Hippocampal Morphometry in AD with Surface Fluid Registration and Multivariate Tensor-Based Morphometry

Yalin Wang, Yuting Wang, Arthur W. Toga, Paul M. Thompson

Introduction:

Hippocampal morphometry is increasingly used in studies of Alzheimer's disease, mild cognitive impairment, and schizophrenia, with several recent approaches modeling the hippocampus as a 3D parametric surface mesh (Morra et al. 2009, Styner et al. 2004, Bansal et al. 2007). However, a major question in these analysis is how to align corresponding regions of the surface across subjects, and what surface-based statistic to analyze (distance to a medial curve, surface metric tensors, or some spectral measure from e.g., the Laplace-Beltrami expansion of the surface). Here we show how the mutual information (MI) method may also be used to drive a diffeomorphic fluid flow that is adjusted to enforce appropriate surface correspondences in the surface parameter domain. Since they generate diffeomorphic mappings, conformal and fluid mappings are composed to generate 3D shape correspondences that are diffeomorphic (i.e., smooth one-to-one correspondences across subjects). We then assessed whether multivariate tensor-based statistics, or local statistics based on its eigenvalues, gave greater effect sizes than we previously obtained in a prior study of hippocampal surface differences between 12 individuals with AD and 14 matched healthy control subjects (Thompson et al., 2004).

Methods:

Hippocampal surfaces were manually traced on 3D MRI scans for greatest accuracy, and converted to 3D parametric meshes (Thompson et al., 2004). We then induced conformal coordinates on each surface (Wang et al., 2007), and computed a map of the conformal factor and mean curvature (Figure 1), which uniquely determine a closed surface, up to a rigid motion. The mean curvature was computed from the derivatives of the conformal factors, instead of the three coordinate functions and the normal, to reduce the effects of noise in the surface.

To nonlinearly register the 3D surfaces, we compute intrinsic geometric features from the conformal mesh and align them in the parameter domain with a fluid registration technique. Using conformal mapping, we essentially convert the surface registration problem to an image registration problem. A diffeomorphic surface-to-surface mapping is then recovered that matches surfaces in 3D. Using the chain rule, we express the gradient of the mutual information between surfaces in the conformal basis of the source surface so that the updated parameterization remains conformal. After the cross-subject mappings were computed with one target surface selected, we examined shape differences using the eigenvalues of the surface deformation tensor, and using log-Euclidean metrics (Arsigny et al., 2006), which allow multivariate statistics on the tensors to be computed easily using standard Euclidean formulae. We applied Hotelling's T^2 test to the log-transformed surface deformation tensors.

Results:

Synthetic Surface Results. Figure 2 shows a synthetic surface example. A pair of simple S-shape surfaces was generated. Corresponding 2D images were generated based on the sum of the local conformal factor and the mean curvature, expressed in conformal coordinates. The locations of the highest and lowest intensities are different (shown by horizontal stripes). Using surface-based fluid registration, in the last image, the obtained horizontal line positions demonstrate improved matching between features lying in the two surfaces.

Hippocampal Surface Morphometry in AD. For hippocampal modeling, we leave two holes at the front and back of the hippocampal surface, representing its anterior junction with the amygdala, and its posterior limit as it turns into the white matter of the fornix. Thus it becomes an open boundary genus zero surface, i.e. a cylinder. Figure 3 illustrates our experimental results on a group of hippocampal surface models extracted from 3D brain MRI scans of 12 individuals with AD and 14 matched healthy control subjects (Thompson et al., 2004). With surface-based fluid registration and multivariate tensor-based morphometry, we detected large areas with statistically significant group differences in the surface parameterization tensor, which is a measure of to the relative surface area for hippocampal subregions in disease versus normality. In Figure 4, the cumulative distribution function of the p-values observed for the contrast of patients versus controls is plotted against the corresponding p-value expected under the null hypothesis of no group difference. We note that the deviation of the statistics from the null distribution generally increases with the number of parameters included in the multivariate statistics; statistics on the full tensor outperfored scalar summaries of the deformation based on the eigenvalues.

Conclusions:

We present a unique mutual-information based method to match intrinsic surface geometric features in the 2D parameter domain. Results on synthetic data and comparing AD patients with matched controls show the effectiveness of the proposed method. Ongoing work is applying this method to map hippocampal surface changes in Alzheimer's disease and those at risk.

