A combined Surface And VOlumetric Registration (SAVOR) framework to study cortical biomarkers and volumetric imaging data

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Abstract. Constructing a one to one correspondence between whole brain MR image scans is a problem of critical importance in neuroimaging analyses. We present a framework to combine the strength of both surface-based and volumetric-based analyses for consistent, bijective data transfer between brain coordinate systems.

1 Introduction

Constructing a one to one correspondence between whole brain MR image scans is a problem of critical importance in neuroimaging analyses [1]. This underlies the ability to transform several types of data that are acquired or computed in the native brain's structural coordinates to a common central template brain space [2]. One type of data to transform is two-dimensional cortical surface-indexed measures such as cortical thickness, curvature, sulcal locations/depths or projected functional activation maps on the surface. A second type of data to be transformed are the 3D volumetric Cartesian grid-indexed measures such as structural images, or 3D functional activation maps from fMRI. Comprehensive neuroanatomical analysis of these two kinds of data necessitates that the distinct surface-indexed and Cartesian grid-indexed coordinate systems be consistently transformed bijectively between the brains being registered.

There now exist several volume to volume registration (VVR) methods that attempt to register brain images by minimizing the overlap of grayscale MR image intensities; these give good results for most internal areas of the brain but cannot handle the thin and highly convoluted nature of the cerebral cortex. On the other hand, surface to surface registration (SSR) methods are able to preserve cortical topology and still give good registrations, however, either these lead to large distortions in the cortical mesh, or require quality controlled point or curve landmarks, the variability in natural occurrence or the uncertainty injected in the labeling process of which also influences heavily the quality of this registration. More generally, these SSR methods give cortical surface correspondence, but these are not easily extendable to construct a volumetric matching between

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the spaces. Hence, the important bridge that should exist between the two methods is not yet available. Instead, researchers have tended to use one or the other type of data and the corresponding registration, and have made comparisons to justify which one is suitable in what conditions [3], [4] and for surface-indexed measurements, generally conclude that surface based registrations offer better alignment than volumetric registration methods [5]. Some hybrid methods leverage VVR to bootstrap SSR [6]; others use SSR to initialize VVR [7,8] improving cortical alignment; however, these methods still use either VVR or SSR alone as the final registration.

Instead of choosing between grid-indexed or surface-indexed data while studying neuroanatomy, a better solution is a consistent combination of both of these methods to reach a comprehensive neuroimaging analyses framework. What is needed is a method that performs accurate whole brain matching such that volumetric and surface data can be consistently mapped to a given template space. The construction of such a framework, that yields consistent mapping between cortical surfaces and volumetric domains, is the focus of this paper.

2 Proposed Combined Surface and VOlumetric Registration (SAVOR) framework

The neuroanatomical volumetric coordinate system Ω_i in the brain scan I_i of the i^{th} brain consists of the Cartesian grid-based coordinates indexing volumetric subdomains $V_i \subset \Omega$, and additionally, imbedded in Ω_i are the 2-dimensional surface manifolds S_i representing the whole brain cortical surface. Our method for constructing a whole brain and surface bijective and accurate correspondence relies on accurate VVR, followed by a surface constrained optimal approximation of the VVR using SSR. This process is outlined in Figure 1.

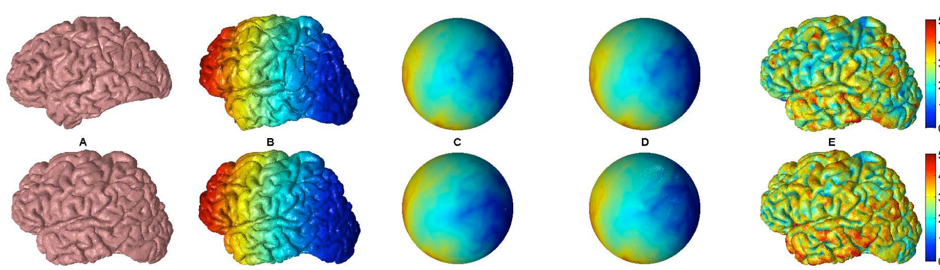


Fig. 1. Framework Pipeline. (A) Two pial surfaces (B) Upper surface registered to lower surface via image registration, with identity coordinate functions overlaid (C) surfaces mapped to the spherical domain via FreeSurfer mapping with coordinate functions overlaid (D) surfaces on spherical domain with function on lower surface mapped to that on upper surface (E) Cortical thickness values for upper and lower brains displayed on the domain of the lower brain.

Whole brain smooth and invertible VVR The first step (Figure 1(B)) is to use an accurate whole brain VVR method construct a dense volumetric correspondence $\varphi_{V(i,j)} : \Omega_i \to \Omega_j$. This mapping should accommodate the variability of subcortical structures, as well as do a reasonably good job, although not necessarily perfect, of aligning cortical surfaces. This mapping will be used directly for transforming grid-index data. Additionally, this mapping is used as a reference registration that the following SSR will approximate.

