinates. To achieve simple and robust identification of the same point in each image, infrared light emitting diodes (IR LEDs) are used, and the pulsing of each diode is synchronized to the imaging process. In this way, there is no possible ambiguity in identifying corresponding image points, and reliable estimation of 3D point positions of the LEDs is possible.

This active triangulation system is highly reliable, with an accuracy of about 1 mm at the 1 m standoff from the 3 linear cameras which we normally use. By mounting three LEDs to a rigid object we can track the object's pose (position and orientation) in three-space. Using two LEDs allow us to solve for five degrees of freedom (all but the twist angle around the axis connecting the two LEDs). Using more than three LEDs provides us with some redundancy, allowing for a least-squares pose solution and wide range of motion in which some LEDs may be blocked from view. We use the Pixsys system for tracking head motion (using five LEDs taped to the head) and localizing the position and orientation of the TMS probe (using two LEDs mounted to the probe).

3.3.1 Head Motion Tracking

In order to track the head motion we record the position of the LEDs taped to the patient's head at the time we perform the laser data/MRI registration. This reference position provides a basis for tracking the head. When the TMS probe is stimulated we record the new position of the head-mounted LEDs and compute the transform necessary to return the head to its reference position. This transform is applied to the position/orientation of the TMS probe at the time of the corresponding stimulation in order to apply the laser data/MRI transformation.

Since we may have up to five LEDs to track we use a least-squares solution for the tracking transform. On the subjects on which we have tested this procedure we taped the LEDs to bony surfaces on which little skin movement (relative to the underlying bone) is expected. One LED was taped to the bridge of the nose, two to the sides of the lower forehead, and two to the sides of the upper forehead. We need at least three LEDs visible at all times.

3.3.2 TMS Probe Localization

In order to use the Pixsys data obtained for localizing the TMS probe we perform two calibration steps: calibrate the TMS probe to identify the position of the coil's magnetic field hot spot relative to its Pixsys coordinates and calibrate the Pixsys coordinate system to the laser coordinate system. In order to calibrate the TMS probe itself we mount two LEDs on a rigid rod which is rigidly bracketed to the center of the figure-8 coil. The rod is connected to be perpendicular to the coil such that the hot spot of the coil is along the same line as the two LEDs. Experimentation on the exact position and shape of the hot spot relative to the coil is still on-going. The Pixsys system is then calibrated to output the position where the line formed by the two LEDs intersects the surface on which the underside of the coil is resting along with the orientation of that line.

In order to calibrate the Pixsys coordinate system to the laser coordinate system we use a Pixsys probe to record points on a calibration gauge which have known laser coordinates. Given the correspondences between Pixsys and laser points we solve for the transformation between the two coordinate systems. Since the three linear Pixsys cameras and laser scanner (laser and camera) are all mounted on the same rigid bar, this calibration remains fixed.

3.3.3 Alternative methods

We are also currently investigating the possibility of using a more passive system to track both head position and probe position and orientation. This method [10] utilizes some simple visual markers placed on the objects of interest, which are then tracked reliably and rapidly by observation in a single camera. The advantage of this system is that the passive markers are less intrusive than the LEDs, and that tracking can in principle be done by any camera in any location, rather than relying on the Pixsys cameras.

3.4 Functional Brain Mapping

We combine the registration and tracking data to obtain the functional brain mapping as follows. We have computed the following transforms:

- $\mathbf{P_L}$ — transformation from Pixsys coordinates to laser coordinates; computed from *a priori* calibration.
- $\mathbf{L_M}$ — transformation from laser coordinates to MRI coordinates; computed from dynamic registration procedure.
- $\mathbf{H_r^t}$ — transformation of head from time t to reference position at time 1, computed from calibration of the LEDs at time t to the LEDs at time 1.

We have also collected the following TMS data:

- C_p^t, C_o^t — position and orientation of TMS coil at time t, $t = [1, T]$, in Pixsys coordinates.
- R_j^t — measured response j to stimulation t. Multiple responses are usually collected such as from several different hand, arm, and shoulder muscles.

In order to compute the brain mapping we need to map the TMS responses to the brain surface using the measured coil positions/orientations and associated transformations. To perform this mapping, for each stimulation t, we process those MRI surface points, $S[i]$, that are sufficiently close to $\mathbf{L_M P_L H_r^t} C_p^t$ to have been possibly stimulated by the pulse. Note that closeness here can be determined in a number of ways. We can simply use the transformed position of the tip of the probe, and gather all MRI points within some predefined distance. Alternatively, if we have a detailed model of the shape of the magnetic field generated by the probe, we can use this, together with information about the orientation of the probe, to select the relevant MRI points. For now, we are simply using Euclidean distance from the position of the probe to select $S[i]$.

