Fuzzy Cluster Method based on RV measure for functional MRI data analysis

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***Abstract*—Functional magnetic resonance imaging (fMRI) has become one of the important tools of functional connectivity studies of the human brain. Fuzzy clustering method (FCM) is a common method for analysis of fMRI data. Traditional FCA methods measure the similarity between the BOLD time course of a centroid and the ones of all other voxels in the brain on the basis of Pearson correlation coefficient. This article puts forward a multi-voxel-based RV coefficient similarity measure to overcome the defects of traditional similarity distance measure in FCM. The experimental results show that the RV-based FCA method has not only improved the speed of FCA, but has comparatively raised the accuracy of the method.**

Keywords- fMRI, FCA, Pearson coefficient, RV coefficient

I. INTRODUCTION

Blood oxygenation level dependent (BOLD) fMRI has become one of the important tools in vivo brain function physiological and pathological activities research because of its high spatial and temporal resolution. Fuzzy clustering analysis (FCA) which has the benefit of being exploratory and paradigm independent method was successfully applied to fMRI data analysis to detect functional signals [2,3,4,12,14]. But because fMRI data is of large quantities and contains many kinds of noises, FCA subjects to certain restrictions on several applications of fMRI.

Traditional FCA methods measure the similarity between two single voxels like Euclidean distance or Pearson correlation coefficient [11], which is widely used owing to its sensitivity, simplicity, and ease of interpretation. However, these univariate based distance similarity measures are with certain defects. On the one hand, FCA of fMRI data always costs huge computing time with large quantity of iterations due to the slow convergence speed. Univariate based measure can't reach the steady iterative state in a short period of time. On the other hand, fMRI data always contains a large amount of spatial random noise. However, univariate analysis method is highly susceptible to the noise, which leads to a salt-and-pepper-like connectivity map. Although smoothing could suppress a part of spatial noise, the connectivity map would become blurred and obscure.

The RV coefficient was firstly introduced by Robert and Escoufier [6, 13]. This multivariate statistic provides a very efficient way to measure the similarity between two sets of variables with the same number of sample observations [1]. In the present study, we use RV coefficient to measure the spatial connectivity patterns between a cube centered on the centroid and a cube centered on each datum of the whole brain. We aim to improve the FCA method by adopting the multivariate distance measure, RV coefficient measure, to enhance the convergence rate of each iteration as well as to suppress the spatial random noise.

In the experiment part, we used visual fMRI data to explore whether our RV based multivariate distance measure can be used to extract functional information more quickly and at the same time reduce the influence of spatial random noise. As a comparison, the hyperbolic correlation coefficient (HCC) measure [11] was used as the univariate distance measure.

II. METHOD

A. Fuzzy C-means clustering method

FCA [17] presents an alternative to hard clustering. It attempts to find a partition of a dataset X of n time courses which are considered as points in t dim-dimensional space. They are to be assigned to one of the c cluster centers (representative time courses) which are defined by a matrix V(c, t). Furthermore, the c-partition of X is defined by the matrix U(c, n). The members of U(c, n), u_{ik} are the membership values of the k-th voxel to the i-th centroid.

$$\text{①}\ 0 \le u_{ik} \le 1\ \forall i, k$$
$$\text{②}\ 0 < \sum_{k=1}^{n} u_{ik} \le n\ \ \forall i$$
$$\text{③}\ \sum_{i=1}^{c} u_{ik} = 1\ \forall k\ (\text{i.e. no empty cluster}) \tag{1}$$

The matrices U and V are determined by an enhanced version of the fuzzy C means algorithm proposed by Bezdek [5], which minimizes the functional J_m:

$$J_m(X, U, V) = \sum_{i=1}^{c} \sum_{k=1}^{n} u_{ik}^{m} d^2(x_k; v_i) \tag{2}$$

where d (x_k; v_i) is the distance between the k-th datum and the i-th centroid. The traditional HCC measure was a kind of single-voxel metric measure [11] used as a contrast to the RV distance measure. Its expression as a function of the correlation coefficient ρ_{ik} between each data vector x_k and the prototype v_i, is the following:

$$d(x_k; v_i) = (1 - \rho_{ik})/(1 + \rho_{ik}) \tag{3}$$

The solution of minimizing J_m is found by a two-stage iteration:

$$\text{①}\ \ v_{il} = \sum_{k=1}^{n} u_{ik}^{m} x_{kl} / \sum_{k=1}^{n} u_{ik}^{m}$$
$$\text{②}\ \ u_{ik} = 1/\sum_{j=1}^{c} (d(x_k; v_i)/d(x_k; v_j))^{2/m-1} \tag{4}$$

v_{il} is the element of the matrix V and m> 1 is a parameter which controls the fuzziness of the clusters (we used m=2). The iterations stop when the algorithm satisfies predetermined convergence criteria. The extensive description of FCA can be seen from the references [7, 8].