Smooth and invertible SSR The second step is to construct invertible mapping $\varphi_{S(i,j)}$ between the two surfaces $S_i \in \Omega_i$ and $S_j \in \Omega_j$, proceeding from this dense volumetric mapping $\varphi_{V(i,j)}$ using VVR in step 1. Using the $\varphi_{V(i,j)}$ obtained, get a transformed surface $S_{i'} = \varphi_{V(i,j)}(S_i) = \{\varphi_{V(i,j)}(x), \forall x \in S_i\}$; this now lies in the domain Ω_j. The transformed surface $S_{i'}$ is expected to be close to the target surface S_j but not exactly matched. To achieve an accurate surface to surface correspondence, we need to construct a second mapping, $\varphi_{Si',j}$, between $S_{i'}$ and S_j to be used to ultimately construct the mapping from S_i to S_j. This mapping should approximate $\varphi_{V(i,j)}$ as closely as possible, under the constraint of precisely, aligning the surface domains. We propose the following three steps.

1. Define suitable functions indexed on the surfaces $S_{i'}$ and S_j that should be registered (Figure 1(B)),
2. define a smooth and invertible mapping of each surface to a common intermediate surface where these registrable functions defined in (a) are then transferred (Figure 1(C)),
3. compute a registration of these transformed functions on the common intermediate surface domain (Figure 1(D)).

The functions we choose to construct for registration are the coordinate identity map on $S_{i'}$ and S_j, such that $C(S_{i'}(x)) = x$ and $C(S_j(x)) = x$. These are then mapped to a common surface domain using a surface homeomorphic mapping $\varphi_{S(i',0)}$ and $\varphi_{S(j,0)}$ for each surface $S_{i'}$ and S_j to a common space S_0 along with the coordinate functions from both surfaces. In this common domain, perform a multi-dimensional registration of the mapped coordinate functions from the two surfaces, producing a mapping $\varphi_{S(0)}$. This mapping between surface coordinate identify maps transferred to a common domain in effect minimizes the distance between corresponding original surface points. Once these coordinate map functions are matched on the common domain via $\varphi_{S(0)}$, then an invertible mapping between the surfaces $S_{i'}$ and S_j is created by composition. By further composition with mapping between Ω_i and Ω_j, the final invertible map that preserves topology between the surfaces S_i and S_j is given to be:

$$\varphi_{S(i,j)} = \varphi^{-1}_{S(j,0)} \circ \varphi_{S(0)} \circ \varphi_{S(i',0)} \circ \varphi_{V(i,j)} \tag{1}$$

Interpolation and Transfer of Coordinate-indexed Data The third step is interpolation of surface-indexed data to a common domain; using the surface mapping $\varphi_{S(i,j)}$ to transform the surface-index data. In the general case, where the surface-indexed functions are continuously defined on the surface domains, and all the mappings are continuous mappings between domains, there is no need for interpolation. However, implementations of this proposed framework may use sparse representations of the domain (as in the triangulated mesh-based surfaces in the illustrative example below). In this case, interpolation is necessary, as the point $x' \in S_j$ corresponding to point $x \in S_i$ will in general not lie on a point where the data to transform, F_{S_j}, is defined. This final interpolation step completes the transfer of surface-indexed functions between surfaces.

3 Our Implementation of the Proposed Framework

In implementing the framework, several algorithmic components must be selected: the VVR method for volumetric image registration, the homeomorphic mapping to bring surfaces into to a common domain, the method of registration of coordinate functions on this common domain and finally, the method of interpolation. Our choice of these components and the selection rationale follow.

Data T1-weighted MR images (N=8 subjects), each scanned at 2 time points were taken from the ADRC dataset [9]. Subjects having CDR 0 score at baseline and CDR 0.5 at followup were chosen. Three types of comparison were implemented: 1) transforming cortical surface-index data from each subject to a common template (cross-sectional); 2) transforming data from the followup scan for each subject to compare to the baseline data (longitudinal); and finally a combined approach to compare these longitudinal results across subjects in a common template. For each brain, the cortical pial surface, corresponding to Ω_{S_i}, was extracted using FreeSurfer [10]. Biomarkers defined on these surfaces include curvature measures generated by FreeSurfer, and our in-house implementation of cortical thickness measurements measured using Laplacian streamlines [11].