For each such $S[i]$ we compute the distance, $d^t[i]$, to the line defined by the point $\mathbf{L_M P_L H_r^t} C_p^t$ and the orientation $\mathbf{L_M P_L H_r^t} C_o^t$. We are currently using a Gaussian weighting function proportional to that distance to "spread" the response R_j^t to the points $S[i]$. The purpose of this (simple) weighting function is to interpolate across the stimulation to obtain a smooth and visible map. If we let $map_j^t[i]$ represent the mapping of response j to stimulation t on the selected surface, then $map_j^t[i] = G(d^t[i], \sigma) R_j^t$, with G being the Gaussian weighting function. We then let $map_j[i]$, the composite mapping from all stimulations, be the maximum $map_j^t[i]$ over all t, which are then normalized over i.

While we generally are most interested in the mapping of the TMS responses to the cortical surface of the brain, we may perform this mapping onto to any underlying segmented surface. The white matter surface is often useful since it highlights some of the major sulci. The skin surface itself is also sometimes useful to examine coverage range of stimulations.

4 Test Results

We have performed the TMS brain mapping on two subjects thus far, one of whom was a neurosurgery patient. Although both mappings were positively reviewed by radiology and neurology specialists, it is difficult to validate the results. A qualitative solution is to validate the results in the operating room in the case of craniotomy surgeries. In the case of the neurosurgery patient, the patient had a tumor on the surface of the brain near the right motor and sensor strips. We mapped part of the motor cortex by collecting muscular responses of the index finger, forearm, and biceps muscles. These responses were mapped to the surface of the brain as well as to the white matter. Figure 3 shows the brain surface overlaid with the TMS probe positions/directions used. The color coding of the TMS probing vectors and surface indicates the strength of the finger muscle response. In this visualization and the remaining ones, the mapping of the other arm muscles looked very similar to the finger muscle.

Figure 4 shows the finger muscle response overlaid on the brain surface. The hot spot identifies the location of the motor strip—even with just this one muscle mapped, medical practitioners can identify the motor strip location based on physiological knowledge on how the motor cortex is organized in terms of muscle control groups. This mapping was exploited by the surgeons to appropriately plan the tumor excision. Furthermore, once in surgery, our results were validated using conventional electrical stimulation made directly on the surface of the brain. According to the surgeons, our functional mapping was localized exactly in the

