# SPHARM-Based Shape Analysis of Hippocampus for Lateralization in Mesial Temporal Lobe Epilepsy

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*Abstract*— **Spherical harmonics (SPHARM) is a powerful tool for modelling and processing of 3D connected objects of any shape. SPHARM popularity lies in its capability of revealing surfaces global discrepancies in a multi-scale manner. In medical image analysis, this capability is of great importance in diagnosis of diseases that are related to deformations in the brain structures, such as mesial temporal lobe epilepsy that is associated with the hippocampus deformation. In this paper, we present a simple and practical method for SPHARM registration, which is required for conducting shape comparisons. The method utilizes concepts of principal components and solves the challenging problem of SPHARM registration. Our method benefits from characteristics of SPHARM coefficients that have independent [*x*,*y*,*z*] elements; so registration is easily performed in the SPHARM feature space. Then, we propose our feature selection methods that summarize 1536 SPHARM-based features of each subject into three lateralization indices. These three indices measure the distances between left and right hippocampi of healthy and epileptic subjects to detect the epileptogenic hippocampus. This work improves the lateralization accuracy from 78% of conventional volumetric method to 85%, and also in cases where volumetric analysis is uncertain, 16% improvement is achieved. This method could be used as a compliment to other methods to decrease lateralization error.**

***Keywords-magnetic resonance imaging (MRI); hippocampus shape analysis; mesial temporal lobe epilepsy (mTLE); spherical harmonics; 3D representation and registration***

## I. INTRODUCTION

Shape analysis of brain structures has achieved great importance in the context of medical image computing in the recent years. The importance of neurodegenerative disorders (such as Alzheimer's, Schizophrenia, Parkinson and Epilepsy) and also evidences that show relations between these diseases and deformation of the brain structures [1-3] have increased research in this field.

Hippocampus (HC) is a brain structure that belongs to the limbic system and is located in the medial temporal lobe. It plays important roles in the short-term memory, the formation of memories and language tasks [4]. In the above mentioned disorders, HC is usually vulnerable to damage at the very earliest stages and is the main target of deformation. So as a biomarker, accurate and timely morphologic assessment of this structure may be beneficial in prognosis and diagnosis of those diseases. In mesial temporal lobe epilepsy (mTLE), lateralization is referred to finding of the epileptogenic side, which is frequently associated with the hippocampus. This is critical for hippocampal resection, a surgical solution for patients with refractory epilepsy.

Hippocampal volumetry along with some other MRI measures are the conventional methods for such assessment. Although volumetry is capable of revealing major deformations and global differences in some disorders [5], it is blind to minuscule shape changes. So in order to better compare the HCs, researches have focused on quantitative shape analysis methods with better discriminant features. Some researchers have proposed to apply deformable registration to a template [1,6,7]. Despite problems of template selection and high dimensionality of transformation, these studies achieved reasonable results. The methods in [8,9] were among the first methods proposed for 3D shape analysis based on sampled descriptions. Cootes, et al. [10] proposed Point Distribution Model for 3D shape analysis and deformation study. Other shape analysis methods based on medial shape descriptions in 3D and 2D were proposed by Styner [11] and Golland [12], respectively. Besides these, some methods build a simplified representation of anatomical structure by utilizing shape descriptors, such as spherical harmonics (SPHARM) [13], spherical wavelets [14], and Laplace-Beltrami operator [15]. In these methods, shape or surface is decomposed into series of bases and the coefficients are used as descriptive features.

SPHARM, a 3D extension of Fourier analysis, is what we utilize in this paper. Applications of SPHARM have been widely reported in many articles. Styner et al. [16] developed a framework using SPHARM to analyze caudate and hippocampus shape in schizophrenia. Zhao, et al. [17] used the same framework to analyze hippocampus shape in late-life depression. McKeown et al. [18] employed SPHARM for thalami shape analysis in Parkinson's disease (PD). They found some differences between "control and PD thalami" and also "left and right" thalami in each group that volumetric analysis was unable to distinguish between them. SPHARM has been widely used for hippocampus shape analysis in Alzheimer's disease (AD) [19-21]. Gerardin et al. [22] obtained 88% accuracy in distinguishing AD from normal aging by hippocampus shape analysis using SPHARM.

