Pattern Classification of Hippocampal Shape Analysis in a Study of Alzheimer's Disease

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1. Objective

Under the auspices of the Brain Morphometry Biomedical Informatics Research Network (BIRN), a processing pipeline is being developed to enable seamless processing of brain morphometry data for subcortical structures through the integration of multiple site applications. The pipeline produces metric distances between anatomical structures. The metric distances give a precise mathematical description of the similarity of shapes. To test this, pattern classification of metric distances between hippocampal structures was used to classify shapes in a study of Alzheimer's Disease.

2. Methods

We investigate the 45-subject BIRN data set. This data set consists of 21 control subjects, 18 subjects diagnosed with Alzheimer's, and 6 with semantic dementia. The subjects were scanned using high resolution T1-weighted structural MRI at Washington University. The anonymized scans were analyzed at MGH's Martinos Center using Freesurfer [1]. The resulting segmented data sets were aligned and processed at JHU's Center for Imaging Science (CIS) using the Large Deformation Diffeomorphic Metric Mapping (LDDMM) tool [2].

The feature vectors are MR imagery and should properly be considered as taking their values in a non-Euclidean space endowed with a metric ρ. We will consider both the 3 class case with control denoted as class 1, Alzheimer's denoted as class 2, and semantic dementia denoted as class 3, and 2 class case with control denoted as class 1 and Alzheimer's and semantic dementia grouped together as class 2.

Our approach is a three step classification process involving extraction of interpoint distances via large deformation diffeomorphic metric mapping (LDDMM) ℓ, subsequent mapping to Euclidean space via multidimensional scaling (MDS) m, and ultimate classification via linear discriminant analysis (LDA) h [3].

Briefly, LDDMM computes the velocity vectors that transform one binary image i to another j giving the metric distance

$$\rho(i,j) = \sqrt{\int_0^1 \|v\|_V^2 dt}$$

where the norm $\|\cdot\|_V^2$ ensures smoothness in the space of velocity vector fields that are generated by the group of infinite dimensional diffeomorphisms (which is the generalization of rotation, translation and scale group), the necessary group for studying shape. For our data set, we obtain 45x45 left and right LDDMM matrices $\mathcal{D}_n$ with the (i,j)-th entry of left matrix (respectively right matrix) representing the LDDMM from the i-th subject to the j-th subject for the left (respectively right) hippocampus. Thus these matrices are non-negative matrices with zeros on the diagonal. However, these metrics are not distance metrics (the triangle inequality is not guaranteed to hold) and in fact are not even dissimilarity matrices (they are asymmetric).

Multidimensional scaling is a general method for taking a dissimilarity matrix and obtaining a set of points (a configuration) in some pre-specified finite-dimensional Euclidean space $\mathbb{R}^d$ such that the distances between the configuration points are approximately equal to the given dissimilarities [4]. While there are many versions of MDS, for simplicity we use here what is known as "classical" multidimensional scaling. Here we are using multidimensional scaling as a dimension reduction method for subsequent statistical pattern recognition as opposed to the (more common) use of technique for visualization.

We write $Z = m_{d_L,d_R}(\ell(\mathcal{D}_n))$ to represent the n x (d_L+d_R) feature matrix thus obtained; Z_i is the (d_L+d_R) vector obtained by extracting the i-th row of this matrix (corresponding to the feature vector X_i) and Z_{-i} is the $(n-1)$ x (d_L+d_R) feature matrix obtained by eliminating the i-th row. We also write the class label Y_{-i} to denote the $(n-1)$ class labels, excepting the i-th. Our performance criterion is the deleted (leave-one-out cross validation) estimation of the probability of misclassification,

$$\widehat{L}^{(D)}_{d_L,d_R} = \frac{1}{n}\sum_{i=1}^{n} I\{h(Z_i; Z_{-i}, Y_{-i}) \neq Y_i\},$$

which is a function of the MDS dimensionalities d_L and d_R.

