MRI-based Biomarker Detection using Conformal Slit Maps and Machine Learning

Yalin Wang, Rudy Senstad, Arthur W. Toga, Paul M. Thompson

Introduction:

Many voxel-based morphometric studies focus on describing structural differences at the group level – i.e., between different diagnostic groups. More recently, morphometric maps have also been used to classify individual subjects into diagnostic groups. In one study (Sun et al. 2009), maps of cortical gray matter density achieved 86.1% accuracy in discriminating psychotic patients from control subjects, in leave-one-out tests. In related work, Ferrarini et al. 2008 proposed the notion of biomarker nodes, i.e. regions on surface meshes that contribute most to diagnostic classification; they tested their approach on ventricular surface models from Alzheimer's disease patients and controls. Here we developed a new approach, based on conformal slit mapping, tensor-based morphometry (TBM), and a multinomial logistic regression classifier, to identify cortical biomarkers for classification problems. We tested the approach on Williams syndrome data from a prior study (Thompson et al., 2005).

Methods: Cortical surface data from 42 subjects with genetically confirmed WS and 40 age-matched healthy controls were analyzed. Cortical surface models were cut along sulcal landmark curves, to obtain multiply connected domains. By computing a sequence of differential geometric features on these surfaces - exact harmonic one-forms, closed harmonic one-forms, and holomorphic one-forms - we built a circular slit map, which conformally maps each surface onto an annulus with a set of embedded concentric arcs and a rectangle with a set of embedded slits (Figure 1). This mapping is stable, and is based on solving a linear system. In the slit domain, the 3D curved features on the cortex are mapped either to straight lines or concentric arcs. A surface-based tensor-based morphometry (TBM) approach (Wang et al. 2009) was then used to locate cortical regions with abnormally large or small surface areas, based on the Jacobian determinant of the parametric grids and the eigenvalues of the surface metric.

A machine learning method, termed PyMVPA (the Multivariate Pattern Analysis in Python machine-learning package; Hanke et al., 2009; also used in Sun et al., 2009), was then applied to the surface maps for group classification. We used the leave-one-out cross-validation method to determine classification accuracy. The classifier was trained using a set of 6 TBM-derived local morphometric features including the 3 log-Euclidean coordinates of the Jacobian of the surface grid, the Jacobian determinant and its two eigenvalues. Leave-one-out validation was applied to each subject, and the accuracy of diagnostic predictions was calculated.

Results:

Figure 2 shows the profile of group differences detected between WS and matched control groups, using the Jacobian determinant as a measure of local surface area (p=0.0004 for the

left and p=0.0005 for the right hemisphere). Focusing on the 1050 vertices with greatest effect sizes, we trained the diagnostic classifier using 6 tensor-based morphometry (TBM) features derived from the surface mesh at each vertex. An example of these biomarker vertices overlaid on an average shape model of the right hemisphere is shown in Figure 3. Using these biomarkers as predictors, we achieved 92.7% accuracy for classifying patients as Williams syndrome or as controls. We also tested using different numbers of biomarker vertices from the left and right hemispheres. The best result was achieved when we only selected biomarker vertices from the right hemisphere (Figure 3).

Conclusions:

We presented an MRI-based biomarker detection system that finds vertices and local features on cortical surface models that best discriminate groups of subjects. In leave-one-out tests, the system performed well in classifying individuals into the correct diagnostic groups. Our ongoing work is testing this framework for studying structural imaging biomarkers of neurodegenerative diseases such as Alzheimer's disease.

Figures:

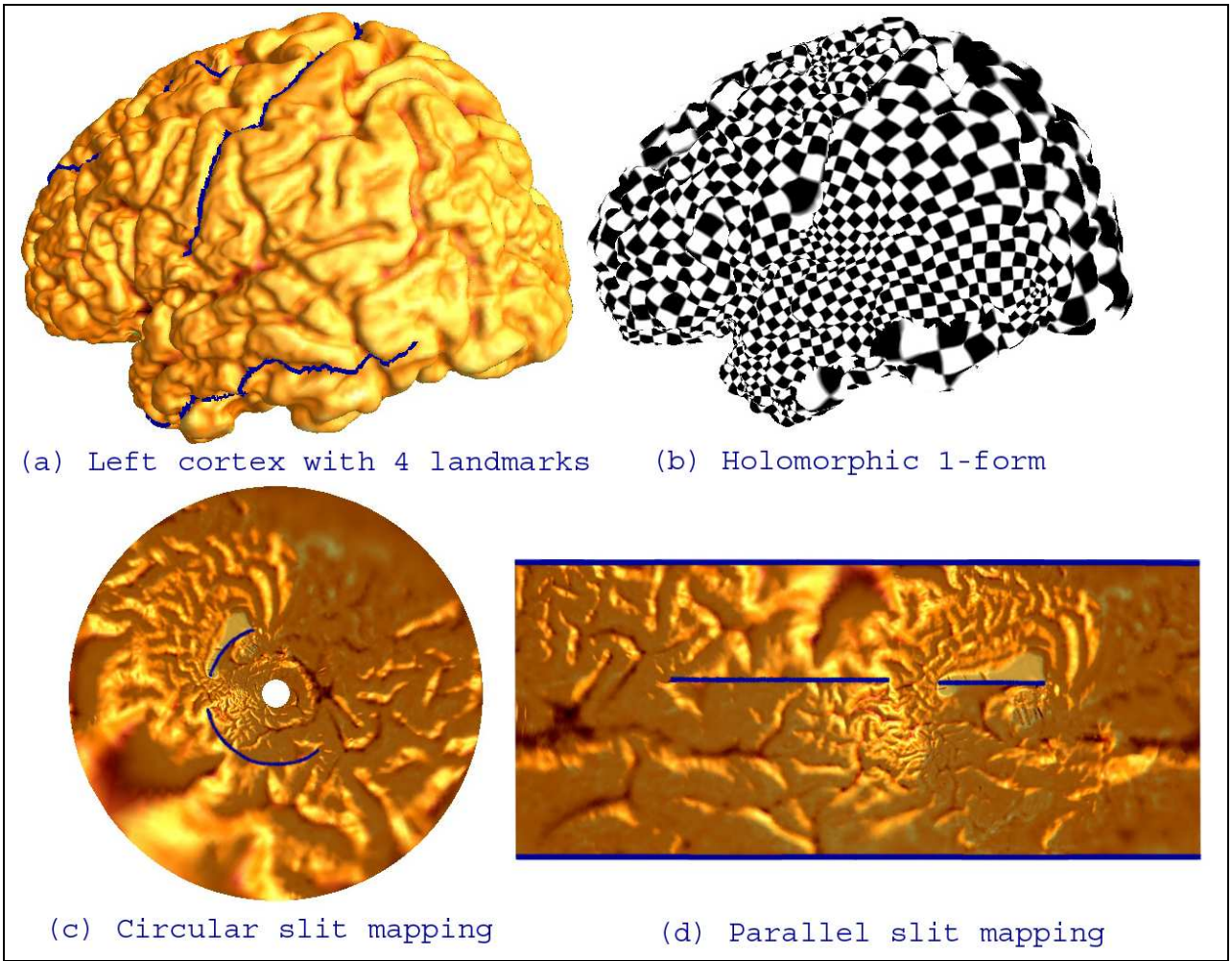

Figure 1. Conformal slit mapping. After cutting along several landmark curves, we turn a cortical surface to a genus zero open boundary surface (a). By computing the holomorphic 1-form (b), this can then be conformally mapped onto either a circle (c) or a rectangle (d) where the landmarks are mapped to concentric or parallel lines in the slit domain. We then perform nonlinear surface registration in these parameter domains.

