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STUDY OF CONNECTIVITY PROPERTIES AND NETWORK TOPOLOGY FOR NEUROIMAGING CLASSIFICATION BY USING ADAPTIVE NERO-FUZZY INFERENCE SYSTEM

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ABSTRACT

Neuro imaging techniques are used to study the structural and functional connectivity of the human brain to identify abnormalities, Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) can be identified by quantitative measurement of brain connectivity. In this paper, Multi kernel based approach is employed. Two types of Kernels i.e., vector based kernel and graph based kernel are used to study the local and global topology properties of a network. Then Adaptive Neuro Fuzzy Inference System (ANFIS) is adopted for neuroimaging classification. This analyses two different yet complementary properties of the network.

Keywords: mild cognitive impairment (MCI), connectivity network, topological property, ANFIS.

1. INTRODUCTION

Alzheimer's disease (AD) causes changes in the brain of the patient even before any physical changes are observed. Studies proposed that by analysing the neuroimaging data MCI can be found [1] Machine learning and pattern classification are used [2]. This focuses on the Region of Interest (ROI) which is extracted from Magnetic Resonance Imaging (MRI). Researchers prove that psychiatric disorders are closely associated to disrupted synchronisation and integration of brain regions [3].

Neuroimaging techniques provide a mechanism to study the structural and functional connectivity of brain [4] states the association pattern among brain regions.
Studies state that AD/MCI can be inferred from large scale highly connected functional network and not in single isolated region [5]. Connectivity network based methods identify an individual with AD and MCI accurately from healthy controls (HCS) [6].

In this paper we propose to use kernel based methods to identify AD and MCI affected individuals from HCS. Two types of kernels, graph kernel and vector based kernel are used. Vector based kernel is associated to local network property and graph kernel corresponding to global topological property of network.

2. MATERIALS AND METHODS

A. Selecting data

The required data is collected from Alzheimer's Disease Neuroimaging Initiative (ADNI) data collection is performed using standard set of protocols and procedures to eliminate inconsistencies [7]. The fMRI data of various subjects with MCI and HCS is taken into account.

B. Method

Studies show that the connectivity patterns and properties of the brains with AD/MCI differ from those of the normal brain [8]. Firstly to identify this, the functional connectivity network has to be found from the fMRI data to remove insignificant connections a threshold value is used in the functional connectivity network. Then, a vector based kernel and graph kernel are used to quantify network properties. Finally ANFIS is adopted to fuse two kernels and distinguishes the individuals with MCI from HCS. Here we combine different

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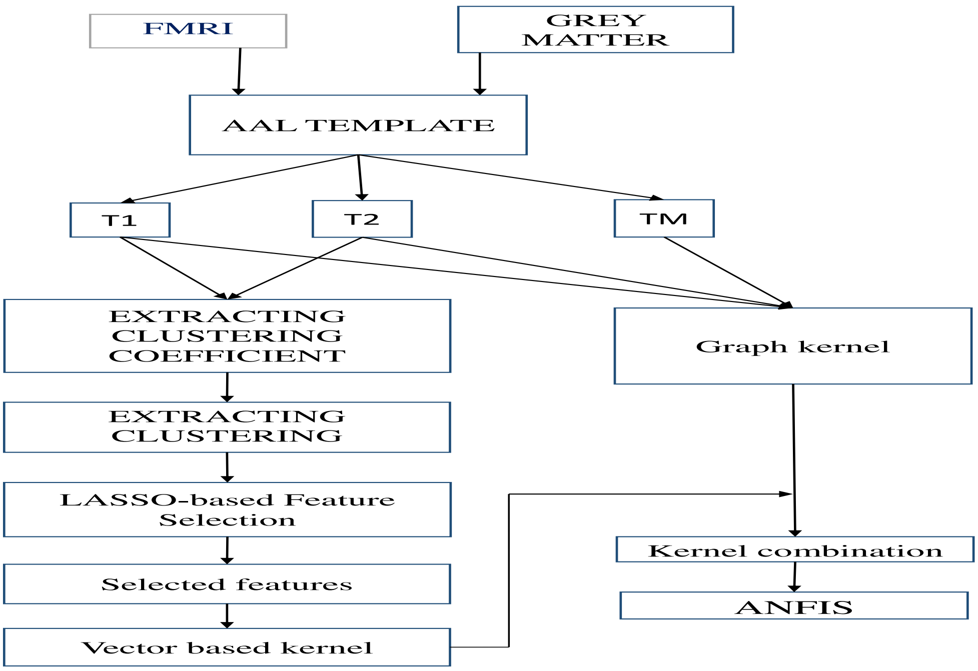

Figure-1. Block diagram showing the proposed method.