In epilepsy, there is evidence of hippocampus deformation due to the neuronal loss caused by the seizures [23]. Most of the previous works in epilepsy have focused on statistical analysis of the hippocampus deformation [24,25]. Vemuri and his research group [26,27] used hippocampus shape analysis for lateralization in epilepsy. In this paper, we employ hippocampus shape analysis using SPHARM for lateralizing mTLE.

When using SPHARM, challenges include accurate hippocampus segmentation by drawing regions on interest (ROIs) and registration of different subjects' ROIs. In this paper, registration challenges are discussed and a simple method utilizing principal component analysis (PCA) is proposed for faster and more efficient registration.

The outline of the rest of the paper is as follows. In Section II, we introduce the datasets and the necessary pre-processing steps. We then describe SPHARM-based shape representation and our proposed method for SPHARM registration. Next, we describe our feature extraction and selection methods. In Section III, we provide the lateralization results using SPHARM and hippocampal volumetry. We conclude in Section IV with a discussion and future works.

## II. Material and Methods

### A. Data

We use T1-weighted (T1W) MR images from two databases: (i) 12 healthy and 65 epileptic subjects from Henry Ford hospital (HFH) and (ii) 18 healthy subjects from Internet Brain Segmentation Repository (IBSR, publicly available from http://www.cma.mgh.harvard.edu/ibsr/data). HFH T1W images were either 256×256, voxel size=0.78×0.78×2 $mm^3$ or 512×512, voxel size=0.39×0.39×2 $mm^3$ (Slice thickness=2 mm).

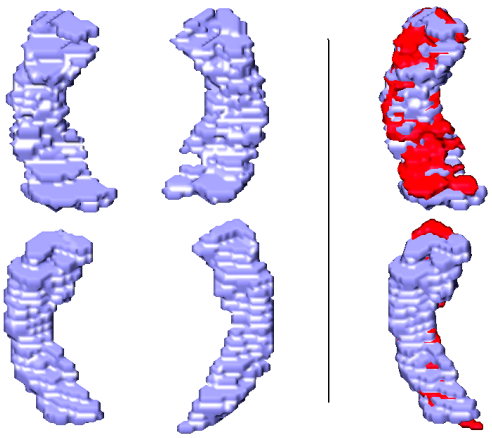

Figure 1. Segmented hippocampi mapped on the MNI template; (up) IBSR, (bottom) HFH – epileptic, (left) both hippocampi of a subject, (right) mirrored right HC [red] on the left one [blue].

IBSR images were 256×256 with and voxel size of 0.84×0.84×1.5 $mm^3$ or 0.94×0.94×1.5 $mm^3$ or 1×1×1.5 $mm^3$ (Slice thickness=1.5 mm). Therefore, structural standardization should be done for all images.

IBSR dataset provides manual segmentation of 43 brain structures including the hippocampi. Manual hippocampus segmentation of HFH images was also available, with reference to an MRI atlas identifying the hippocampus [4].

### B. Data Pre-processing

We rigidly register the datasets to the Montreal Neurological Institute (MNI) atlas using the FSL software [28].

This generates a common framework for all the images: 3D 182×218×182 volume matrices with voxel size of 1×1×1 $mm^3$. Obviously, the ROIs undergo the same transformation.

Moreover, right segmented HCs are mirrored for having a unique framework for all left and right HCs. Instances of HFH and IBSR HCs mapped on MNI template are shown in Fig. 1.

