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Functional Feature Embedded Space Mapping of fMRI data

Jin Hu, Jie Tian*, *Senior Member, IEEE*, Lei Yang

Abstract—**We have proposed a new method for fMRI data analysis which is called Functional Feature Embedded Space Mapping (FFESM). Our work mainly focuses on the experimental design with periodic stimuli which can be described by a number of Fourier coefficients in the frequency domain. A nonlinear dimension reduction technique Isomap is applied to the high dimensional features obtained from frequency domain of the fMRI data for the first time. Finally, the presence of activated time series is identified by the clustering method in which the information theoretic criterion of minimum description length (MDL) is used to estimate the number of clusters. The feasibility of our algorithm is demonstrated by real human experiments. Although we focus on analyzing periodic fMRI data, the approach can be extended to analyze non-periodic fMRI data (event-related fMRI) by replacing the Fourier analysis with a wavelet analysis.**

Keywords—**fMRI; Functional Feature Embedded Space Mapping (FFESM); Isomap; Fuzzy c-means clustering**

I. Introduction

With the coupling between neuronal activity and haemodynamics in the brain fMRI allows the non-invasive localization and measurement of brain activity. The most common technique, blood oxygenation level dependent (BOLD) fMRI, is sensitive to the changes of deoxyhemoglobin concentration in small local blood vessels [1]. fMRI measures a BOLD response which reflects a number of factors due to the task/stimulation. This technique has opened a new era for human brain investigation. However, changes in BOLD signal during brain activation are very small even with a high magnetic field (2 − 5% in 3T scanner). The ultimate success of the neurocognitive research depends on the accurate modelling of the relationship between the measured fMRI signal and the neuronal activity.

A popular way to analyze fMRI data is to consider the relationship as a linear invariant system of which GLM is the most widely used method [2]–[4]. Obviously, this method heavily depends on the prior knowledge of the experimental design and the assumption of the relatively simplified hemodynamic function. An alternative means which avoids these shortcomings is clustering method. The existing clustering methods usually suffer from the curse of dimensionality. The large amount of data reduces the algorithm performance and sometimes even makes them useless. Luckily, a time series is usually not only independent but also highly correlated. To take the advantage of the existing correlations between time series, we consider each time series as a vector in a high dimensional space. But there is a lot of redundancy due to the correlations. Feature extraction should be applied to get a fine low dimensional representation of the original high dimensional data. Features in a low dimensional space not only improve the algorithm performance but also achieve a more accurate representation of the original data model. A fine low feature representation provides a direct view of the original data set.

Popular feature extraction techniques for time series include the Discrete Wavelet Transform (DWT) and Discrete Fourier Transform (DFT). Nowadays, most of the BOLD fMRI experiments are block design and the corresponding BOLD signals are periodic ones. And for those signals, the Fourier basis provides the most interesting projection of the data. It has been shown that the BOLD response to periodic stimuli can be well described by a small number of Fourier coefficients [5]. Traditional fMRI analysis algorithms such as Statistical Parametric Mapping (SPM) [2]-[4] and deconvolution model [6] have considered the system as time invariant. The existing variation in delay is often overlooked and assumed constant over all activated voxels, and the results is not robust. When applying DFT to the periodic BOLD signal, the delay in the time domain creates a shift in the phase, but the energy level is left unchanged [5].

To avoid the curse of dimensionality problem, we have used an appropriate representation of the data. Two of the most common dimension reduction methods are the principle component analysis (PCA) and Multidimensional Scaling (MDS). They are valuable for extracting low dimensional representations for a certain kind of data, but do not attempt to explicitly model the underlying manifold. Recently, several nonlinear methods have been proposed for nonlinear dimension reduction, such as Laplacian Embeddings [14], Isomap[13] and Locally Linear Embeddings (LLE) [15]. These methods can directly model the manifold of the dataset. We choose Isomap since it is an instance of a large family set of unsupervised learning algorithms-unlike Laplacian Embeddings which is a semi-supervised learning method, and only Isomap holds the computational efficiency and global optimality-unlike LLE. And the guarantee of asymptotic convergence is Isomap's major features. Moreover, LLE's maintenance of the global structure is through the fitting of simple local linear models [15] and thus may distort the global structure. As far as know, it is the first time to apply Isomap to dimension reduction of the feature space of fMRI

Jin Hu and Jie Tian* are with Medical Image Processing Group, Institute of Automation Chinese Academy of Science, Beijing, 100080, China (corresponding author to provide email: tian@ieee.org)

data. Here we present a framework called Functional Feature Embeded Space Mapping (FFESM) for fMRI data analysis.