Types of kernels from different properties of the same connectivity network [9]. A summary of the methods followed is given. Extraction of topological properties of connectivity network using multiple thresholds. Graph kernel is used to measure topological similarity. Feature selection using the least absolution shrinkage and selection operator (LASSO) method. ANFIS is used to integrate the network properties.

1) Image processing and network construction

The fMRI images should be pre-processed by slice timing correction which is done by using statistical parametric mapping software package (SPMS). The white matter (WM) of the brain contains noise caused by cardiac and respiratory cycles [10]. Therefore the grey matter (GM) tissue of the brain consists of Blood Oxygen Level Dependent (BOLD) signals. From the MR image of each subject only the GM is used to mask the corresponding fMRI images. The CSF (Cerebro Spinal Fluid) and White Matter is eliminated. The fMRI scan will be integrated into ROIs by warping the Automated Anatomical Labelling (AAL) [11]. Finally the mean time series of subject's ROI was computed by averaging the fMRI time series over all pixels in that particular ROI. A frequency internal [0.025 ≤ frequency ≤ 0.1 Hz] is used to filter the ROI. It is explained in [12] that the frequency band (0.027 - 0.073) Hz having high reliability.

By using pair wise Pearson coefficient a functional connectivity network is constructed. The ROI is considered as node and weight of edge is equal to Pearson correlation coefficient between a pair of ROIs. Later, Fisher's r–to–z transformation is applied; this improves normality of correlation coefficient.

2) Kernel based method

Kernel based methods do pattern analysis like classification and clustering on different types of data. It performs mapping of data from input space. A kernel quantifies the similarities between two subjects. Given two subjects x and x' the kernel can be defined as

$$k(x,x') = \left(\emptyset(x),\emptyset(x')\right)$$

Where, Øis mapping function that maps data from input space to the feature space.

a. Topology based graph kernel

A graph in a connectivity network can be defined by a kernel. A graph kernel maps the graph data from original graph space to feature space and measured its similarity in the topology [13]. We use Weisfeiler Lehman sub tree kernel to measure the topological similarity between paired connectivity networks. It is proved in [13] that are the type of graph kernel has high efficiency.

A graph has finite number of nodes and edges. A labelled graph will contain a label associated for each node. A subtree can be defined as a part of a graph where every node will have a path to the root node. A graph kernel is constructed from a subtree pattern using Weisfeiler Lehman test of isomorphism [31]. For a pair of graphs G and G', let $L_i = \{l_{i1}, l_{i2}, \ldots\ldots, l_{i|l_i|}\}$ (i=0,1,…,h) be the set of letters that occurs as node labels in G or G' at the end of ith iteration of the Weisfeiler Lehman test of polymorphism. In this Lo is the one which denotes the set of initial labels of graph G or G'. Assuming that all Li are pair wise disjoint.

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$k(G,G') = (\emptyset(G), \emptyset(G'))$
Where,
$\emptyset(G) = (\rho_0(G, l_{01}), \ldots., \rho_0(G, l_{0|l_0|}), \ldots\ldots,$
$\rho_h(G, l_{n1}), \ldots\ldots, \rho_h(G', l_{h|L_h|}))$
And
$\emptyset(G') = (\rho_0(G', l_{01}), \ldots., \rho_0(G', l_{0|L_0|}), \ldots,$
$\rho_h(G', l_{n1}), \ldots, \rho_h(G', l_{n|l_n|}))$
Each compressed label denotes a sub tree pattern.

b. ANFIS

Adaptive Neuro Fuzzy System (ANFIS) uses a hybrid technique. It is an adaptive network incorporates the concepts of fuzzy logic into neural networks and has been widely used in many applications. These networks are the one which maps the relationship between input and output. By using a hybrid learning procedure the proposed ANFIS can construct input output mapping. ANFIS represents Sugeno e Tsukamoto fuzzy model. In Sugeno model x and y are input. Z is the output. There are two rules in this model.

Rule-1

If x = A_1 and $y = B_1$, then $f_1 = p_1x + q_1y + r_1$.