### C. SPHARM

SPHARM was proposed by Brechbühler et al. [13] for modelling arbitrarily shaped but simply connected 3D objects. SPHARM, similar to volume, is a global shape analysis framework, but its multi-scale characteristics make it superior over simple volumetric analysis. Fig. 2 gives an overall view of the SPHARM processing pipeline for hippocampus shape analysis. Three steps are often taken in a typical SPHARM analysis:

(1) Surface parameterization
(2) SPHARM expansion
(3) SPHARM registration

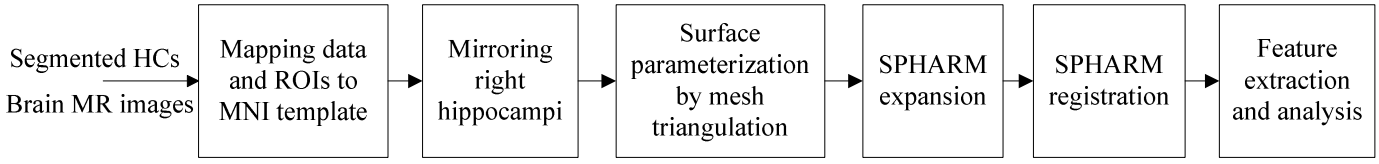


Figure 2. The proposed procedure for shape analysis of hippocampus using SPHARM.

In the first step, we parameterize the segmented HC surface by triangular meshes. This method considers a number of points (also called vertices) on the HC surface with their $(x,y,z)$ coordinates stored in a $N_v \times 3$ matrix, where $N_v$ is the total number of vertices. The connections between vertices in the triangular meshes are stored in another matrix named Faces. Each row of this matrix represents a face on the surface. Since triangular meshes are of interest, Faces is an $N_f \times 3$ matrix, where $N_f$ is the total number of faces. Finally the [Vertices, Faces] matrices provide the parameterized surface.

Equation (1) is a relation between $N_f$ and $N_v$, which could be used for testing correctness of surface parameterization of a 3D closed object:

$$N_f = 2(N_v - 2) \tag{1}$$

SPHARM basis functions of degree $l$ and order $m$ ($Y_l^m, -l \le m \le l$) are defined as follows:

$$Y_l^m(\theta,\phi) = \sqrt{\frac{2l+1}{4\pi}\frac{(l-m)!}{(l+m)!}} P_l^m(\cos\theta)\, e^{im\phi} \tag{2}$$
$$\theta \in [0:\pi], \phi \in [0:2\pi)$$

where $P_l^m(\cos\theta)$ are the associated Legendre polynomials defined by the differential equation:

$$P_l^m(w) = \frac{(-1)^m}{2^l l!}(1-w^2)^{m/2}\frac{d^{m+l}}{dw^{m+l}}(1-w^2)^l \tag{3}$$

Therefore, considering a parameterized surface $\vec{v}(\theta,\phi)$ in spherical coordinate, the SPHARM expansion takes the form:

$$\vec{v}(\theta,\phi) = (x(\theta,\phi), y(\theta,\phi), z(\theta,\phi))^T = \sum_{l=0}^{\infty}\sum_{m=-l}^{l} \vec{c}_l^{\,m} Y_l^m(\theta,\phi) \tag{4}$$
$$\vec{c}_l^{\,m} = (c_{lx}^m, c_{ly}^m, c_{lz}^m)^T$$

The coefficients $c_l^m$ up to a user-desired degree ($L_{max}$) can be estimated by solving a set of linear equations in a least squares fashion. The object surface can be reconstructed using these coefficients. Using more coefficients leads to a more detailed reconstruction [19]. This is depicted in Fig. 3.

We set $L_{max} = 15$ to keep appropriate amount of details of HC shape. This results in $(L_{max}+1)^2 = 256$ $c_l^m$ coefficients for each HC. So considering $x$, $y$, and $z$ elements of $c_l^m$, the total number of features for each HC will be $256 \times 3 = 768$. We carry out the same process for every HC, but before comparing these 768 features, some normalization is required. Applying the same methods discussed in [16] can easily handle translation, but SPHARM registration remains challenging.