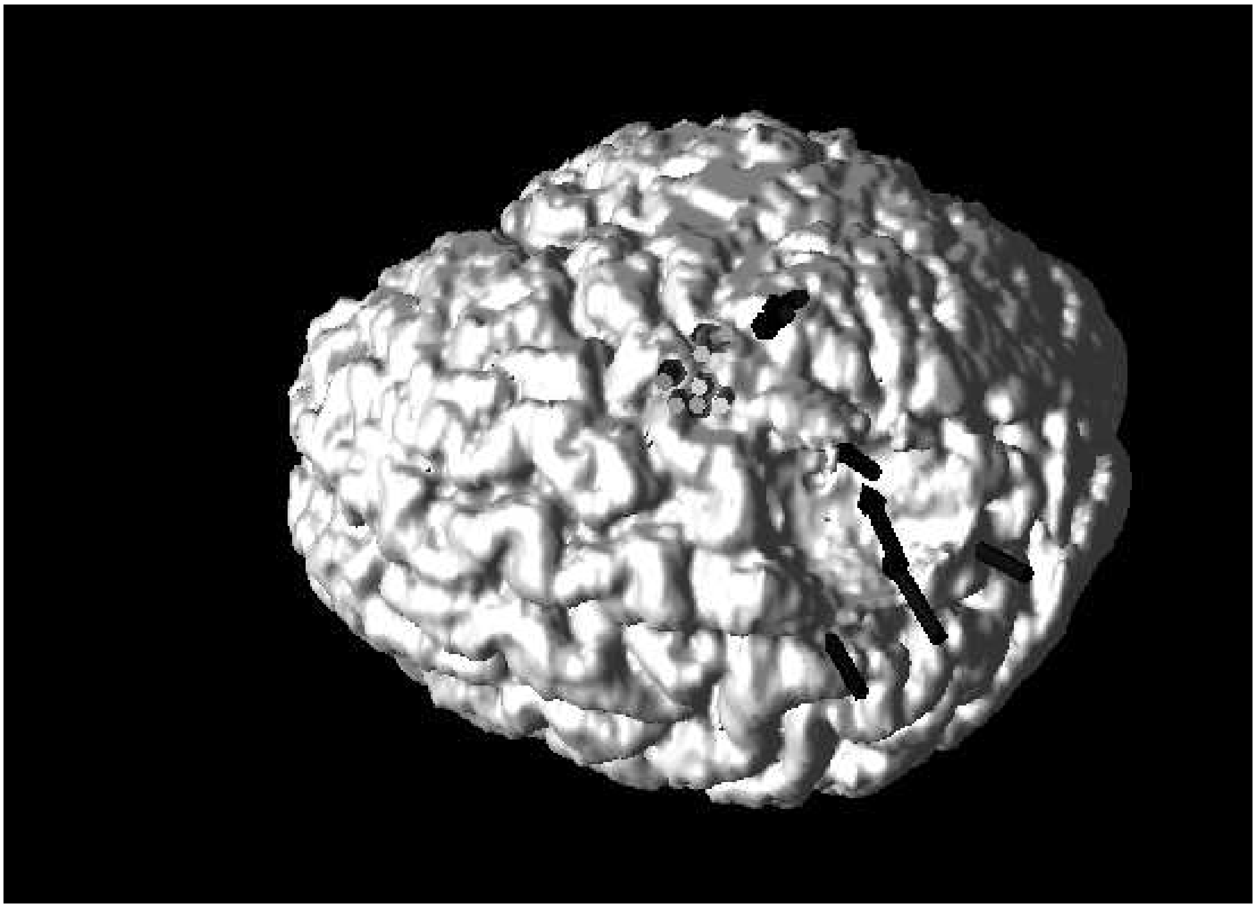

Figure 3: Patient's cortical surface overlaid with TMS probe positions/directions. Color coding indicates finger muscle response: black = no response, green-to-yellow-to-red = minimal to maximum response obtained.

right place.

For reference, we also generated functional maps on the surface of the white matter, Figure 5, and skin, Figure 6. The presence of the hot spot on a gyrus of the white matter further increases the confidence of the correct localization of the motor map. It is interesting to note that the mapping on the skin surface is more diffuse than the brain or white matter mapping, a result of several stimulations originating from different points, but intersecting very near each other in the brain.