B. RV coefficient measure

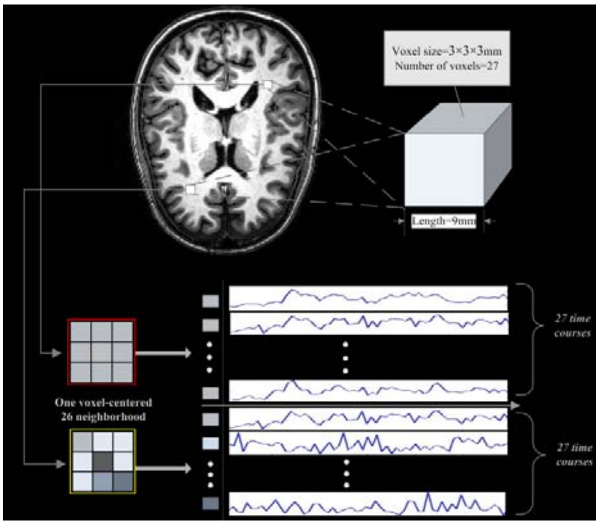

Figure 1. The multivariate similarity framework for the analysis of the functional connectivity. The region surrounded by the red closed curve is one of the local regions falling into the datum search cube. The region surrounded by the yellow closed curve is the centroid search cube. The datum search cube is moved through the entire brain volume voxel by voxel. The centroid search cube is just moved through the entire centroids. At each location, the multivariate similarity is measured between the time courses from the voxels within these two search cubes.

To investigate the intensity of functional connectivity between each location in the brain with a particular centroid, we obtain the search cube centered on a particular voxel (see Fig.1). We define the centroid search cube as the search cube centered on the center of a cluster, and datum search cube as the search cube centered on the voxel to be classified. The cube contains multiple neighboring voxels with a particular size and shape. We move the datum search cube through the entire brain volume voxel by voxel. At each location, we measure the multivariate similarity between the time courses of the voxels falling into the centroid search cube and the time courses of the voxels falling into the datum search cube. We can map the connectivity patterns of different spatial scales by choosing the search cube with different sizes and shapes.

To measure the similarity between two sets of time courses, we utilize the multivariate statistic of RV coefficient. RV coefficient can be described as:

$$\mathrm{RV}(\mathrm{X},\mathrm{Y}) = \frac{\mathrm{tr}(\mathrm{XX^tYY^t})}{\mathrm{tr}(\mathrm{XX^tXX^t})^{\frac{1}{2}} \times \mathrm{tr}(\mathrm{YY^tYY^t})^{\frac{1}{2}}} \quad (5)$$

where X and Y are n×p and n×q matrix from two data sets, which involve p and q numerical variables respectively on the same sample of n time points, X^t is the transpose of matrix X, and tr(·) is the trace operator of square matrix. In our study, X is a data set composed of voxels falling into the datum search cube centered by x_k, Y is a data set composed of voxels falling into the centroid search cube centered by v_i. So the distance can be described as:

$$\mathrm{d}(\mathrm{x_k}; \mathrm{v_i}) = \mathrm{D}(\mathrm{X},\mathrm{Y}) = \sqrt{2(1-\mathrm{RV}(\mathrm{X},\mathrm{Y}))} \quad (6)$$

The value of RV coefficient ranges from 0 to 1. If RV coefficient is 0, the two sets are independent, which denotes no correlation or similarity between the two data sets. If RV coefficient is 1, the eigen components of data set X can be derived from Y through a homothetic transformation, which means that there exists a rotation matrix H and a scaling factor c such that cXH=Y. For RV calculation, X and Y must be firstly mean centered by column [19].

III. EXPERIMENT

A. Data acquisition

In this study, a healthy subject participated with informed consent. In experiment, the visual paradigm of the subject was OFF-ON-OFF-ON-OFF-ON-OFF. Each block lasted 20s. At 'ON' state, visual stimulus was corresponding to a radial blue/yellow checkerboard, reversing at 7 HZ. And at the 'OFF' state, the participant was required to focus on the cross at the center of the screen.