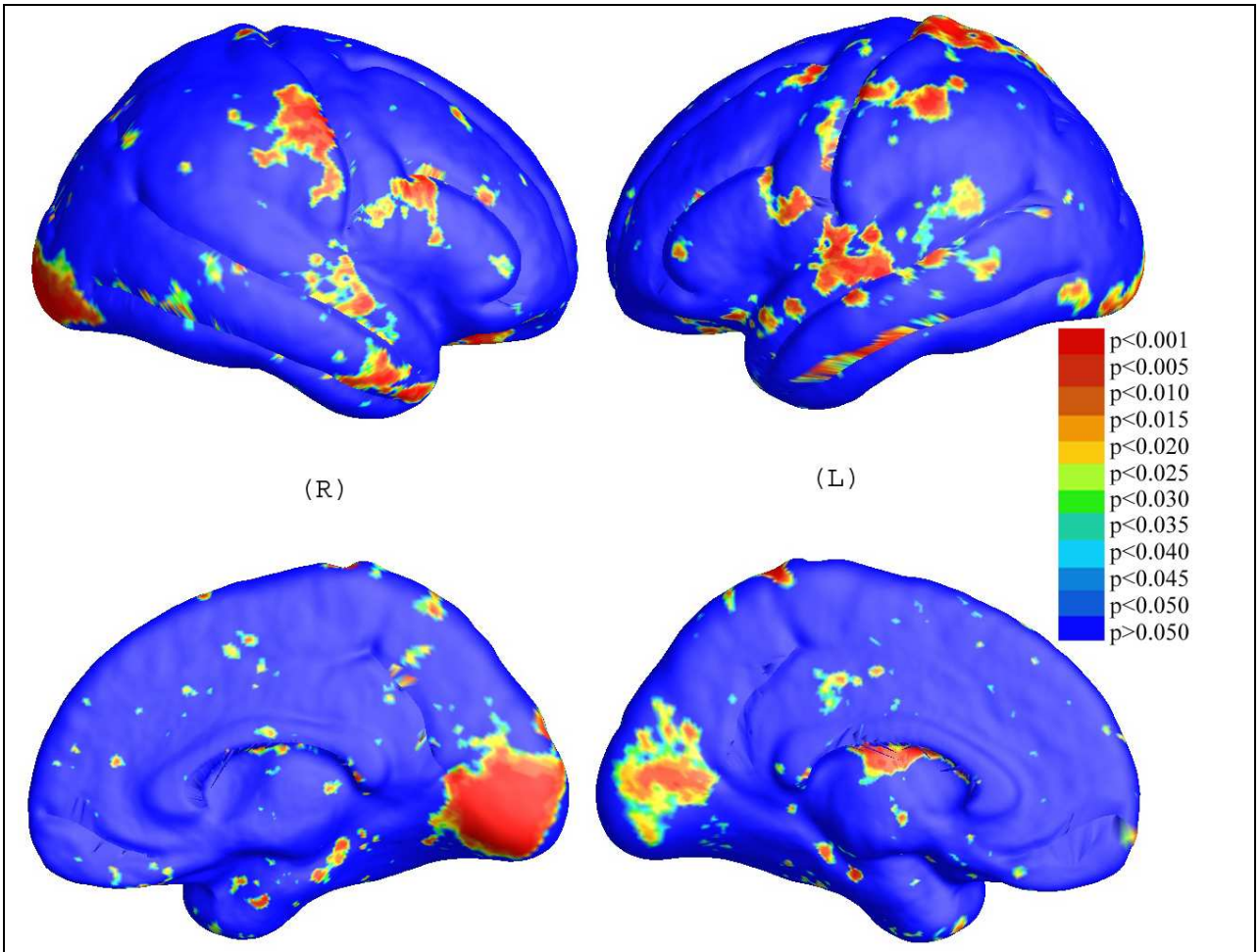

Figure 2. Statistical significance (uncorrected *p*-maps) show group differences in regional cortical surface area between 42 WS patients and 40 healthy controls (Thompson et al., 2005). The local statistic analyzed is the determinant of the Jacobian matrix of the cortical parameterization. On the color-coded scale, non-blue colors denote the vertices where there is a significant group difference, at the uncorrected p=0.05 level.