3. Results

Figure 1 presents $\widehat{L}^{(D)}_{d_L,d_R}$ as a function of d_L and d_R. The figure is for the **two-class** version of the problem, in which Alzheimer's and semantic dementia are grouped together. A region of dimensionality-space yielding statistically significant classification improvement is apparent.

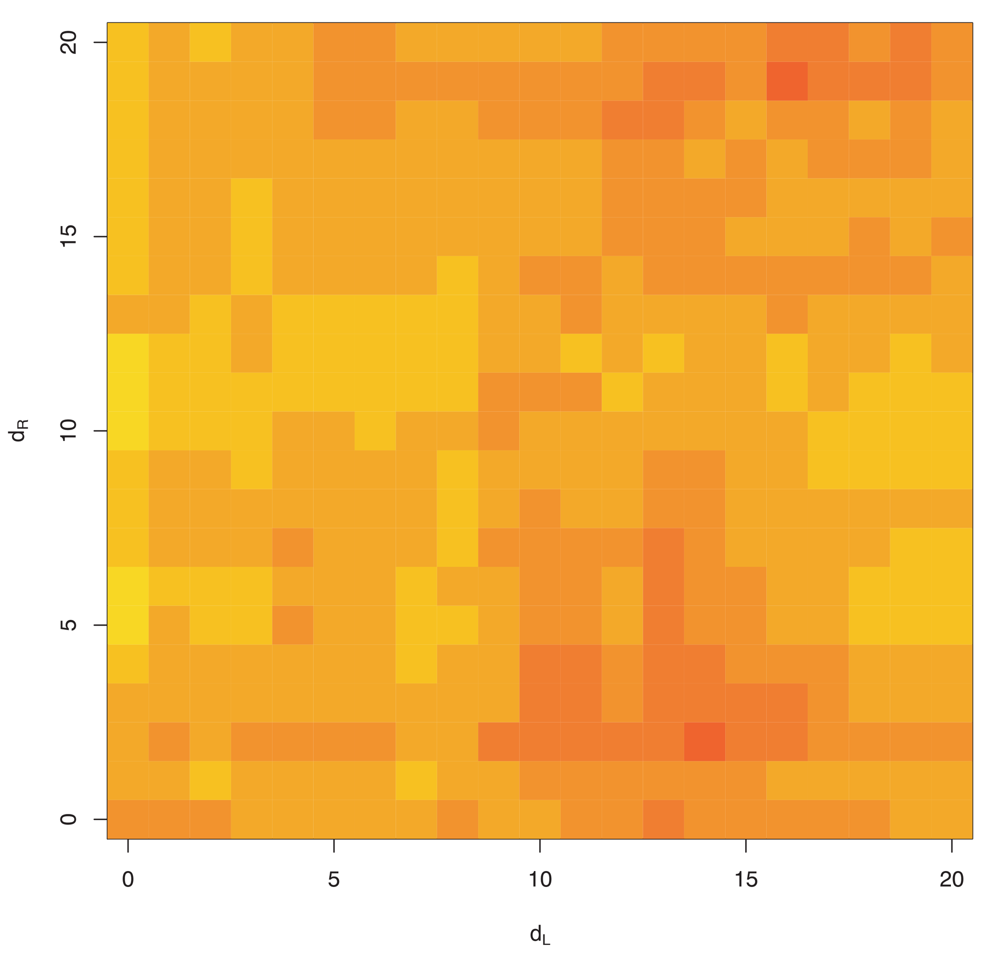

Figure 1. A contour plot of $\widehat{L}^{(D)}_{d_L,d_R}$, the classification error using LDA with 2 classes. The plot shows that min($\widehat{L}^{(D)}_{d_L,d_R}$) is 0.22, and $\text{argmin}_{d_L,d_R}\ \widehat{L}^{(D)}_{d_L,d_R}$ yields d_L=14, d_R=2.

Figure 2 presents the LDA scatter plot. Since the range space of the LDA map is 2 dimensional, this plot necessarily requires the **three class** version of the problem. Significant class-conditional structure is apparent.

