

# Groupwise shape analysis of the hippocampus using spectral matching

Mahsa Shakeri<sup>\*ab</sup>, Hervé Lombaert<sup>c</sup>, Sarah Lippé<sup>bd</sup>, Samuel Kadoury<sup>ab</sup>

<sup>a</sup>MEDICAL, Polytechnique Montréal, Montréal, QC, Canada; <sup>b</sup>CHU Sainte-Justine Hospital Research Center, Montréal, QC, Canada; <sup>c</sup>Centre for Intelligent Machines, McGill University, Montréal, QC, Canada; <sup>d</sup>Department of Psychology, Université de Montréal, Montréal, QC, Canada;

## ABSTRACT

The hippocampus is a prominent subcortical feature of interest in many neuroscience studies. Its subtle morphological changes often predicate illnesses, including Alzheimer's, schizophrenia or epilepsy. The precise location of structural differences requires a reliable correspondence between shapes across a population. In this paper, we propose an automated method for groupwise hippocampal shape analysis based on a spectral decomposition of a group of shapes to solve the correspondence problem between sets of meshes. The framework generates diffeomorphic correspondence maps across a population, which enables us to create a mean shape. Morphological changes are then located between two groups of subjects. The performance of the proposed method was evaluated on a dataset of 42 hippocampus shapes and compared with a state-of-the-art structural shape analysis approach, using spherical harmonics. Difference maps between mean shapes of two test groups demonstrates that the two approaches showed results with insignificant differences, while Gaussian curvature measures calculated between matched vertices showed a better fit and reduced variability with spectral matching.

**Keywords:** hippocampus, groupwise shape analysis, correspondence, spectral matching

## 1. INTRODUCTION

The hippocampus is the main target of deformation in many neurodegenerative diseases [1]. Extracting its morphological characteristics is an important and challenging problem in medical image analysis. Early morphological studies on the hippocampus were based on volumetric analysis, which had the advantage of simplicity [2, 3]. However, structural changes at specific locations were not accurately detected using volumetric frameworks. Thus, hippocampal shape analysis has emerged as a way of evaluating morphology location and magnitude in the brain anatomy.

Several works have proposed hippocampal shape analysis via deformable registration to a template, where population-wise comparisons are performed by analyzing the individual deformable transformations [4, 5]. Another type of shape analysis method is based on medial surface descriptions, which allows for the quantification of local positional changes by assessing morphological variation of the skeleton extracted from a given object [6, 7]. Besides these, some methods use spherical harmonics description combined with Point Distribution Models (PDM) to discover structural differences across a population [8, 9]. However, these surface-based frameworks depend on establishing vertex correspondence across subjects, which are prone to inter-subject variability and are more adapted to sphere-like shapes.

SPHARM-PDM is a popular groupwise shape analysis method based on spherical harmonic combined with point distribution models. This method solves the correspondence problem by the alignment of the spherical parametrization using a first order ellipsoid [9]. In this method the spherical description of surface meshes is sampled into triangulated surfaces via icosahedron subdivision. These surfaces are then spatially aligned using rigid Procrustes alignment. However, as this method establishes correspondence on simplified spherical models of surfaces, it is restricted to surfaces with spherical topology and is computationally expensive.

In this work we propose an alternative groupwise hippocampal shape analysis approach based on spectral matching in which the correspondence maps are computed using a new surface matching approach presented in [10]. In spectral matching relationships are modeled as graphs and an eigendecomposition of these graphs enables us to match similar features. The objective of this work is to investigate whether a shape analysis method based on

spectral matching could produce similar shape geometries on hippocampus and identify groupwise differences to SPHARM-PDM method.

## 2. METHODS

The inputs to the proposed method include two groups of hippocampus meshes. Our framework establishes correspondences across surface points for each group using spectral matching and creates two mean shapes as outputs. The workflow for the procedure is illustrated in Fig. 1.

In the proposed method, an initial reference is randomly selected and all vertices of all other surfaces are matched to the reference image. A spectral matching approach presented in [10] is used to find the correspondence between each mesh and the selected reference image. This approach is able to provide a diffeomorphic correspondence map between two surfaces. Before applying this method, a preliminary correspondence map has to be generated between two meshes. We used a conventional spectral matching method presented in [11] to compute this initial correspondence map. In section 2.1, the spectral method for matching two surface meshes is briefly described. Section 2.2 presents the groupwise hippocampal shape analysis approach, in which the vertex correspondence between meshes is established using the spectral matching method described in section 2.1.