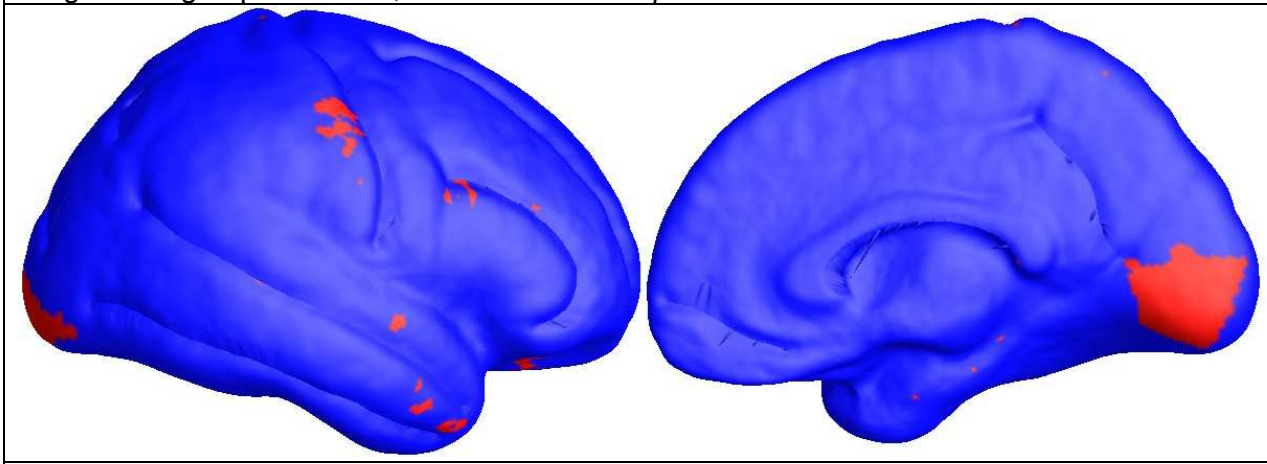

Figure 3. Biomarker vertices on the average right hemisphere. The red pixels are selected as useful for group discrimination and diagnostic classification at the individual level: a total of 1050 vertices are selected. Using surface-based features, measured at these biomarker vertices, as

inputs to the sparse multinominal logistic regression classifier (Krishnapuram et al., 2005), we achieved a 92.7% diagnostic classification accuracy.

References:

ARSIGNY, V., FILLARD, P., PENNEC, X. & AYACHE, N. 2006. Log-Euclidean Metrics for Fast and Simple Calculus on Diffusion Tensors. *Magn. Reson. Med.,* 56, 411-421.

Ferrarini L, Palm WM, Olofsen H, van der Landen R, van Buchem MA, Reiber JH, Admiraal-Behloul F. Ventricular shape biomarkers for Alzheimer's disease in clinical MR images. Magn Reson Med. 2008 Feb;59(2):260-7.

HANKE, M., HALCHENKO, Y. O., SEDERBERG, P. B., OLIVETTI, E., FRUND, I., RIEGER, J. W., HERRMANN, C. S., HAXBY, J. V., HANSON, S. J. & POLLMANN, S. 2009. PyMVPA: A Unifying Approach to the Analysis of Neuroscientific Data. *Front Neuroinformatics,* 3, 3.

KRISHNAPURAM, B., CARIN, L., FIGUEIREDO, M. A. T. & HARTEMINK, A. J. 2005. Sparse multinomial logistic regression: fast algorithms and generalization bounds. *Pattern Analysis and Machine Intelligence, IEEE Transactions on,* 27, 957-968.

Sun D, van Erp TG, Thompson PM, Bearden CE, Daley M, Kushan L, Hardt ME, Nuechterlein KH, Toga AW, Cannon TD (2009). Elucidating a magnetic resonance imaging-based neuroanatomic biomarker for psychosis: classification analysis using probabilistic brain atlas and machine learning algorithms. Biol Psychiatry. 2009 Dec 1;66(11):1055-60. Epub 2009 Sep 3.

THOMPSON, P. M., LEE, A. D., DUTTON, R. A., GEAGA, J. A., HAYASHI, K. M., ECKERT, M. A., BELLUGI, U., GALABURDA, A. M., KORENBERG, J. R., MILLS, D. L., TOGA, A. W. & REISS, A. L. 2005. Abnormal Cortical Complexity and Thickness Profiles Mapped in Williams syndrome. *J. Neuroscience,* 25, 4146-4158.

THOMPSON, P. M., WOODS, R. P., MEGA, M. S. & TOGA, A. W. 2000. Mathematical/Computational Challenges in Creating Deformable and Probabilistic Atlases of the Human Brain. *Human Brain Mapping.*

WANG, Y., CHAN, T. F., TOGA, A. W. & THOMPSON, P. M. 2009. Multivariate Tensor-based Brain Anatomical Surface Morphometry via Holomorphic One-Forms. *Med. Image Comp. Comput.-Assist. Intervention, Proceedings*.