Rule-2

If x=A_2 and y=B_2 , then
$f_2 = p_2x + q_2y + r_2$

x and y are inputs, Ai and Bi are fuzzy sets, fi is the output and pi,qi,ri are design parameters.

3) Properties of connectivity network

Connectivity of a network is defined as a frequency dependent correlation between spatially distinct brain regions. Inorder to eliminate the weak connections certain connections are ignored by using a threshold approach which makes the network simple [14]. An arbitrary value is considered as a threshold value [8]. To improve the classification performance, network with different threshold are taken so that complementary properties can be used. Given a threshold Tm (m=1… M), the connectivity network G = [tij] n*n is threshold as

$$T_{ij}^{m} = f(x) = \begin{cases} 0, & if T_{ij} < T_m \\ T_{ij}, & otherwise \end{cases}$$

Where Tij denotes the connection weight between the i-th and j-th network nodes. Numerous studies have showed that the local clustering of functional connectivity network has been disrupted in the AD and MCI patients [8]. In [4] local weighted clustering coefficients are extracted from threshold connectivity network.

$$c_p^m = \frac{2\sum ij\left(T_{pi}^m T_{ij}^m T_{jp}^m\right)^\wedge {}^1\!/_3}{d_p^m(d_p^m - 1)}$$

Least absolution selection and shrinkage operator (LASSO) is implied in the threshold connectivity network to remove redundant and irrelevant features. Vector-based kernel is performed on the selected features to measure the similarity of two connectivity networks using local clustering property. Since it is known that the topological properties of the whole brain network has been changed for AD and MCI patients [15]. The graph kernel only reports the local and global structure information of connectivity network but it will not consider the weight information of edges. In vector-based kernel the connectivity strength of edges is considered. It is found by using the local clustering property of connectivity networks.

4) LASSO- based feature selection

It removes many irrelevant and redundant features to form an effective subset for data classification. In LASSO a penalised objective function is used which assigns zero to most irrelevant and redundant features.The loss function of LASSO is defined as

$$\min_{w,b} \frac{1}{2}\sum_{i}^{N}(y_i - w^T x_i - b)^2 + \lambda\,||w||_1$$

Where xi represents a feature vector extracted from all threshold connectivity networks on the i-th subject, yi, is the corresponding class label, w denotes the regression coefficients for the feature vector, b is the intercept and N is the number of training subjects. W1 shows the regression coefficient shrunk to zero. The features with non zero coefficient will be selected and used for constructing a vector-based kernel.

5) Implementation details

To enhance the performance of the classification leave out one (LOO) cross validation method is adopted. It is reported the connectivity densities interval of [25% to 75%] provides better classification performance [16]. The extracted features are normalised and by using SLEP package and LASSO feature selection is done and a vector-based kernel is used.

3. RESULTS

A. Classification performance

The classification performance is evaluated based on the classification accuracy and the area under receiver operating characteristics (ROC) curve (AUC). The proposed method is compared with multi network properties with those using only single network property. In the linear -kernel-based method (LK) firstly LASSO is performed for feature selection but in graph kernel five threshold connectivity networks GK1, GK2, GK3, GK4, GK5 which represent different levels of topological properties of connectivity network are combined as GK-C. All experiments are performed using LOO cross-validation. The classification performance is listed in the Table-1.

Table-1. Classification performance.

method	Accuracy (%)	Balanced accuracy (%)	AUC
LK	81.1	79.5	0.84
GK1	73.0	60.5	0.51
GK2	73.0	64.7	0.79
GK3	70.3	58.5	0.63
GK4	73.0	60.5	0.83
GK5	75.7	64.7	0.71
GK-C	81.8	75.2	0.87
Proposed	91.9	89.7	0.87

These results indicate that different properties of the connectivity network contain complementary information and thus can be integrated for further improving the classification performance as shown in Figure-2 [17].

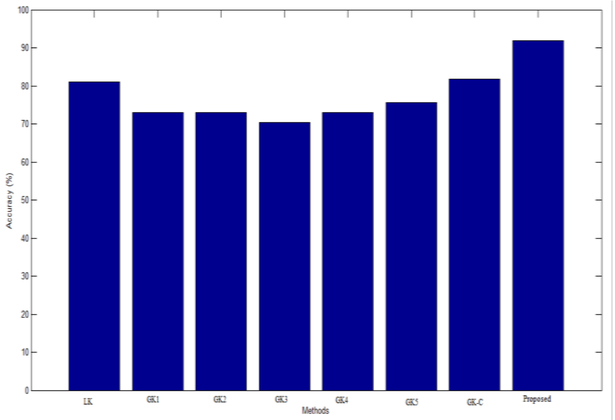

Figure-2. Classification performance.