Image Registration Accuracy of the VVR registration is important to the quality of the final mapping; thus a high-dimensional nonlinear VVR method was chosen. Specifically, VVR registration between MR images I_i and I_j was carried out using a multi-structure extension of a high dimensional nonrigid diffeomorphic (smooth and invertible) transformation [12] that incorporated channels for MR image intensity, subcortical binary segmentation and volumetric cortical segmentations to concurrently guide the registration. The simultaneous usage of the automated segmentations as separate cost terms allows the overall MR image matching to better avoid local minima, while providing flexibility in setting weights for different channels to emphasize certain properties, such as emphasizing smaller structures, or deemphasizing less reliable channels. The use of 34 cortical parcellations, as listed in [13] and computed using FreeSurfer, allows for higher accuracy in the cortical mantle. Parcellations were voxelized, then smoothed to eliminate the sharp boundaries, and used in guiding the volumetric registration. This multi-structure framework is observed to transform the surfaces to within 1.5 mm of template surface in cross-sectional registration.

Homeomorphic Surface to Common Domain Mapping To apply the second step for SSR, we map the surfaces to a common spherical domain. The specific mapping to a spherical domain is drawn from an intermediate step in the FreeSurfer segmentation, and is described in detail in [14]. In brief, each cortical surface is first inflated to a smooth surface and then projected on to a sphere. The surface is then evolved to minimize metric distortion, including spherical folds introduced by the projection.

Registration of Functions on Common Domain The registration of the coordinate functions on the spherical domain is performed using Spherical Demons registration [15]. The Spherical Demons algorithm uses representations of mappings, and regularizations that are particularly suited to fast computation on the spherical domain, and know to perform well on cortical surfaces.

Interpolation Each cortical surface was represented by a triangular mesh, and surface-indexed function was given on the vertices. Additionally, the homeomorphic mappings to the common domain are defined only at the vertices, extended via linear interpolation along the entire face, and for interpolating function value from neighboring vertices. This linearity allows us to compute the interpolation weights from a discretization of the spherical common domain.

4 Results

Using our multi-structure VVR registration, the dice coefficients found for subcortical structure mappings are shown in Figure 3(b). For the subsequent SSR registration of the cortical surface manifolds between the baseline scans to a common template image(I_T)/surface(S_T) and from baseline scans to the followup scan, we transformed all baseline surfaces S_i and corresponding baseline FS labels F_i to the template domain. We compute, for each vertex v on the template surface, the surface registration error map (SREM) by comparing the transformed labels $F_{i,T}$ to the template label F_T via $\delta_{(F_T=F_{i,T})}$ giving value 1 for a mismatch, and 0 otherwise. Across N subjects, we define the probability of registration error to be the average SREM or ASREM via $P(error(v) = 0) = (1/N)\sum_{i=1}^{N} \delta_{(F_T=F_{i,T})}$. The ASREM, shown in Figure 2 (a) shows the average registration errors across our 8 subjects, and panel (b) shows the individual SREMs in matching to template space and (c) shows the SREMs for baseline to longitudinal matching. Using these registrations, we transformed the cortical curvature and mantle thickness functions longitudinally to baseline, and further, cross-sectionally to template. Longitudinal cortical thickness change, normalized for inter-scan time for each subject, is shown in Figure 4(a), and mapped further to a common template, as in Figure 4(b). Pearson's linear correlation, comparing the overlap of values transformed from followup to baseline, was done using our framework and using solely FreeSurfer's cortical surface registration [14], is shown in Figure 3(a). Dice metrics for alignment of cortical parcellations are given in Figure 3(b).