Figures:

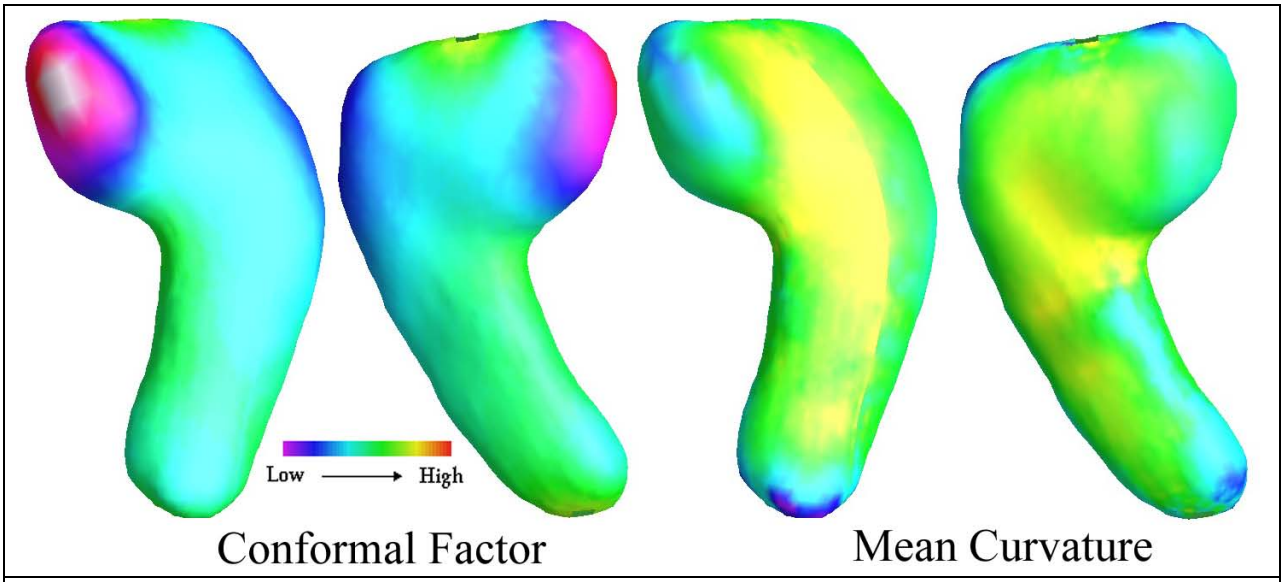

Figure 1. The conformal factor and mean curvature color-coded on a hippocampal surface.

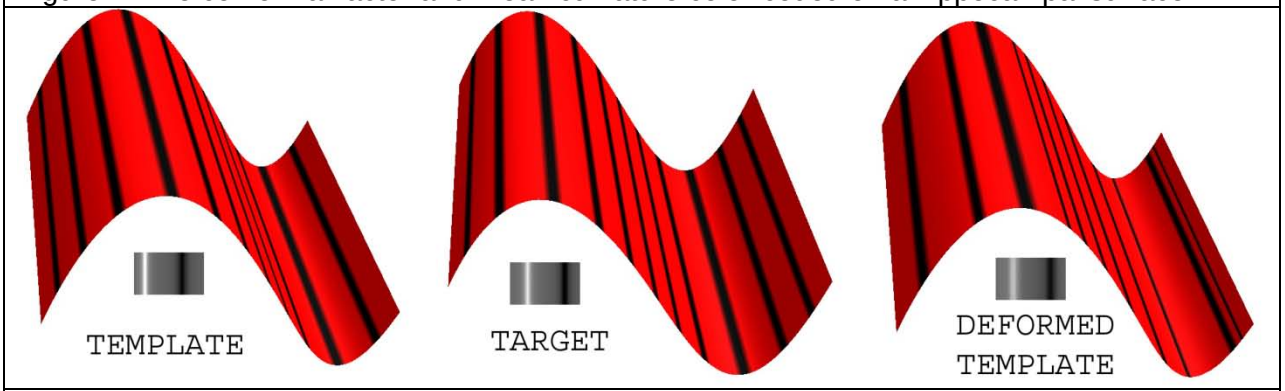

Figure 2. Matching of geometric features in the 2D parameter domain using mutual-information based fluid registration of two synthetic surfaces. The lines show the effect of the flow.