Figure-3 represents the comparison of proposed method with SVM+ANFIS. The proposed method shown as promising results.

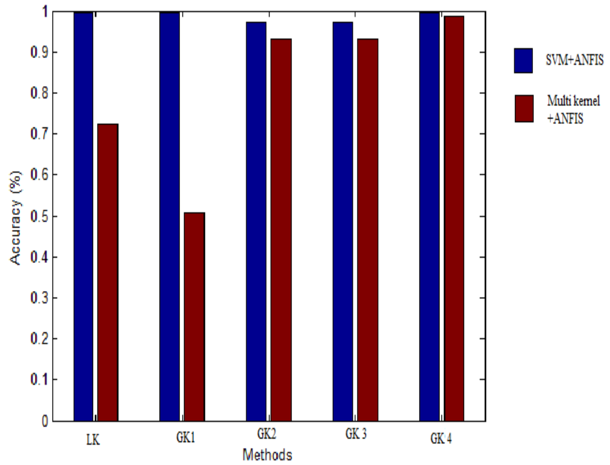

Figure-3. Performance comparison of proposed method with SVM+ANFIS.

B. Selection of brain region

Table-2. Top 12 ROIs that are selected based on the local clustering property.

Selected ROI	Threshold connectivity network	Number of occurrence
Left temporal pole	T2	37
Right caudate	T1	37
Right temporal pole	T3,T5	37,17
Right orbito frontal cortex	T2	36
Right orbito frontal coretex medial	T3,T4	36,36
Left heschl gyrus	T2	36
Right orbito frontal cortex middle	T2	34
Left posterior cingulated gyrus	T2	33
Left hippocampus	T1	32
Left lingual gyrus	T2	32
Right middle singulate gyrus	T2	15
Left interior temporal	T2	15

The important parameter in classification is identifying the region of interest. The most important features are selected by the selection frequency by LASSO method and LOO-cross validation. The t-test is performed on the features to identify patients from normal controls. The TABLE 2 shows the brain regions that are selected based on local clustering property. P-values should be calculated for the region which shows the discriminative power between patients and controls.

On the other hand, to further evaluate the discriminative power of different ROIs, we also characterize the top brain regions based on their global topological property. Let $R = \{R1, R2,...,Rn\}$ be the set of ROIs. For each ROI Rp , a sub-network can be built according to the connectivity between Rp and the remaining ROIs Rq ($q = 1, 2, . . . , n, q = p$)on the m-th threshold connectivity network, and the graph kernel $kpm(Gim,Gjm)$ between the samples Gi and Gj on the corresponding sub-network is computed using the method introduced in the previous section. Then, the group difference of ROI Rp on the m-th threshold connectivity network can be defined as follows:

$$d_m(\rho) = \frac{1}{n_1 n_2} \sum_{i \in L^+, j \in L^-} k_m^p(G_m^i, G_m^j)$$

Where $L+$ is the index set of patients, and $L-$ is the index set of normal controls, with number of subjects of $n1$ and $n2$, respectively. The group difference dm (p) represents the discriminative power of ROI Rp between patients and normal controls on the$m$-th threshold connectivity network. The top 12 ROI are selected with the highest group distance. It is also worth mentioning that the function connectivity between posterior cingulated cortex and other regions is less in MCI patients [18].

4. LIMITATIONS

The following drawbacks are present in the current study. In this study the topological information of the whole connectivity network is used in classification where as the disease related sub network is not given high priority. The network construction is the major activity in the proposed paper various methods of network construction may have different level of accuracy that is not fully explored in this paper. Thus, the future work will be focused on improving these factors.

5. CONCLUSIONS

To conclude, this paper explains a new framework in which the graph obtained from the ROI of the brain is split into multiple levels based on thresholds. Then two different kernels are used to quantify the network properties and an ANFIS technique is used to integrate the heterogeneous kernels. This method detects the ROIs that are more sensitive to disease and detects an MCI affected brain image from a normal control.

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