### 2.1. Matching two surfaces using spectral matching

Given two surface meshes  $S^{(1)}$  and  $S^{(2)}$ , the matching between these two shapes is conducted in a two-step process (Fig 2.a and b). At first, we build the graph  $g^{(i)} = \{V^{(i)}, E^{(i)}\}$  from the set of vertices and edges of each surface  $S^{(i)}$ . Then, the weighted adjacency matrix  $W^{(i)}$  is defined in terms of node affinities. The diagonal node degree matrix  $D^{(i)}$  is determined as the sum of all point affinities. The general Laplacian operator on a graph  $g^{(i)}$  is formulated with  $L^{(i)} = G^{-1}(D^{(i)} - W^{(i)})$  where  $G$  is a diagonal node weighting matrix ( $G = D^{(i)}$ ). The eigendecomposition of each graph's Laplacian matrix  $L^{(i)}$  reveals its spectral components. After reordering the spectral components by finding the optimal permutation of components between the pair of meshes, regularization is performed by matching the spectral embeddings. The correspondence map  $c$  between each pair of vertices on  $S^{(1)}$  and  $S^{(2)}$  is established with a simple nearest-neighbor search between spectral representation of  $S^{(1)}$  and  $S^{(2)}$ . An overview of the procedure of finding the correspondence map  $c$  is shown in Fig 2.a.

In the next step, the final map (diffeomorphic match) between two surfaces  $S^{(1)}$  and  $S^{(2)}$  is obtained as shown in Fig2.b. In this procedure, an association graph  $g_a = \{V_{1,2}, E_{1,2,c}\}$  is defined as the union of the set of vertices and edges of two surfaces  $S^{(1)}$  and  $S^{(2)}$  with an initial set of correspondence links  $c$  between both surfaces. The spectral decomposition of this unique association graph creates a shared set of eigenvectors that enables a direct mapping  $\varphi_{1 \rightarrow 2}$  between two meshes (see [10] for more details).

### 2.2. Morphological Analysis

Let  $\{S^{(i)}\}_{i=0, \dots, n}$  be a set of  $n+1$  surface meshes. We would like to compute the mean shape  $\bar{S}$  as the geometric mean of all surface meshes in the set. For that purpose, at first an initial reference mesh  $S^{(0)}$  is selected randomly. Then, all vertices of all meshes  $S^{(i)}$  are matched to the reference mesh  $S^{(0)}$ , using the spectral mapping  $\{\varphi_{i \rightarrow 0}\}_{i=0, \dots, n}$  described in section 2.1. In the next step, the mean surface  $\bar{S}$  is defined by averaging the 3D coordinates of corresponding surface points across the group. The position of point  $\bar{x}_j$  on mean surface  $\bar{S}$  is defined as follows:

$$\bar{x}_j = \frac{1}{n+1} \sum_{i=1}^n x_j^{(i)} \quad (1)$$

Where  $x_j^{(i)}$  is the interpolated position of point  $i$  on surface  $S^{(i)}$  computed using the mapping  $\varphi_{i \rightarrow 0}$ .