This paper is organized as follows. In Section 2 provides a general description of our method. In Section 3, real human experiments are presented to evaluate the efficiency of our work. The discussion and conclusion are addressed in Section 4.

II. Methods

Fig. 1 shows the schema of our method. When the image series are ready for analysis (usually after preprocessing–realignment and smoothing), a single voxel time series is picked. For periodic time series, we use DFT to find the features in frequency domain called functional feature space. It is often a high dimensional functional feature space and suffers from the curse of dimensionality. Then nonlinear dimension reduction technique is applied to obtain the low dimensional representation of the functional feature space which is called functional feature embedded space. Finally, we apply clustering method in the functional feature embedded space and get the desired brain activation area.

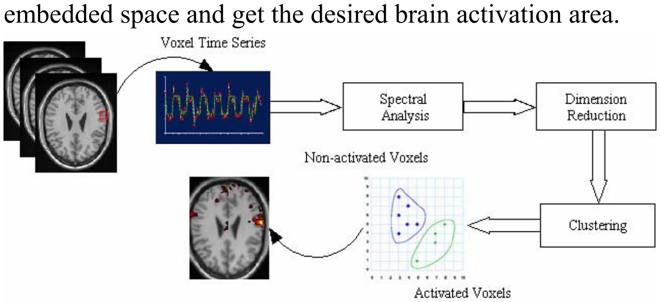

Fig. 1 Schema of Functional Feature Embedded Space Mapping

A. Preprocessing

The first step is to realign the data in order to 'undo' the effects of subject movement during the scanning session. After realignment, the data are spatially smoothed before entering the analysis proper. Finally a number of voxels in the data are selected for analysis by image intensity thresholding segmentation to exclude the voxels outside the brain.

B. Spectral Analysis

In a standard block paradigm, control and active states are cycled in a periodic manner during the fMRI experiment. Therefore, the response signal should also be periodic. In this case, Fourier Transformation has the following virtues as [5] mentioned.

The Fourier basis can provide the most interesting projection of the data. And it has been shown that the BOLD response to periodic stimuli can be well described by a small number of Fourier coefficients. The existing variation in delay is often overlooked and assumed to be constant over all activated voxels, and the results are not robust. In the Fourier domain the delay creates a shift in the phase, while the magnitude is left unchanged. Although we focus on analyzing periodic fMRI data, the approach could be extended to analyze non-periodic fMRI data (event-related fMRI) by replacing the Fourier analysis with a wavelet analysis.

After DFT, each data set is DC corrected to remove any linear drift in the data over time. Prior to the following analysis, each voxel features in the frequency domain is demeaned, detrended and normalized to variance 1.

C. Dimension Reduction

After DFT, a high dimensional functional feature space is obtained. Then Isomap algorithm is performed to find its concise low dimensional representation as functional feature embedded space.

Isomap inherits the advantages of PCA and MDS and extends these to learn nonlinear structures that are hidden in high dimensional data. Computational efficiency, global optimality and the guarantee of asymptotic convergence are its major features [13].

Here Isomap assumes that local area is linear and the neighbor points lie on a linear spanning patch of the manifold. Isomap first define k nearest neighbor points or within some fixed radius ε . The points in one local area can be characterized by Euclidean distance. For the points in different local areas (or to say for the points in long path), Isomap uses a subsection linear technique to characterize the distance that is adding up neighboring distance along the manifold. When constructing Isomap, neighborhood are first determined by using input space Euclidean distance $d_x(i,j)$ where point i and point j are neighbors. Thus these neighborhood relations are represented as a weighted graph G over all the data points, with edges of weight $d_x(i,j)$ [13]. In the Isomap second step, it estimates the geodesic distances $d_M(i,j)$ between the pair points i and j using Floyd's Theorem and computes their shortest path distances $d_G(i,j)$ in the graph G . Finally Isomap applies classical MDS to the matrix of graph distances $D_G = d_G(i,j)$, constructing an embedding of the data in a d-dimensional Euclidean space Y which best preserves the manifold's intrinsic geometry.

The coordinate vectors y_i for points in Y are chosen to minimize the cost function

$$E = \left\| \tau(D_G) - \tau(D_Y) \right\|_{L^2}$$

where D_Y denotes the matrix of Euclidean distances $\left\{ d_Y(i,j) = \left\| y_i - y_j \right\| \right\}$ and τ function converts distances to inner products and is defined as follows[13]:

$$\tau(D) = -HSH/2$$

where S is the matrix of squared distances $\left\{ S_{ij} = D_{ij}^2 \right\}$ and H is the centering matrix $\left\{ H_{ij} = \delta_{ij} - 1/N \right\}$.