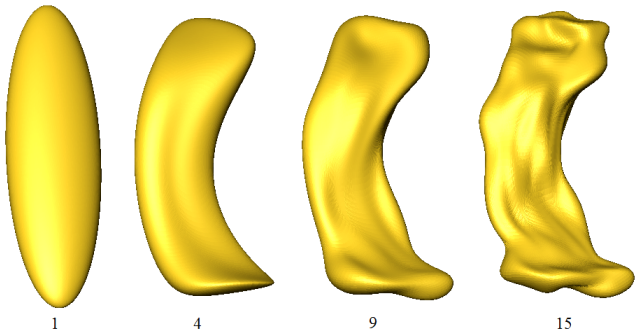


Figure 3. SPHARM shape description of right HC of the IBSR example shown in Fig. 1 at 4 different degrees (1, 4, 9, 15). Degree 1 description is called *first order ellipsoid* (FOE) and is used in SPHARM registration.

### D. SPHARM Registration

The whole brain registration introduced in section II-B can slightly help with bringing the HCs to a common framework. But due to the variable HC orientation in different subjects, fine tuning is still of great importance. In other words, without SPHARM registration, the coefficients are not useful.

To cope with this problem, some methods have been proposed in the literature. Mckeown et al. [18] uses the 3D invariants proposed in [29]. In this method, SPHARM coefficients are considered as tensors. By applying the concepts of *tensor theory*, any dependency upon orientation is eliminated. Shen et al. [20] uses landmarks for registration of SPHARM objects. In his method, landmarks are manually placed on some corresponding surface points of all objects. By minimizing the root mean square distance between landmark vectors of two subjects, they are aligned. This step is not performed in the object space; rather it is performed in the SPHARM feature space.

Both of the above methods are efficient but very complicated. The latter is greatly subjective too. We propose a simple yet practical method. The following steps can briefly express this method:

1- Compute the FOE of each hippocampus (which is degree 1 SPHARM description).
2- Represent it using [vertices, faces] format described in Section II-C
3- Calculate principal components (PCs) of the matrix 'vertices' (3 principal components exist, more details on PCA in [30]).
4- Compute the 3×3 matrix M for mapping these three principal components on the three main axes.
5- Multiply SPHARM coefficients by M to obtain new coefficients $c'^m_l$.

As $c_l^m$ consists of $x$, $y$, and $z$ elements, applying the same mapping on the corresponding coefficients is possible. An example is provided in Fig. 4.

Modified coefficients generated by this method are representative of shapes with complete alignment on the Cartesian axes, so $c'^m_l$ will be used to compare different hippocampi, such as normal and epileptic ones. Fig. 5 depicts a sample result of our method for fine alignment.

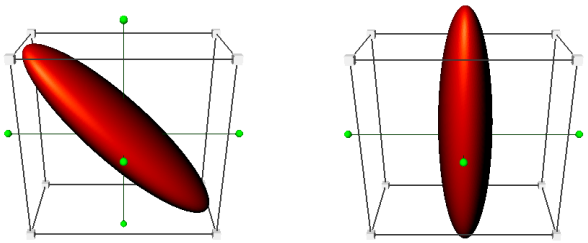


Figure 4. Mapping PCs of FOE to main axes for SPHARM coefficients registration.

### E. Feature Extraction

In this section, we test four features for lateralization. Only the first one, hippocampi volume ratio for each subject, is calculated for both HFH and IBSR images. The other three that are extracted from SPHARM coefficients are calculated only for the HFH images. These three features detect the differences between left and right hippocampi of each subject, as well as the differences between the hippocampi of normal and epileptic subjects. Since manual hippocampus segmentation varies among experts, this variation (between HFH and IBSR segmentation) could make a difference in calculation of distance between coefficients of healthy and epileptic subjects. Hence, IBSR is eliminated in the SPHARM analysis.