The fMRI data was acquired on a Philips 3.0 Tesla scanner using a multi-element receiver coil to allow partially parallel image acquisition. BOLD fMRI data was acquired using single-shot SENSE gradient echo EPI with 40 slices providing whole-brain coverage, a SENSE acceleration factor of 2.0, a TR of 2.0 s and scan resolution of 80×80. Nominal in-plane resolution was 3mm × 3mm; slice thickness was 3 mm; slice gap was 1 mm.

Preprocessing was performed on visual fMRI data. Scans were slice timing corrected, spatially realigned and removal of non-brain voxels,. All the procedure was implemented with SPM8 software and in-house Matlab codes.

B. Analysis of fMRI data

The following three types of analytic methods were used to detect the functional signals and assess the activation maps:

A. HCC-based FCA on unsmoothed fMRI data
B. HCC-based FCA on smoothed fMRI data
C. RV-based FCA on unsmoothed fMRI data

In Method B, the full width at half maximum (FWHM) of the Gaussian kernel for smoothing was 6mm.The variances of the Gaussian kernel were 1. In Method C, the size of the search cubes was 9mm×9mm×9mm (3×3×3 voxels). To determine the number of clusters, we applied the above three methods for a range of values between 2 and 15. After visual assessment of the topography and time course of the resulting clusters, we selected the relatively optimal values which were close agreement with literature wrote by Fadili [9].

C. Results and methods comparisons

Fig.2 shows the activation maps of visual fMRI data obtained by the above three methods. Three activation maps all show that, during the visual task-related state, occipital lobe region is activated. However, the activation map obtained by Method A shows a salt-and-pepper pattern, which makes it difficult to distinguish the actual activated patterns from the spatial noise. The activation maps obtained by Methods B and C are homogeneous within a particular local region. This suggests that Methods B and C could remove some spatial random noise and make the activated regions more localized.

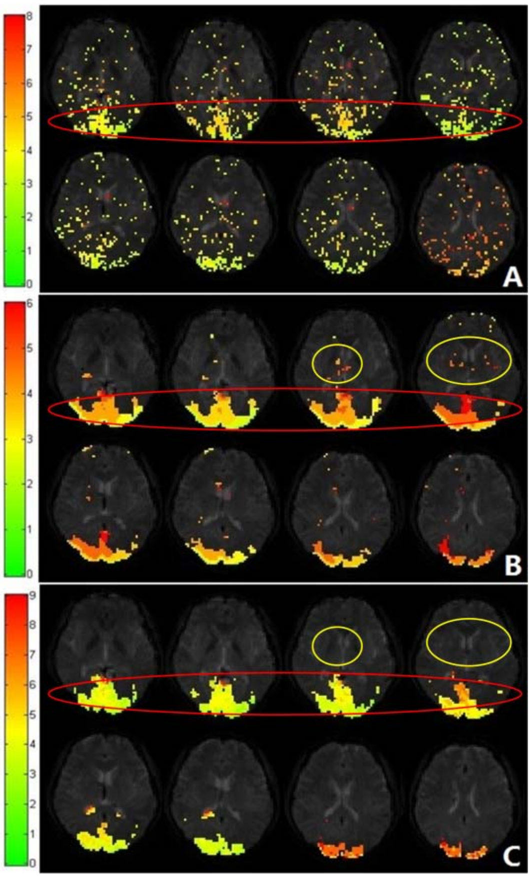

Figure 2. Spatial maps related to visual stimulus from the 14th to 21st slices. A and B denote the spatial maps corresponding to the HCC-based FCA on the unsmoothed and smoothed data respectively; C denotes the spatial maps corresponding to RV-based FCA on the unsmoothed data. The regions surrounded by the red curves represent demonstration areas for comparison among Methods A-C. The regions surrounded by the yellow curves represent demonstration areas for comparison among Methods B and C.

However, from the regions surrounded by the red curves in each method, we could see that the activated local regions obtained by Methods B and C are larger than those obtained with Method A, which indicates that Methods B and C both have a expanded phenomenon, while the regions of Method C expand lesser. The maps obtained by Method B still show a noise pattern which can be seen from the regions surrounded by the yellow curves (Fig.2B). This suggests that although smoothing the data with Gaussian kernel could suppress the spatial noise and improve the homogeneity of nearby voxels, it has the difficulty in distinguishing the signals from the random noises, rendering the former as the noise and being eliminated from the final activation map. Therefore, Method C has a better performance than Method B in noise suppression (Fig.2B and C).