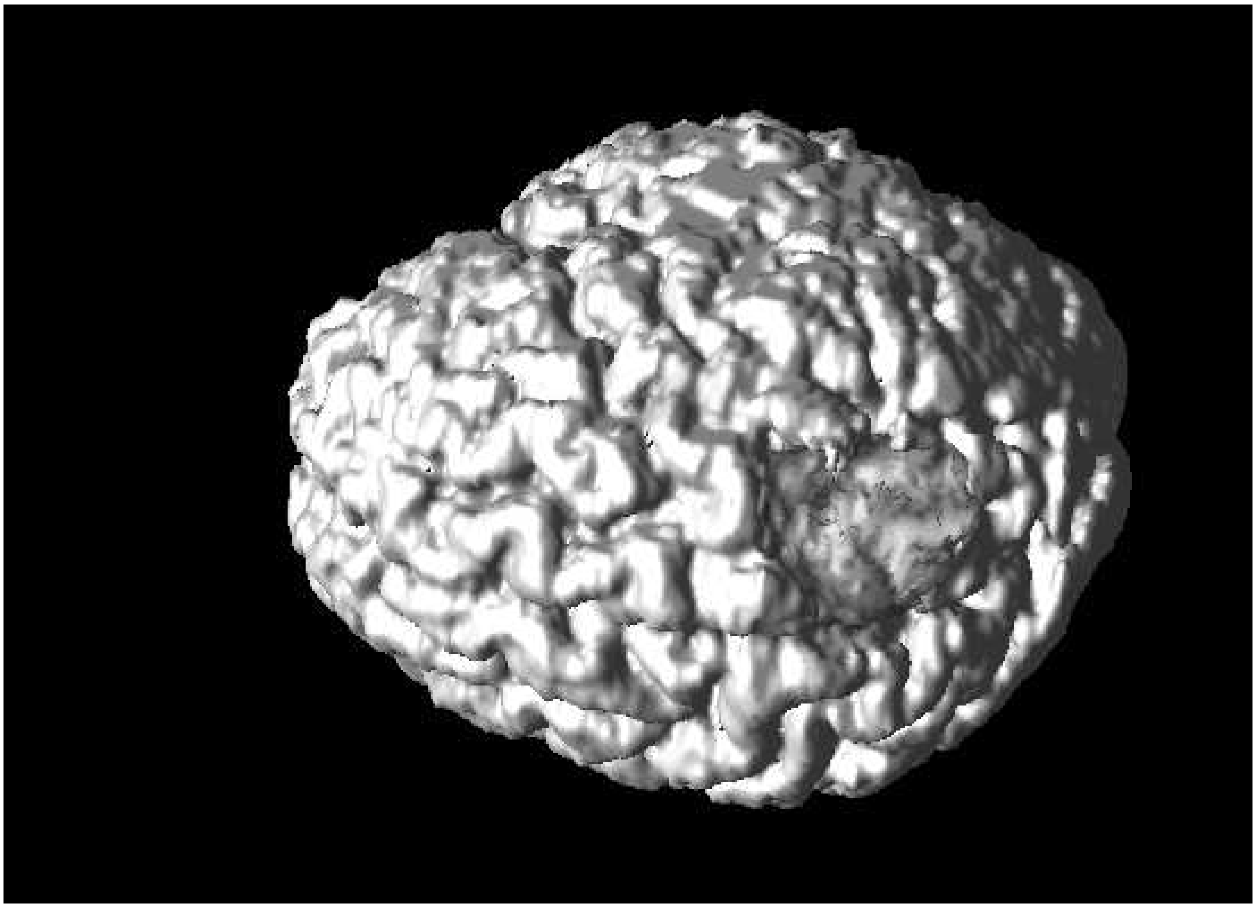

Figure 4: Patient's cortical surface overlaid with functional mapping of index finger control. Tumor is shown as well. Color coding of muscle response: green-to-yellow-to-red = minimal to maximum response obtained.