#### 1) Volume

Volumetric analysis is the old method for lateralization. We calculate the lateralization index $LI_{vol}$ as follows:

$$LI_{vol} = \frac{L_{vol} - R_{vol}}{L_{vol} + R_{vol}} \tag{5}$$

where $R_{vol}$ and $L_{vol}$ are the volumes of the right and left hippocampi. Negative (positive) values of $LI_{vol}$ indicate smaller left (right) hippocampus. In mTLE, the smaller hippocampus is more likely to be epileptogenic. For normal subjects, this index is usually around zero.

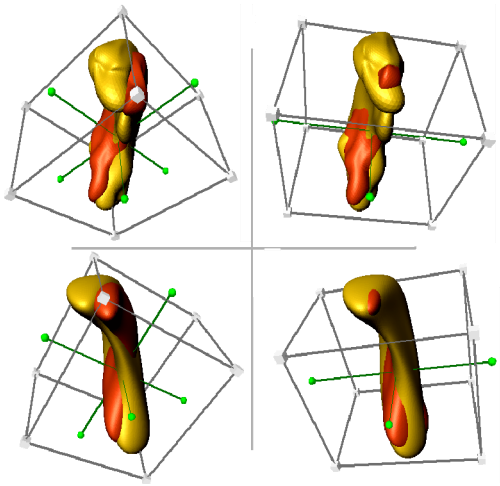

Figure 5. SPHARM description of two subjects' HC; (left) Raw SPHARM description, (right) Aligned SPHARM description by the proposed method, (top) Degree 15 and (bottom) Degree 5 SPHARM description.

#### 2) Self Distance I

As discussed in section II-D, each hippocampus is described by 768 SPHARM coefficients, which are positive and negative real numbers. Since not all of them are useful, some coefficients selection is necessary. We select the coefficients that have the same sign (+ or -) for all 154 hippocampi (77×2=154). This leads to 20 coefficients (*CL* and *CR*) for each hippocampus. This method of selection is justified by the fact that the coefficients with multiple changes in sign for different subjects are not accurate representor of hippocampus shape, as they are not matched sufficiently to the HC shape and thus are not consistent.

After coefficient normalization, the lateralization index based on self distance ($LI_{SD1}$) is calculated by:

$$LI_{SD1} = \sum_{i=1}^{20} \frac{|CL(i)| - |CR(i)|}{|CL(i)| + |CR(i)|} \tag{6}$$

#### 3) Self Distance II

Another method to establish a criterion for measuring left-right hippocampi distance is using the simplest invariants discussed in [29] for each aligned hippocampus. This is a multi scale method and summarizes all the coefficients to $L_{max}+1$ values by:

$$N(l) = \sum_{m=-l}^{l} \left| c_l^{'m} \right| \quad , \quad l = 0,1,..., L_{max} \tag{7}$$

The following equation generates another lateralization index based on self distance ($LI_{SD2}$):

$$LI_{SD2} = \sum_{l=0}^{L_{\max}} \frac{|NL(l)| - |NR(l)|}{|NL(l)| + |NR(l)|} \tag{8}$$

#### 4) Distance to Normal Subjects

Another approach for finding the abnormal hippocampus in one subject is to find which hippocampus is less similar to a normal hippocampus. For this purpose, we utilize the 20 coefficients selected in II-E-2. Since there are 12 normal subjects in HFH, 24 healthy hippocampi are available. The following equations are used to measure the distance between each hippocampi of the epileptic subjects and the normal hippocampi:

$$\begin{aligned} DIST\_L(i,j) &= \sum_{k=1}^{20} \left(CL_i(k) - CN_j(k)\right)^2 \\ DIST\_R(i,j) &= \sum_{k=1}^{20} \left(CR_i(k) - CN_j(k)\right)^2 \\ i &\in [1,65] \quad j \in [1,24] \end{aligned} \tag{9}$$

*CN* represent the 20 coefficients for 24 left and right hippocampi of normal subjects. Smaller distance shows more similarity to normal hippocampi. So, we calculate another lateralization index as defined in (10):

$$LI_{D2N}(i) = \sum_{j=1}^{N} sign\left(DIST\_R(i,j) - DIST\_L(i,j)\right) \qquad (10)$$
$$i \in [1,65]$$

The maximum value of $N$ is 24, but in cases where *DIST_R(i,j)/DIST_L(i,j)* is around 1, that $j$ is ignored. The interpretation of this index is just the same as other three LIs: negative (positive) value show healthier right (left) hippocampi.