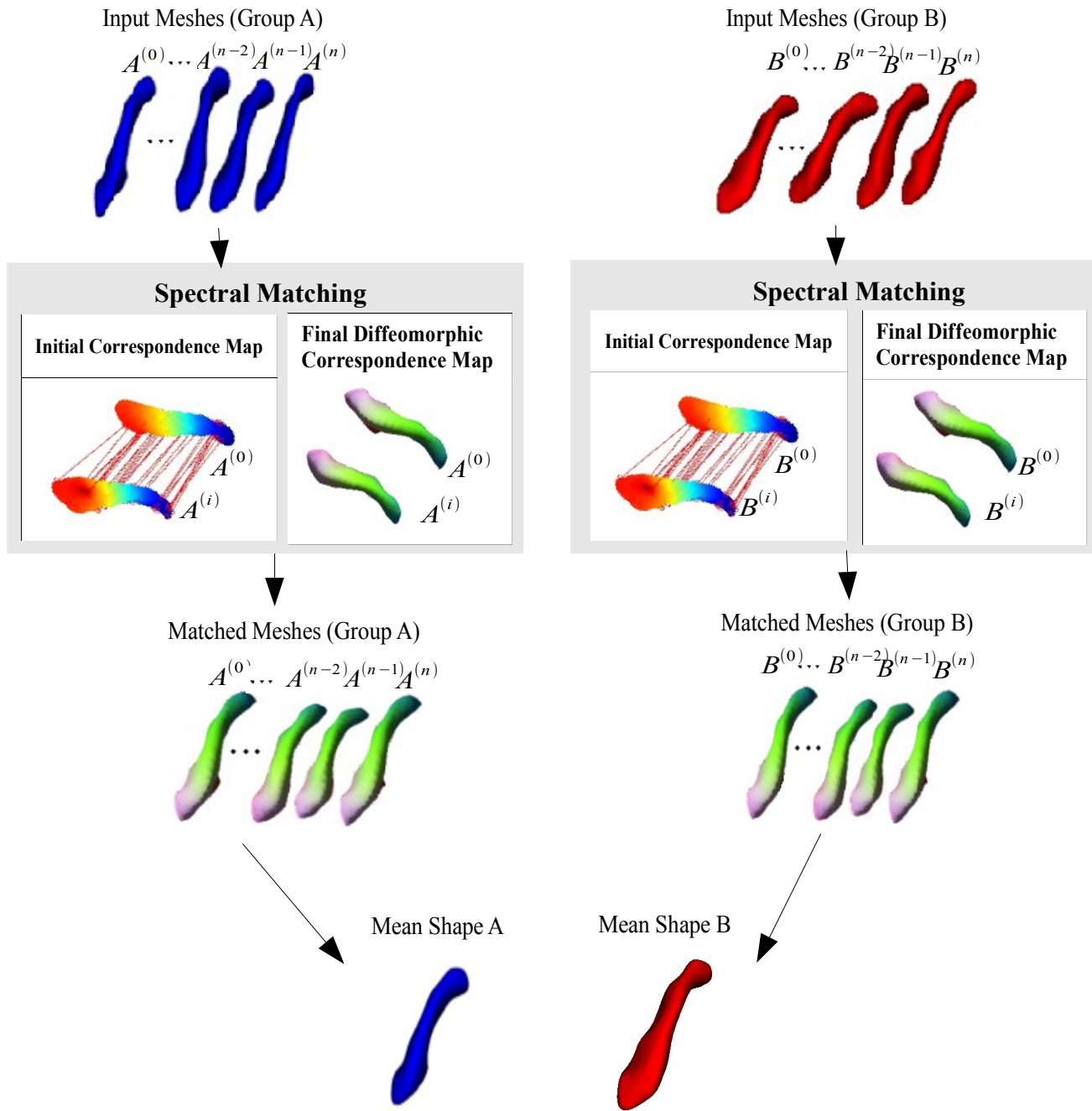


Figure 1. Hippocampal shape analysis between two groups of subjects (group A and B) using spectral matching. At first, an initial reference image is selected randomly in each group ( $A^{(0)}$  and  $B^{(0)}$  in top row). Then, all vertices of all meshes are mapped to the reference image using the spectral matching algorithm (second and third rows). Finally, the mean surface of each group is created (bottom row).

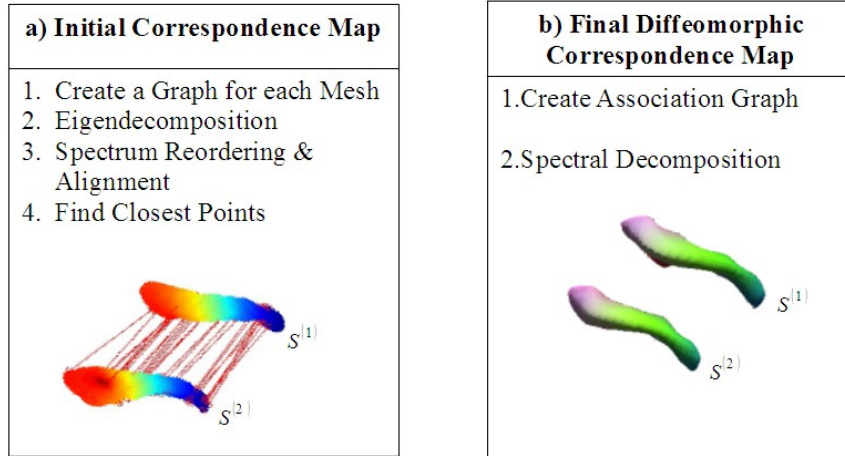


Figure 2. (a) Initial matching of two meshes using the algorithm proposed in [11]. (b) Final correspondence mapping between two surfaces based on diffeomorphic spectral matching approach in [10].

By applying the proposed approach to two groups of surface meshes (A and B) and obtaining a mean shape for both groups (Fig. 1), the local shape differences between groups can be detected by computing a difference map between two mean shapes after registering them together.