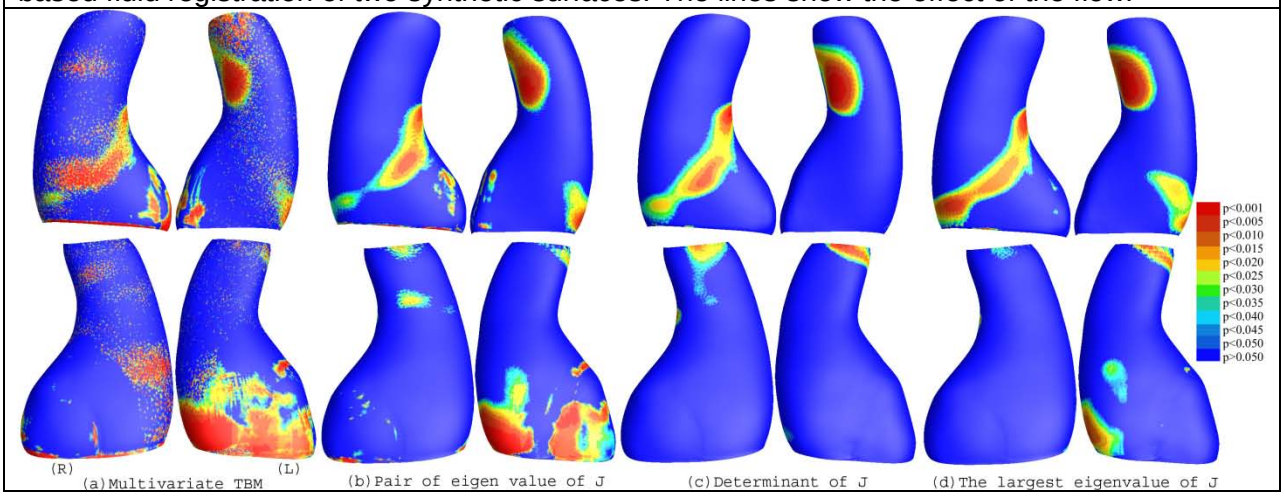

Figure 3. Geometric features on 3D surfaces were computed and mapped to 2D conformal parameter domains. In the 2D domain, data from healthy normal subjects was matched to data from AD patients. Maps of local shape differences (*p*-values) are shown, based on the multivariate TBM method, comparing hippocampal surfaces in 12 AD versus 14 control subjects.

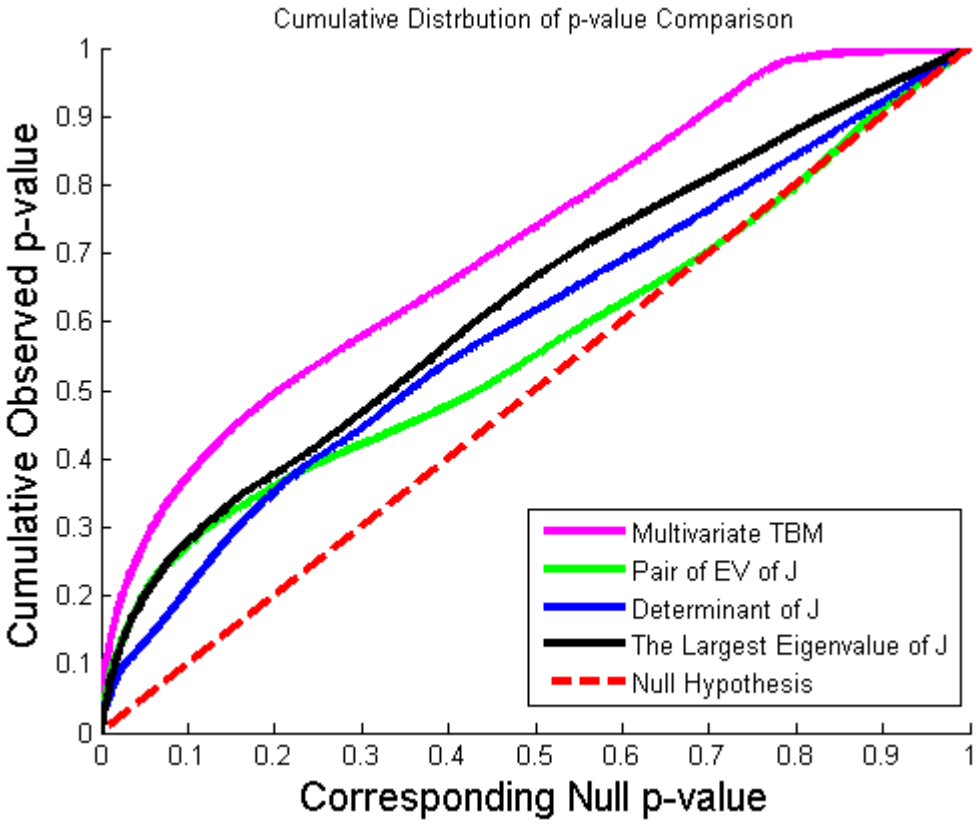

Figure 4. The cumulative distribution of p-values versus the corresponding cumulative p-value expected from a null distribution is shown, for multivariate TBM (magenta) and various tensor-based morphometry results, including the pair of eigenvalues of Jacobian matrix (green), the Jacobian determinant (blue), the largest eigenvalue (blue) and the smallest eigenvalue (black) of the Jacobian matrix, on a group of hippocampal surfaces from 12 AD patients and 14 matched control subjects. Multivariate TBM separates the two groups with greatest power.

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