## III. Results

### A. Volumetric Analysis

Using (5) for finding the epileptogenic hippocampus, correct classification ratio of 78% (51 out of 65) is achieved. However, Table I reveals the overlap between range of $LI_{vol}$ for epileptic and normal subjects.

So, if statistical distribution of normal $LI_{vol}$ is considered $N(\mu,\sigma)$, only those epileptic with $LI_{vol}$ outside $[\mu-2\sigma, \mu+2\sigma]$ could be confidently classified as right or left, but those $LI_{vol}$ within this range will remain as the input to the next analysis step, which is SPHARM analysis. Here, by considering $\sigma$=0.04 and $\mu\approx$0, 40 subjects are outside the bound and 25 are inside. Table III contains the detailed results of volumetric analysis.

### B. SPHARM Analysis

Here, we calculate the three SPHARM-based features, defined by (6), (8), and (10), for all normal and epileptic subjects. Again, we find the confidence interval of normal state for each of these features, and classify those subjects outside the bounds. Table II gives some information about these LIs. Almost in all epileptic cases (except two of them), three LI values have the same sign, and all subjects have at least one LI outside the normal state intervals. So, the classification is performed and the results are provided in Table III.

TABLE I. $LI_{VOL}$ FOR HFH AND IBSR DATASETS, EP=EPILEPTIC, N=NORMAL.

| | No. of subjects | Mean $LI_{vol}$ | STD $LI_{vol}$ | Max $LI_{vol}$ | Min $LI_{vol}$ |
|---|---|---|---|---|---|
| **N-HFH** | 12 | -0.003 | 0.037 | 0.079 | -0.06 |
| **N-IBSR** | 18 | -0.005 | 0.034 | 0.056 | -0.072 |
| **N-Total** | 30 | -0.004 | 0.035 | 0.079 | -0.072 |
| **EP-HFH** | 65 | -0.033 | 0.189 | 0.349 | -0.539 |

TABLE II. MEAN, STANDARD DEVIATION, MAXIMUM, AND MINIMUM VALUE FOR SPHARM-BASED LIS. N="12 NORMAL SUBJECT OF HFH", EP="25 EPILEPTIC SUBJECTS OF HFH WITH $|LI_{VOL}| \le 0.08$".

| | | Mean | STD | Max | Min |
|---|---|---|---|---|---|
| $LI_{SD1}$ | **N** | 0.33 | 4.92 | 7.67 | -11.74 |
| | **EP** | 1.15 | 8.57 | 14.96 | -19.66 |
| $LI_{SD2}$ | **N** | 0.07 | 1.12 | 2.11 | -1.78 |
| | **EP** | 0.32 | 2.12 | 4.52 | -3.13 |
| $LI_{D2N}$ | **N** | 0.08 | 1.08 | 3.00 | -1.00 |
| | **EP** | -0.19 | 2.13 | 6.00 | -5.00 |

TABLE III. RESULTS OF VOLUMETRIC AND SPHARM ANALYSIS FOR EPILEPTIC HIPPOCAMPUS LATERALIZATION, CC=CORRECTLY CLASSIFIED.

| | No. of subjects | No. of CC, VOL | No. of CC, SPHARM |
|---|---|---|---|
| $\|LI_{vol}\| \le 0.08$ | 25 | 14 (56.0%) | 18 (72.0%) |
| $\|LI_{vol}\| > 0.08$ | 40 | 37 (92.5%) | 37 (92.5%) |
| **EP - total** | 65 | 51 (78.0%) | 55 (85.0%) |

Considering the above results, it is clearly shown that the SPHARM method produced exactly the same result for those with $|LI_{vol}| > 0.08$, of course not only in overall CC ratio, but also in subject wise analysis.