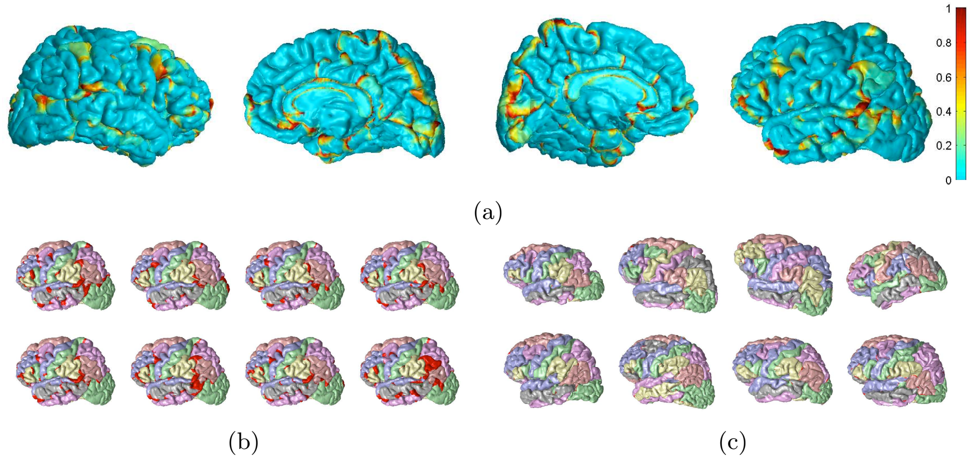


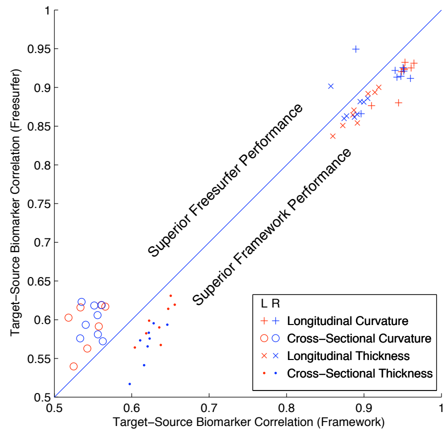
Fig. 2. The average surface-registration error map (ASREM), shown as a color map (a) on the template surface, quantifies the variability in label overlaps after registration, capturing the variability in folding patterns accuracy in the assignment of labels and errors in registration. (b) shows the individual cross-sectional registration error (red: labels were not matched), and (c) shows the longitudinal registration errors.

5 Discussion and Conclusion

While direct surface registration has many proponents, there are limitations to the types of data that can be expressed on surfaces, and to the quality of registration achievable by directly mapping two surfaces. Furthermore, this step necessarily assumes that there is no error in the definition of the surface. Hence, the 'correct' registration may lie outside of the space of considered registrations in direct SSR. In the SAVOR framework, the correct registration would lie within the space of considered registrations, and errors in surface definition would be accounted for by the manifold registration on the common domain.

Our suggestion to use an arbitrary homeomorphic mapping to a common domain as an intermediate stage for mapping surfaces needs some justification. In the general sense, the mapping may be arbitrary; however, this requires that the manifold registration must also be capable of producing arbitrary mappings. In practice, manifold registration algorithms use regularization techniques that limit the space of achievable manifold registrations, limiting the choice of acceptable homeomorphic mappings. The Spherical Demons algorithm was used with the FreeSurfer spherical mapping based on evidence that this registration was powerful enough to align cortical surfaces with this mapping [15].

Our demonstrated implementation performed better at overlaying longitudinal cortical thickness and data mapping. For longitudinal and cross-sectional mapping of thickness and curvature, our implementation performed better except for cross-sectional curvature mapping. This may be attributed to the under-



(a)

Gyri	Cross-sect.	Long.
Precentral	.94(.01)	.99(.01)
Postcentral	.93(.02)	.99(.01)
Sup. Frontal	.94(.03)	.99(.01)
Sup. Temporal	.91(.03)	.99(.01)
Inf. Temporal	.86(.04)	.99(.01)
Sup. Parietal	.92(.02)	.99(.01)
Inf. Parietal	.87(.08)	.99(.01)

Structure	Cross-sect.	Long.
White Matter	.66(.03)	.80(.12)
Ventricle	.85(.04)	.91(.02)
Thalamus	.85(.04)	.92(.02)
Caudate	.71(.06)	.83(.07)
Putamen	.78(.04)	.90(.02)
Hipocampus	.73(.06)	.85(.05)
Amygdala	.73(.07)	.86(.05)

(b)

Fig. 3. (a) Comparison of our framework vs. FreeSurfer cortical registration. Points below the line correspond to mappings where our framework had higher correlation between source and mapped target data. (b top) Mean dice metrics for selected surface parcellations. (b bottom) Mean dice metrics for selected subcortical structures

lying mechanism of the FreeSurfer data mapping which includes a minimization of intersubject curvature in its cortical registration.

In conclusion, we have introduced a comprehensive framework for bijectively transporting both volume-indexed and surface-indexed data using a powerful combination of image-based and surface-based registration (SAVOR). We demonstrate the use of this framework for assessing general trends in longitudinal studies, and show results from one such assessment. This work simplifies the use of cortical surface biomarkers for proponents of image-based registration; enables combined surface and volume based data-mapping; and provides a new means for evaluating image-based registrations relative to surface-based registrations. However, the framework relies on a set of subcomponents, and the full potential of this framework can be realized with optimized combination of each of the subcomponents.

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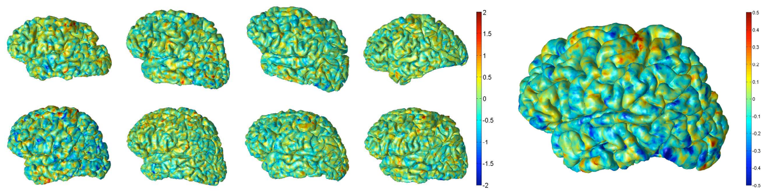

(a) (b)

Fig. 4. (a)Longitudinal change in cortical thickness overlaid on the baseline surface for left hemisphere of all subjects. (b)Mean longitudinal change in cortical thickness mapped on to the common template. These thickness maps have not been smoothed.

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