Furthermore, we use receiver-operating characteristics (ROCs; Fig.3) [10, 15] to quantitatively assess how well different methods distinguishthe effective regions and the background noise. The visual fMRI data entered into the General Linear Models (GLM) for parameter estimation. By comparing the visual region obtained by GLM with the ones obtained by each FCA method, we could evaluate the detecting performance of each method using ROCs.

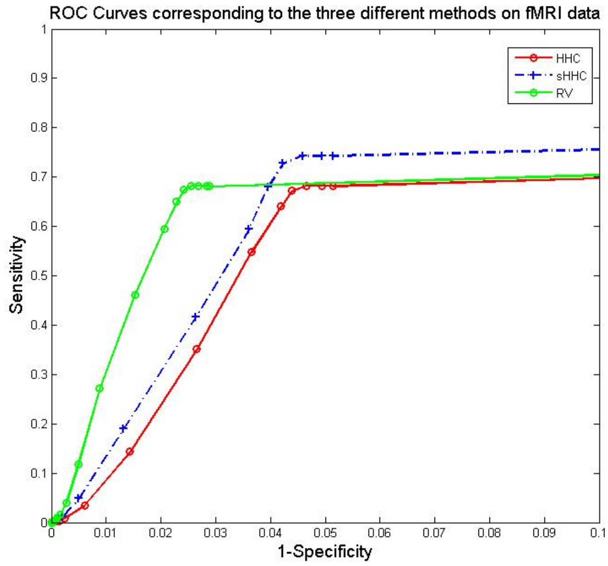

Figure 3. ROC curves corresponding to the three different methods on visual fMRI data.

As shown in Fig.3, the curve of Method A are at the bottom of all curves, which indicates the worst performance. This is mainly due to that univariate analysis method is highly susceptible to the noise and thus reduces the detection performance. The curve of Method C is located above that of Method B when the false positive rate (1-specificity) is between 0 and 0.04 while it is located under that of Method B when the false positive rate is more than 0.04. This phenomenon indicates that RV calculation on unsmoothed data outstands the HCC-based FCA on smoothed data at a low false positive rate. At the same level of true positive rate, univariate metric measure has a higher false positive rate. For Method A, that's mainly due to the large amount noises. For Method B, it is probably for the reason that smoothing cannot distinguish the signals with the random noises and extends the functional region. In summary, RV-based FCA produces relatively the optimal performance at detecting the local activation regions.

Additionally, we repeat 3 times both for HCC-based FCA and RV-based FCA. The average numbers of iterations corresponding to these two methods were 80 and 4. For both methods, each iteration time is similar since the processed data is an order of magnitude. So it can be seen from the comparison of the numbers of iterations that the RV-based FCA has faster convergence speed. That's mainly because at each iteration RV-based FCA not only considers the correlation between two single voxels, but also takes voxels' surrounding information into account, which makes it more easily to achieve iterative steady state in a short period of time.

IV. DISCUSSION

In this paper, to address the issue that univariate measure method is highly susceptible to the noise and has a slow convergence rate in FCA, we develop an RV-based FCA method according to the hypothesis that the function-homogeneous voxels of brain volume are spatially clustered within a local region to detect task-related functional region [18].

In the experiment, this improved method can quickly find the location of the visual stimulate signal and our result is consistent with the findings of GLM analysis where extensive prior knowledge has to be added. This shows the effectiveness of our method. The result analysis shows that the RV-based FCA method achieves a better performance in mapping the activation patterns of functionally specialized brain network. The success of this method is due to that we use local multivariate voxels instead of one single voxel for measuring the distance between a datum and a centroid, so more information of local spatial structure is kept.

The application of the RV-based FCA focuses on detecting the task-related functional region in this paper. However, it can also be extended to detect resting-state functional connectivity, which needs to be explored in the near future. Moreover, we can improve RV-based FCA aiming at the problem of extending the boundaries of the functionally connected region by adding a weight value to each voxel in the search cube which could take more fine spatial information into account. Furthermore, the search cube used in our study is not the optimum, so the shape and the size of the search cube in RV-based FCA can be further studied.

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