D. Clustering Method

The goal of this step is to group voxels in functional feature embedded space into groups that represent similar shapes. Fuzzy c-means (FCM) is a data clustering technique wherein each data point belongs to a cluster to some degree that is specified by a membership grade. The method for estimating the number of clusters C is performed by minimizing the minimum description length (MDL) criterion.

III. Results

A healthy right-handed subject participated in a finger tapping experiment with written consent. A typical block design was employed with alternating control condition. The whole scan took 300 seconds. The control and experimental conditions were alternated every 30s (10 scan) and repeated 5 times. The experiment was performed on a 3.0-T GE Signa system (GE Medical Systems, Milwaukee, WI, USA) at Tiantan Hospital Beijing China with a standard head coil. Prior to MR imaging, the subjects were visually familiarized with the procedures and the experimental conditions to minimize anxiety and to enhance task performance as well. The participants were placed in the scanner in a supine position with earplugs to muffle the noise. Head fixation was assured through a foam-rubber device mounted on the headcoil. T2*-weighted images were acquired using a gradient-echo EPI sequence (TR=3000ms, TE=30ms, flip angle = 900, FOV=240 ×240mm, matrix 64 ×64, 100 repetitions). Each volume consisted of 24 slices and the spatial resolution was 3.75 ×3.75 ×5 mm. T1-weighted anatomic images were acquired for reference (512 × 512). Fig. 2 indicates a diagram of paradigm timing.

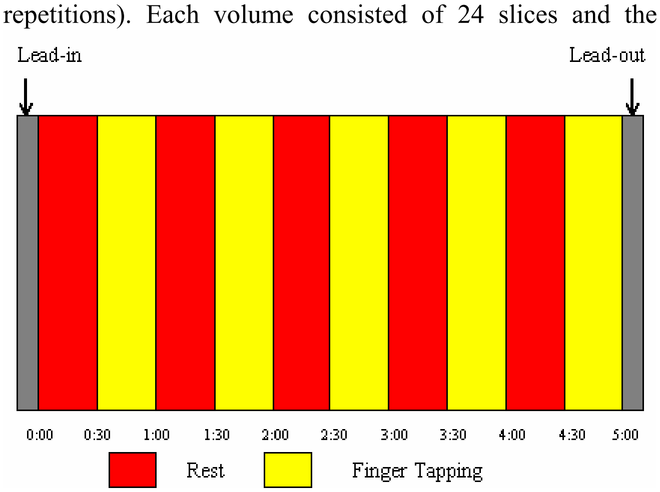

Fig.2 Experimental Paradigm Timing

We focus on the comparison of PCA as a linear method and Isomap in dimension reduction of the functional feature space. From Fig. 3, we find that the residual variance of dimension reduction by Isomap appears far more stable and lower than PCA when the reduced dimension is less than 16. Moreover, Fig. 4 presents the Isomap 2D representation of fMRI data in the functional feature embedded space and PCA 2D in the functional feature subspace respectively. The comparison of 2D representations obtained with two methods confirms the ability of the Isomap to put in evidence geometry structures of interest, while PCA with little or no structure. The voxel cluster corresponding to the detected active region is marked with red color, which is the one from the north arm in the Isomap 2D view but mixed with other points in the PCA 2D view. Time courses of the detected region with two methods are shown in Fig. 5. Obviously, the one with Isomap was less noisy than PCA.

To validate our method, we have applied it to the fMRI data of five different slices (from slice 19 to 23). The Isomap 2D representations in the functional feature embedded space in these slices are shown in Fig. 6. Fig. 7 shows the detected region during human motor tasks in each slice on T1 images. The results demonstrate a successful separation of activation sources in motor cortices. And the 2D view of fMRI data in different slices reveals a similar property of structures.

IV. Discussion and Conclusion

In this paper, we have proposed a new framework as FFESM for fMRI data analysis. FFESM has provided a novel 2D view to 4D fMRI data by using the descriptive numerical features of the data by nonlinear dimension reduction method Isomap which is first applied to fMRI data as the authors know. Our method takes advantages of data-driven and the ability in representation of intrinsic manifold of nonlinear fMRI data. The real human experimental results demonstrated a successful separation of human motor activation areas. This preliminary study confirms that the framework is feasible for detection brain activations from task-related fMRI series. Moreover, our method can be extended to analyze event-related fMRI by replacing the Fourier analysis with a wavelet means. The method can also be used to detect functional connectivity as well.

We will further improve this preliminary work by making the voxel neighboring constraint in the functional feature space extraction during the extraction of the functional feature embedded space.