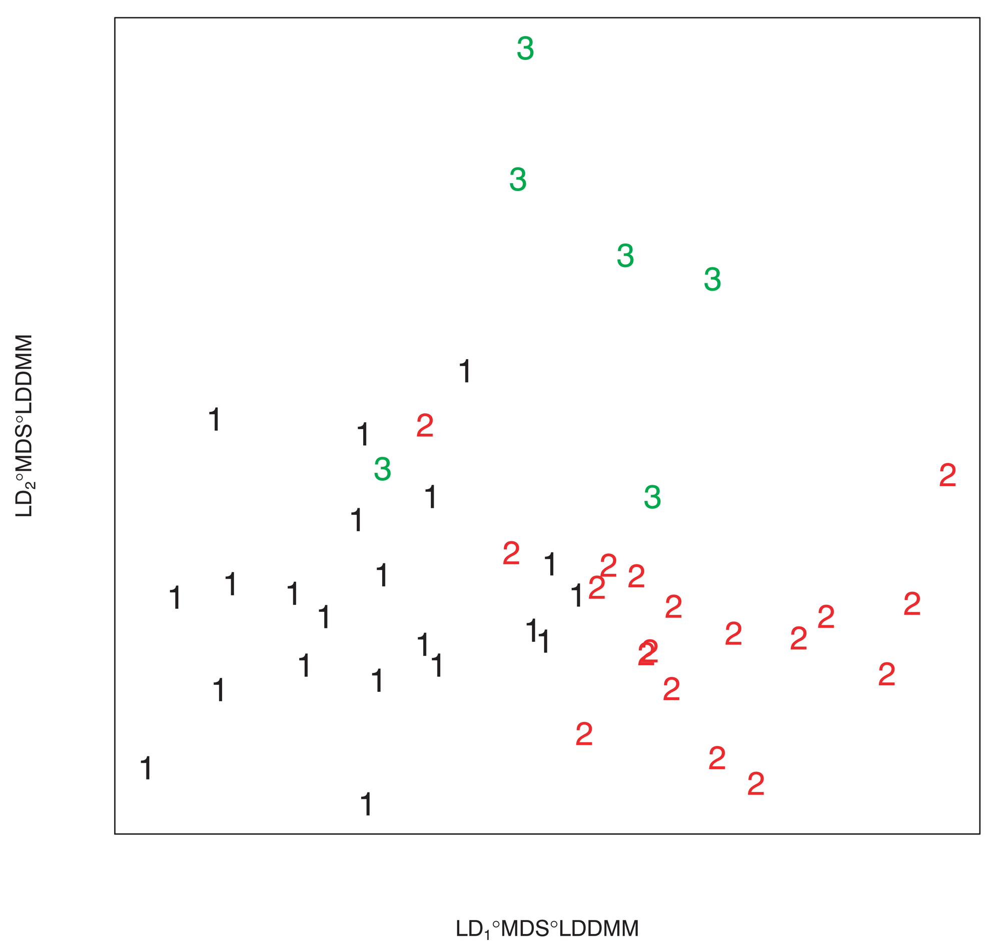

Figure 2. A scatter plot of combined dimensions of (1:d_L) U (1:d_R). The legends are 1: controls, 2: Alzheimer's patients, and 3: semantic dementia.

4. Conclusions

Pattern classification of metric distances provides a powerful means of distinguishing shapes and providing the neuroanatomist an increased understanding of diseases and disorders with greater statistical power.

References:

[1] B. Fischl, et.al., Whole brain segmentation: automated labelling of neuroanatomical structures in the human brain, Neuron, 33:341, 2005.
[2] M.F. Beg, et.al., Computing Large Deformation Metric Mapping via Geodesic Flows of Diffeomorphisms, Int. J. Comp Vis, 61:139, 2005.
[3] Venables, W.N. and Ripley, B.D., Modern applied statistics with S, S. Springer, 2002.
[4] T.F. Cox and M.A.A.Cox, Multidimensional Scaling, Capman and Hall, 1994.

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