### C. Statistical Analysis of LIs

In this section, we focus on the significance of our LIs for classification. For such purpose, *t*-test is the widely used method. However, the distributions of the LIs are not normal. Since normality is the fundamental assumption in *t*-test, it is not applicable in our case. *Mann–Whitney U*-test [31] is the nonparametric alternative. Here, the null hypothesis is that the distribution of each LI for patients with left seizure focus is identical to the distribution of those with right seizure focus. Table IV shows the *p*-value of this null hypothesis.

Table IV also provides the *p*-values for testing the significance of LIs between healthy and epileptic subjects. Considering the significance value of 5%, all the null hypotheses are rejected, and this supports the power of selected features for lateralization and also classifying normal and epileptic subjects. It should be also noted that if we consider those with $|LI_{vol}| > 0.08$, then the *p*-value of Table IV will be of order $10^{-5}$.

## IV. Conclusion and Discussion

In this article, we made use of a well-known shape analysis framework, SPHARM, for lateralization in mTLE.

To perform a comparison between healthy and epileptic subjects, some pre-processing such as voxel-size unification and rigid registration of the brain images are performed. Next, SPHARM-based representations of the HCs are achieved by calculating the coefficients. Then, we use our simple method for fine alignment of the HCs. The method is based on mapping the principal components of the FOE of each HC on Cartesian axes, and is carried out in the space of SPHARM coefficients. Finally, some features are extracted and the corresponding LIs are calculated.

As Table III suggests, the SPHARM-based method has improved the lateralization accuracy for patients with $|LI_{vol}| \le 0.08$. This improvement is achieved by the extra information in SPHARM coefficients in comparison to volume. If volume of a

TABLE IV. THE *P*-VALUES FOR TESTING SIGNIFICANCE OF THREE LIS FOR PATIENTS WITH $|LI_{VOL}| \le 0.08$. FOR TESTING SIMILARITY BETWEEN NORMAL AND EPILEPTIC SUBJECTS, ABSOLUTE VALUES OF LIS ARE CONSIDERED.

| | $LI_{SD1}$ | $LI_{SD2}$ | $LI_{D2N}$ |
|---|---|---|---|
| **L vs. R** | 0.0175 | 0.0138 | 0.0222 |
| **N vs. EP** | 0.0214 | 0.0050 | 0.0103 |

shape is considered to be equivalent to energy of a signal, then SPHARM coefficients will be the same as Fourier coefficients; obviously the latter provide more information about our signal (shape) of interest.

Also, similar to 1D Fourier expansion, in 3D analysis, the problem of choosing an optimum value for $L_{max}$ (similar to maximum frequency in 1D signals) to keep appropriate amount of details while preventing noise, exists. Hence, the trade-off among dimensionality, accuracy, and sensitivity to noise should be considered.

The above discussion is also applicable to support the method of feature selection in Section II-E-2. In 1D signal processing, we sometimes filter some prominent frequency components to omit other unwanted and irrelevant components, and this is very similar to what we proposed in that section.

To compare our lateralization results to others, the only available studies of this kind we could refer to are [26,27]. In both of these references, a common dataset consisting of 23 healthy subjects and 31 epileptic patients is used. Patients are with epileptic focus of either Left or Right Anterior Temporal Lobe (LATL or RATL), and from this point of view, their dataset is more specific than ours with patients from different types of mTLE. Their best result of 90.32% for classification of LATL and RATL is validated by the leave-one-out method. Beside the differences in the datasets, which contribute to the differences of the results, some local features are used in [26] and all of the subjects are used in the training phase.

In the future work, we will use localized features such as wavelets [14] and will enhance our classification method to improve the lateralization accuracy further.

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