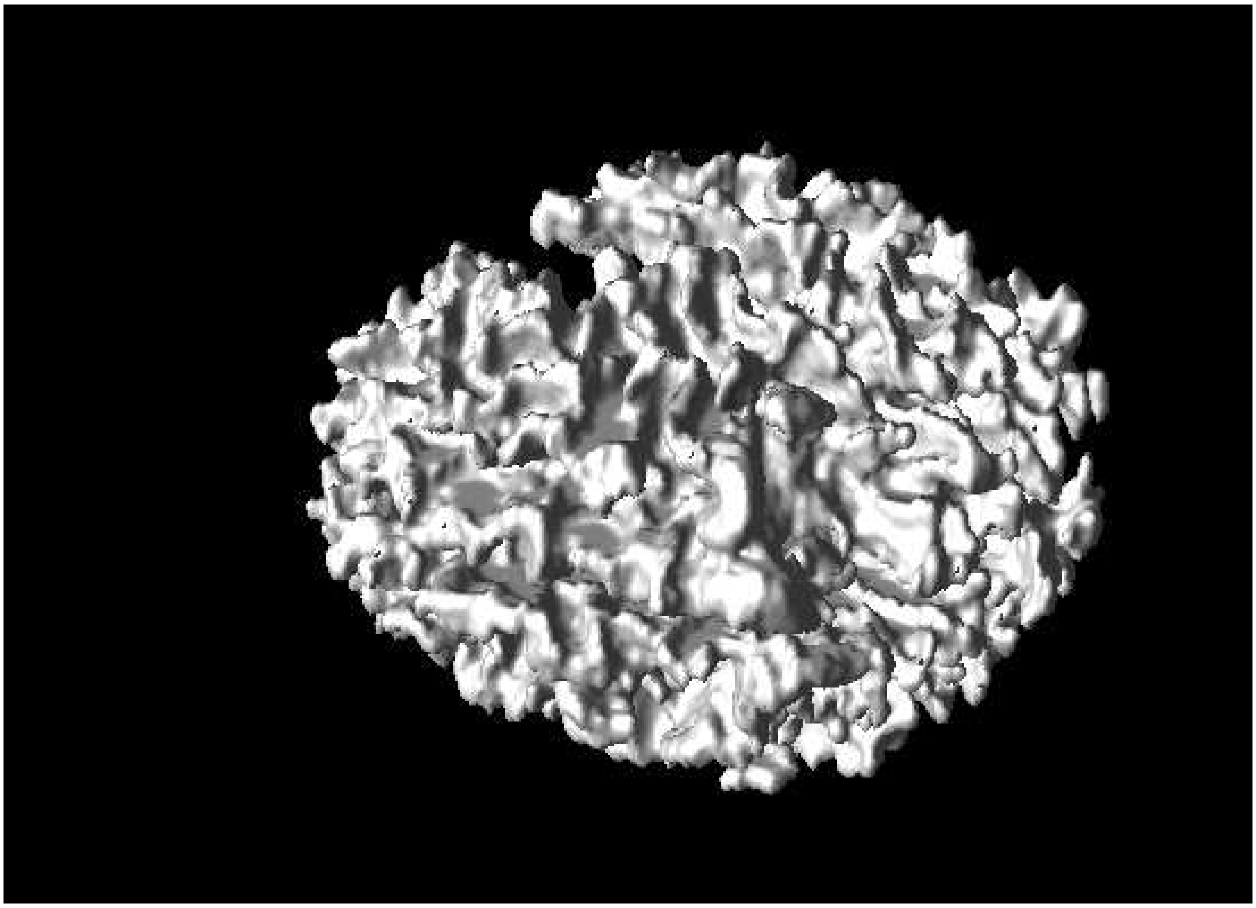

Figure 5: Patient's white matter surface overlaid with functional mapping of index finger control. Color coding of muscle response: green-to-yellow-to-red = minimal to maximum response obtained.