### 3. RESULTS

To evaluate the performance of the proposed spectral matching method, we used a dataset of 42 hippocampus shapes obtained from schizophrenic patients [12]. The hippocampi were segmented from IR-Prepped SPGR (Inversion Recovery-Prepared Spoiled Gradient Echo) data segmented originally at 0.9375x0.9375x1.5mm resolution as part of an adult schizophrenia study (mean age 32, all male gender). All cases have been fully randomized and group association has been performed to create two different groups (group A and group B) with 21 subjects (42 subjects in total). We compared the performance of the spectral matching approach with a state-of-the-art method used for groupwise analysis of anatomical shapes, namely SPHARM-PDM [9].

We generated mean shapes, for both groups of subjects, using our spectral groupwise framework and SPHARM-PDM. The distance maps between the mean shapes produced by both methods are illustrated in Fig. 3. Dice volume difference measures, Hausdorff distance, and average absolute distance between the mean shapes of group A and B are listed in Table 1. These results suggest that the proposed spectral framework produces similar groupwise shape differences as SPHARM-PDM.

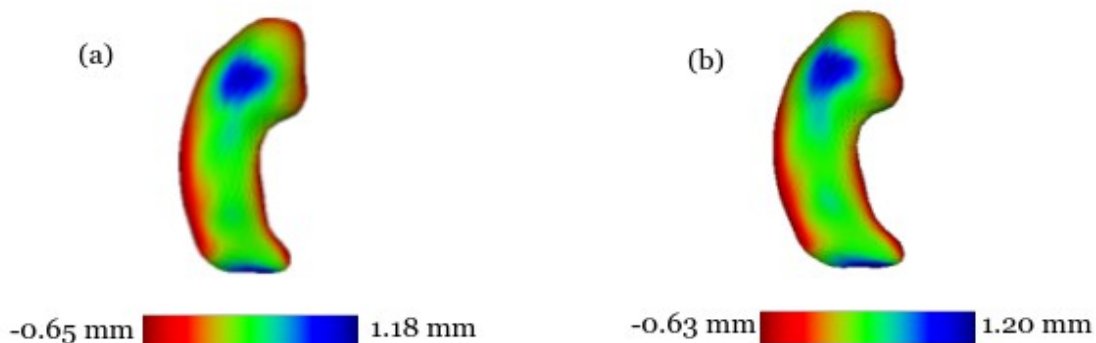


Figure 3. (a) Distance map between group A and B using SPHARM-PDM. (b) Distance map between group A and B with spectral matching. The proposed framework based on spectral matching yield similar results as the state-of-the-art method.

Table 1. Shape differences between mean shape A and mean shape B.

|                                    | <b>Spectral Matching</b> | <b>SPHARM-PDM</b> |
|------------------------------------|--------------------------|-------------------|
| <b>Dice Coefficient</b>            | 0.92                     | 0.92              |
| <b>Hausdorff Distance (mm)</b>     | 1.20                     | 1.18              |
| <b>Mean Absolute Distance (mm)</b> | $0.03 \pm 0.39$          | $0.03 \pm 0.38$   |

Fig. 4 presents the comparison between mean shapes computed using spectral matching and SPHARM-PDM. The Dice coefficient, Hausdorff distance, and average absolute distance are reported in Table 2. This shows that our method yields similar accuracy than the method based on spherical harmonics .

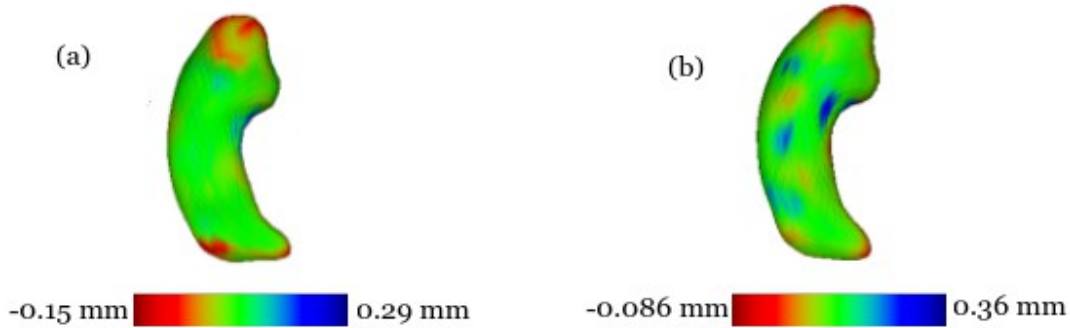


Figure 4. (a) Difference map for mean shape A. (b) Difference map for mean shape B. There is a small difference between mean shapes computed using spectral matching and SPHARM-PDM.