V. Acknowledgments

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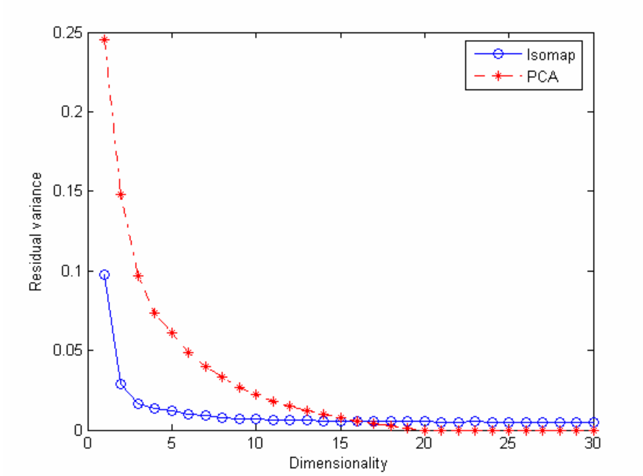

Fig. 3 the residual variance of dimension reduction results by Isomap and PCA.

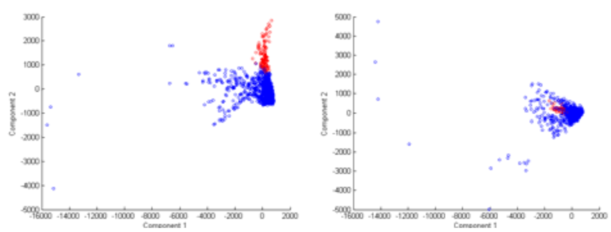

Fig. 4 the Isomap 2D representation of the fMRI data in the functional feature embedded space (left) and PCA 2D in the functional feature subspace (right)

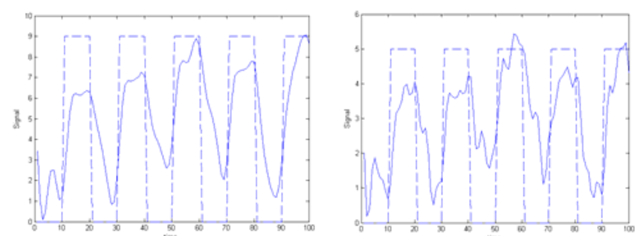

Fig. 5 Time courses of the detected region with Isomap (left) and PCA (right). Solid line: time course, broken line: experimental design matrix.

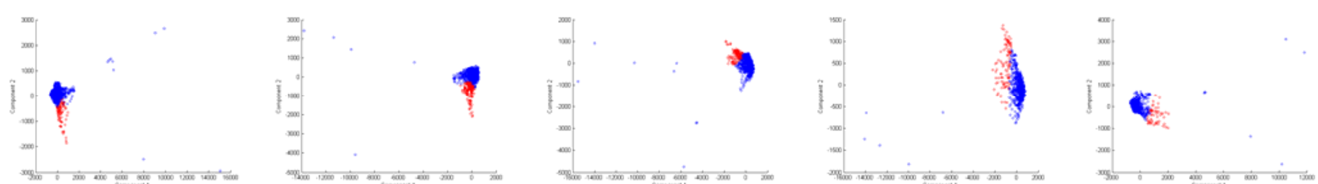

Fig. 6 The Isomap 2D representations in the functional feature embedded space in five slices (from left to right: slice 19, 20, 21, 22 and 23)

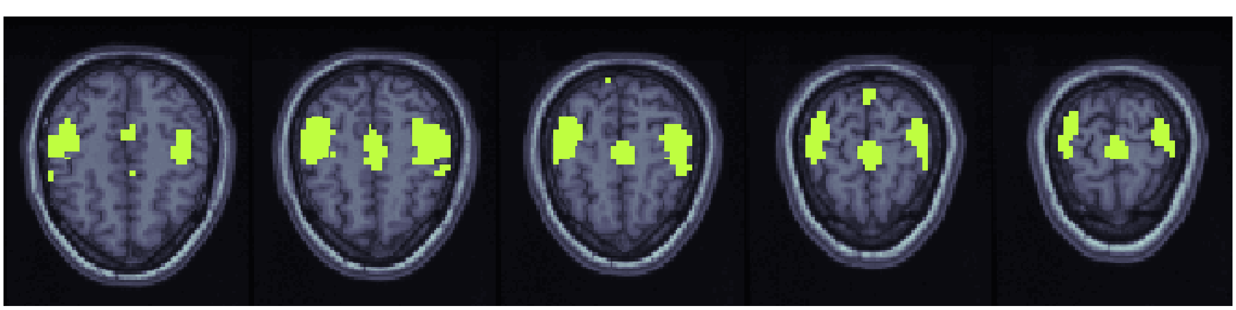

Fig. 7 Detection Results by FFESM from fMRI data of a human motor task (from left to right: slice 19, 20, 21, 22 and 23).