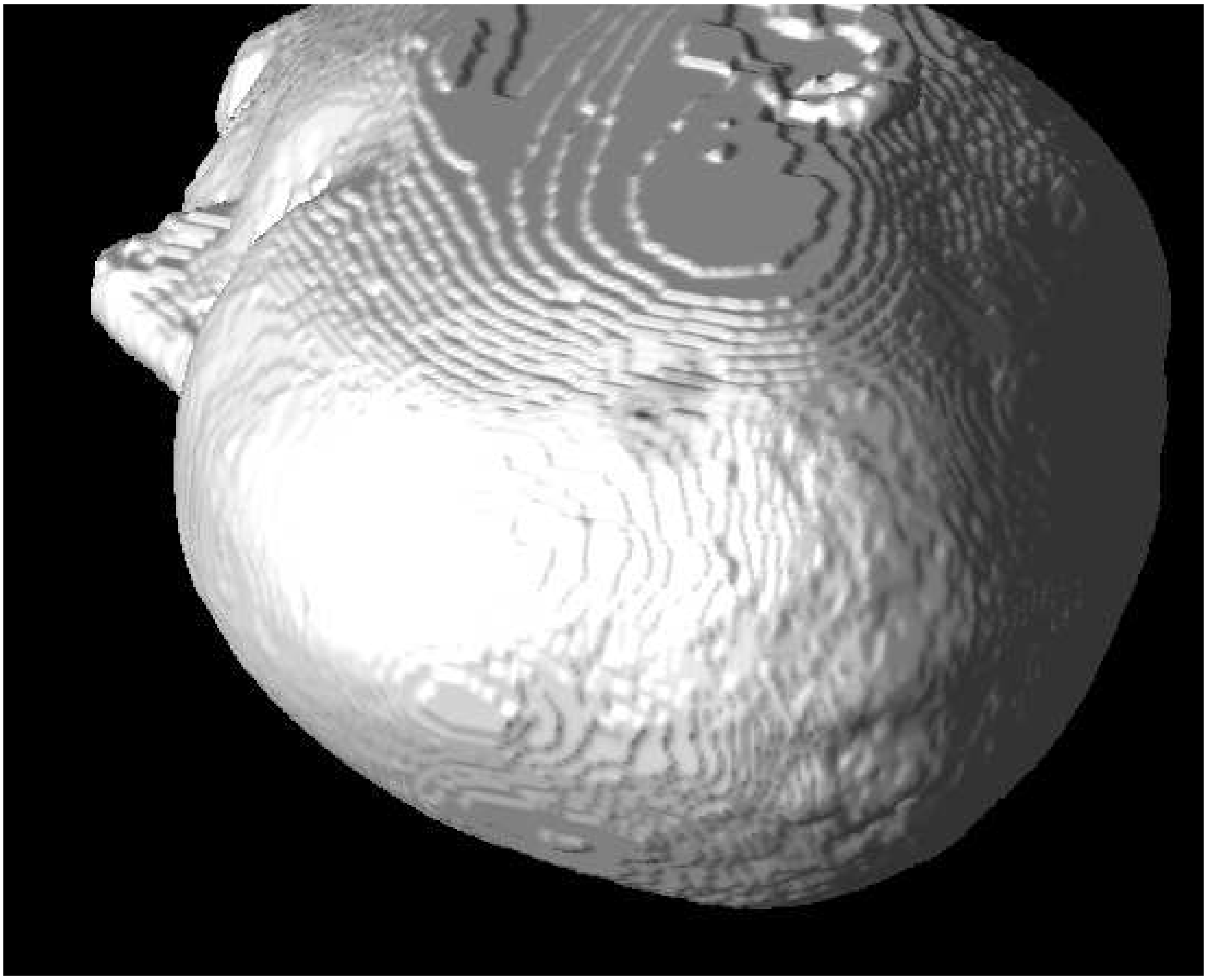

Figure 6: Patient's skin surface overlaid with functional mapping of index finger control. Color coding of muscle response: green-to-yellow-to-red = minimal to maximum response obtained.

5 Related Work

Several other groups have reported registration methods similar to ours, but for different applications. Pelizzari et al [11] have developed a method that matches retrospective data sets, (MRI, CT, PET), to one another. This work also uses a least squares minimization of distances between data sets, although with a different distance function and with more operator guidance required. Lavallee and Szeliski [14] also perform a least-squares minimization of a distance function to match data sets. Here, the distance is weighted by an estimate of the inverse variance of the measurement noise, and a Levenberg-Marquardt method is used to find the minimum. Once an initial solution is found, points with large errors are removed and the minimization is repeated to refine the pose. Thirion et al [7, 15] performs automatic rigid registration of 3D surfaces by matching ridge lines which track points of maximum curvature along the surface. Related registration methods also include [2, 13, 18].

6 Potential Applications of this Functional Mapping

In our discussion above, we have used the example of motor strip stimulation to illustrate our method for registering transcranial magnetic stimulation responses to segmented reconstructions of a patient's brain. There are some natural applications that follow from this scenario.

- **Identification of motor cortex for surgical planning.** Our first demonstration of this technique, as illustrated in the earlier figures, involved mapping out portions of a neurosurgical patient's motor strip, and providing the registered mapping, overlaid onto a segmented MRI reconstruction, to the surgeon for surgical planning. In particular, the surgeon used the registered reconstruction to plan access to a tumor for removal, while avoiding critical structures.

- **Surgical guidance.** Not only is the identification of motor strip useful for planning processes, it can also serve a useful role during the actual surgery. In the case cited above, during the surgical procedure itself, enhanced reality visualizations of the MRI model, registered and overlaid on a live video view of the patient (e.g. [4, 5, 6]), were used to help guide the surgical procedure. This included both guidance for tumor removal while avoiding critical structures and guiding the placement of sensors onto the exposed cortical surface for direct stimulation of the motor cortex. Such stimulation serves both as a check of the noninvasive mapping of cortex, and as a means of monitoring patient status during the surgery.

While mapping of motor cortex is a good motivating example for this approach, many other applications may benefit from the ability to relate noninvasive magnetic stimulation of the brain to MRI reconstructions of the neuroanatomy:

- **Neuroscience.** The method provides the potential for relating functional properties to specific locations in the brain. Examples include detailed mappings of motor or sensory cortex across subject populations. Such mappings could be used in building anatomical atlases, measuring deviations in location, and potentially serving as a base for seeking correlations between functional properties and disease processes. Such functional mapping could extend to other modalities, such as speech and vision, by designing psychophysical protocols that utilize either stimulation or inhibition of percepts via transcranial magnetic stimulation.
- **Diagnostic tools.** The ability to relate induced magnetic stimulation response to anatomical models potentially provides the ability to identify and isolate damage to cortical tissue in a noninvasive manner.
- **Therapy.** Some work has already begun on the utility of TMS as a therapeutic tool [1], in the treatment of depression, akinesia, and related areas. By providing registration tools, we may enable a practitioner to use graphical models and real time registration of a probe to those models and the patient to accurately direct stimulation to desired targets.

7 Summary

We have reported on an initial system combining 3D registration and 3D tracking techniques to generate functional brain maps from transcranial magnetic stimulation responses. In limited testing thus far the system has achieved accurate results which indicate promise to a wide of applications requiring low cost and portable brain mapping. In addition to surgical planning and guidance, this work can benefit growing research efforts into understanding the brain and learning about neurological diseases.

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