Table 2. Shape differences obtained with spectral matching and SPHARM-PDM.

|                                    | <b>Mean shape A</b> | <b>Mean shape B</b> |
|------------------------------------|---------------------|---------------------|
| <b>Dice Coefficient</b>            | 0.99                | 0.98                |
| <b>Hausdorff Distance (mm)</b>     | 0.29                | 0.36                |
| <b>Mean Absolute Distance (mm)</b> | $0.0028 \pm 0.0459$ | $0.0031 \pm 0.0636$ |

In order to assess the variability in curvature between matched vertices in spectral matching and in SPHARM-PDM, the gaussian curvature was computed at each vertex of all meshes in the dataset. We computed the minimum, maximum, mean, and the standard deviation across all correspondent vertices, and obtained the average metrics for vertices (Table 3). These show that the measures are similar between both approaches. More importantly, the spectral matching approach shows a lower standard deviation compared to SPHARM-PDM, indicated lesser variability in the curvature measure for matched vertices.

Table 3. Curvature measures computed with spectral matching and SPHARM-PDM

|                       | <b>Group A</b>           |                       | <b>Group B</b>           |                       |
|-----------------------|--------------------------|-----------------------|--------------------------|-----------------------|
|                       | <b>Spectral Matching</b> | <b>SPHARM-PDM</b>     | <b>Spectral Matching</b> | <b>SPHARM-PDM</b>     |
| <b>Max curvature</b>  | $5.35 \times 10^{-4}$    | $5.46 \times 10^{-4}$ | $5.47 \times 10^{-4}$    | $5.5 \times 10^{-4}$  |
| <b>Min curvature</b>  | $2.9 \times 10^{-4}$     | $2.89 \times 10^{-4}$ | $2.51 \times 10^{-4}$    | $2.42 \times 10^{-4}$ |
| <b>Mean curvature</b> | $4.14 \times 10^{-4}$    | $4.16 \times 10^{-4}$ | $3.90 \times 10^{-4}$    | $3.95 \times 10^{-4}$ |
| <b>Std curvature</b>  | $6.54 \times 10^{-5}$    | $6.89 \times 10^{-5}$ | $7.55 \times 10^{-5}$    | $8.05 \times 10^{-5}$ |

In the final experiment, the Euclidean distance was computed between all correspondent vertices using both spectral matching and SPHARM-PDM. The minimum, maximum, mean, and the standard deviation across all matched vertices are reported in Table 4. These results show that the distances between matched vertices are similar in both methods.

Table 4. Distance measures obtained with spectral matching and SPHARM-PDM

|                           | Group A           |            | Group B           |            |
|---------------------------|-------------------|------------|-------------------|------------|
|                           | Spectral Matching | SPHARM-PDM | Spectral Matching | SPHARM-PDM |
| <b>Max distance (mm)</b>  | 2.61              | 2.53       | 3.24              | 2.91       |
| <b>Min distance (mm)</b>  | 0.43              | 0.43       | 0.57              | 0.62       |
| <b>Mean distance (mm)</b> | 1.36              | 1.37       | 1.58              | 1.61       |
| <b>Std distance (mm)</b>  | 0.57              | 0.56       | 0.66              | 0.62       |

#### 4. DISCUSSION

In this work, a new approach for groupwise hippocampal shape analysis is proposed in order to detect regional alterations of hippocampal morphology in neurological conditions such as schizophrenia and epilepsy. The proposed scheme finds diffeomorphic correspondences among a population of surfaces in the spectral domain. This enables us to create a mean shape and locate the morphological changes between two groups of healthy and pathological subjects.

In this paper the performance of the proposed approach was compared with a state-of-the-art method, namely SPHARM-PDM [9]. Looking at the distance maps between mean shapes created using spectral matching and SPHARM-PDM methods, we find that both methods yield differences which are statistically insignificant. In addition to distance maps, the accuracy of the obtained mean shapes using spectral matching was evaluated using the Dice volume difference measure. According to the reported Dice coefficient, there is almost a perfect overlap between the mean shapes computed using spectral matching and SPHARM-PDM.

In order to indicate the variability of correspondent vertices, we computed curvature measures at each vertex of all meshes in the dataset. Comparing curvature measures obtained from both spectral matching and SPHARM-PDM method, shows that the matched vertices have close variability in both methods. However, the average standard deviation of curvature measure for spectral method is lower compared to SPHARM-PDM, which indicates the reduced variability and better fit of matched vertices in spectral method.

In order to achieve higher accuracy in surface matching, additional information (e.g., texture, anatomical information, or landmark positions) can be incorporated in extended spectral representation. These additional information which can be embedded as weights in graph nodes and as extra coordinates lead to little computational expenses in the mapping part of our framework. Further improvements of the method lies in enhancing the quality of input meshes. The number of vertices, the quality of triangulation, and the smoothing level of the meshes are the effective factors that play an important role in the accuracy of the result. The more accurate the input surface meshes are, the more valid the result of hippocampal shape analysis would be. Therefore, further work seek to incorporate additional features to help improve the matching, and to propose a strategy to provide proper input surfaces.

#### 5. CONCLUSIONS

In this paper, a new approach for groupwise hippocampal shape analysis based on spectral matching is described. Our proposed scheme finds diffeomorphic correspondences among a population of surfaces in the spectral domain which could be an alternative to the current hippocampal morphometry analysis methods. The performance of the proposed approach was compared with the SPHARM-PDM method [9]. According to the experiments, the two methods showed results with insignificant differences. In order to improve the accuracy of our groupwise

hippocampal shape analysis approach, we need to incorporate additional information in spectral matching, as well as enhancing the quality of input meshes.

## REFERENCES

- [1] Andersen, P., Morris, R., Amaral, D., Bliss, T., O'Keefe, J., [The hippocampus book], Oxford University Press, USA, 769-812 (2007).
- [2] Shi, F., Liu, B., Zhou, Y., Yu, C., Jiang, T., "Hippocampal volume and asymmetry in mild cognitive impairment and Alzheimer's disease: meta-analyses of MRI studies, " *Hippocampus*, 19(11), 1055-1064 (2009).
- [3] Hastings, R. S., Parsey, R. V., Oquendo, M. A., Arango, V., Mann, J. J., "Volumetric analysis of the prefrontal cortex, amygdala, and hippocampus in major depression, " *Neuropsychopharmacology* 29, 952-959 (2004).
- [4] Csernansky, J.G., Joshi, S., Wang, L.E., Haller, J., Gado, M., Miller, J.P., Grenander, U., Miller, M.I., "Hippocampal morphometry in schizophrenia via high dimensional brain mapping, " *National Academy of Science, USA*, 95, 11406-11411 (1998).
- [5] Csernansky, J.G., Wang, L. E., Jones, D., Rastogi-Cruz, D., Posener, J.A., Heydebrand, G., Miller, J.P., Miller, M.I., "Hippocampal deformities in schizophrenia characterized by high dimensional brain mapping, " *Am. J. Psychiatry*, 159, 1-7 (2002).
- [6] Joshi, S., Pizer, S., Fletcher, P.T., Yushkevich, P., Thall, A., Marron, J. S., "Multiscale deformable model segmentation and statistical shape analysis using medial descriptions, " *IEEE Transactions on Medical Imaging*, 21(5), 538-550 (2002)
- [7] Bouix, S., Jens, C., Pruessner, D., Collins, L., Siddiqi, K., "Hippocampal shape analysis using medial surfaces, " *NeuroImage*, 25(4), 1077-1089 (2005).
- [8] L. Shen, L., Ford, J., Makedon, F., Saykin, A., "Hippocampal shape analysis surface-based representation and classification, " in *SPIE-Medical Imaging* (2003).
- [9] Styner, M., Oguz, I., Xu, S., Brechbuhler, C., Pantazis, D., Levitt, J., Shenton, M., Gerig, G., "Framework for the statistical shape analysis of brain structures using SPHARM-PDM, " *Insight Journal*, 1-20 (2006).
- [10] Lombaert, H., Sporring, J., Siddiqi, K., "Diffeomorphic Spectral Matching of Cortical Surfaces, " *IPMI*, 376-389 (2013).
- [11] Lombaert, H., Grady, L., Polimeni, J.R., Chriet, F., "FOCUSR: Feature Oriented Correspondence using Spectral Regularization - A Method for Accurate Surface Matching, " *IEEE Transactions on Pattern Analysis and Machine Intelligence*, 35(9), 2143-2160 (2013).
- [12] Styner, M., Lieberman, J. A., Pantazis, D., and Gerig, G., "Boundary and medial shape analysis of the hippocampus in schizophrenia, " *Medical Image Analysis* 8(3), 197-203 (2004).