Principal Component Analysis for Analysis and Classification of fMRI Activation Maps

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Summary
The activity patterns in fMRI data represent execution of different physical and mental tasks. Each of these patterns is unique and located in specific location in the brain. The main aim of analyzing these datasets is to localize the areas of the brain that have been activated in a given experiment. The multi stimuli fMRI data tends to appear scattered because of involvement of multiple activity patterns. The detection of prime activity in the scattered data leads to decision making on prime stimulus. The detection of prime activity is possible through identification of principal components in the multivariate data. The principle components always align along the principal axis with the component with maximum variance nearest to the origin and the minimum variance component at the other extreme end. Clustering of the principle components yields groups of components with most similar variance values. The average linkage clustering aids clustering of principle components. The cluster with maximum variance forms the principal component. This component represents the prime activity. The fMRI data set is huge and also the data size for different tasks is dimensionally dissimilar. Dimensionality reduction of high dimensional data helps reduce computational requirements for subsequent operations on the data, eliminates redundancies in the data, and, in cases where the feature data set dimensionality doesn't match then a common dimension can be arrived at with the available data. All three reasons apply here, and motivate the use of Principal Component Analysis (PCA) a standard method for creating uncorrelated variables from best-fitting linear combinations of the variables in the raw depth data extracted using Statistical Parametric mapping (SPM). This approach is equivalent to finding an orthogonal basis such that the projection onto each successive vector (or\"principal component") is of maximal variance (and uncorrelated with each previous vector). The templates comprising of principal components represent individual activity. These are then fed to the back propagation training algorithm. The trained network is capable of classifying the test pattern into the corresponding defined class.

Keywords: fMRI, Scattered patterns, Prime activity, Principal component analysis, Pattern classification, Statistical Parametric Mapping, Back propagation neural network.Back propagation neural network.

1. Introduction

fMRI(Functional Magnetic Resonance Imaging) is a technique for determining which parts of the brain are activated by different types of physical sensation or activity, such as sight, sound or the movement of a subject's fingers[1][2]. For fMRI data the inherent character is its tendency towards clustered activation [3]. The fMRI activation is more likely to occur in clusters of several contiguous voxels than in a single voxel. This characteristic of fMRI data is explored for identification of the data representing the prime activity. When subject is given multiple stimuli, the activity patterns seem to be scattered because of involvement of multiple brain regions. The prime activity is that region which represents that activity due to prime stimulus. This can be identified among all the other regions by considering those regions which have maximal size as compared to the rest of the regions over multiple slices. Typically data driven procedures/techniques for region selection are implemented. All the techniques can separate different types of Hemodynamic Responses (HR) without the hypothesis of paradigm or Hemodynamic Response Function (HRF). [2]
Principal Component Analysis (PCA) is one more important method used under data driven methods. The tacit assumption made when applying PCA is that the underlying sources have high energy or variability. In practice, the unmixing vectors are found as the eigenvectors of the estimated covariance matrix of the data, thus transforming the original fMRI data matrix with these vectors as rows in a transformation matrix. Most often the dimensionality of the data is also reduced by discarding the principal components with lowest variance [4]. The principal component analysis (PCA) method is used to generate the new feature space. Each brain voxel (or fMRI time series) is described in this feature space with a vector. This vector is described by the projections of the corresponding fMRI time series onto the basis vectors of the feature space.

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After finding the basis vectors of the feature space, each time series is projected onto the basis vectors and the feature vector is generated for the corresponding voxel [5]. In PCA, the first principal component is the linear combination of the variables with maximal variance that is the direction within the original data with the largest variability. The second component is the linear combination with the next largest variability that is orthogonal to the first. Further components are the linear combinations that maximize the variability and are orthogonal to all previous ones [6]. This characteristic of PCA is incorporated in our method to find out both prime activity and the accompanying activities. The number of accompanying activities is decided and the corresponding number of principal components is explored. The component with maximum variance depicts the prime activity. The next successive components represent the accompanying activities in the order of their significance.

2. Analysis[3]

The principal components are random variables of maximal variance constructed from linear combinations of the input features. Equivalently, they are the projections onto the principal component axes. The projections are lines that minimize the average squared distance to each point in the data set. To ensure uniqueness, all of the principal component axes must be orthogonal. PCA allows us to compute a linear transformation that maps data from a high dimensional space to a lower dimensional space.

PCA is an orthogonal linear transformation that transforms the data to a new coordinate system such that the greatest variance by any projection of the data will lie on the first coordinate (called the first principal component), the second greatest variance on the second coordinate, and so on. The derivation of the PCA method [7-8] begins with the application of Lagrange multipliers to maximize the variance of the data. The resulting equation is of the form,

$$\left|\Sigma_x - \lambda I_K\right|\alpha_i = 0$$

Where, $\mathbf{\Sigma_x}$ covariance matrix describing the scatter or spread of intensity values in the vector space of x.

λ eigenvalue of Σx.

I_k (K x K) identity matrix.

α_i Linear transformation of the i^{th} principal component

This system of equations has a rank equivalent to the number of spectral bands, i.e., activity clusters. In other words, the number of possible solutions is the same as the number of activity clusters. In practice the following steps are carried out for each voxel:

1. Calculate the covariance matrix $\mathbf{\Sigma_x}$. The definition of $\mathbf{\Sigma_x}$ is

$$\Sigma_x = E\{(x-m)(x-m)^T\}$$

Where *E* is the expectation operator and m is the mean of *x*. An unbiased estimate of $\mathbf{\Sigma_x}$ is given by

$$\Sigma_x = \frac{1}{K-1}\sum_{i=1}^{K}(x_i - m)(x_i - m)^T.$$

2. Solve the characteristic equation

$$\Sigma_x - \lambda I = 0$$

for the eigenvalues λ.

3. Sort the eigenvalues in order of decreasing value. The number of possible PCA solutions is the same as the number of clusters, and the same as the number of eigenvalues. The first principal component corresponds to the eigenvalue containing the maximum variance and therefore can be considered as the prime activity.

The characteristic feature of identifying the components with highest variance is used in this methodology. The statistical data representing area (Table-1) and the centroid of the activity patterns over multiple slices of the 3-D fMRI data is obtained by image preprocessing techniques. For creating the statistical data experimentation was performed on nine normal subjects.

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Table -1: The area and centroid values of multiple activities obtained over multiple slices

	Rgn1	Rgn2	rgn3	Rgn4	Rgn5	Cen1	Cen2	cen3	Cen4	Cen5
slice1	873	239				124.34	107.78			
slice2	400		1341	237		192.75		128.7	114.95	
slice3	2053	280				140.47	106.44			
slice4	841	1059	346			171.4	105	102.46		
slice5	950	1895				179.92	112.54			
slice6	948	1874				186.08	116.28	136.56		
slice7	931	1180				187.84	113.46			
slice8	661	941				185.22	101.79			
slice9	272	42		941		194.59	179.27		100.44	
slice10	441		21		1137	195.33		194.59		95.44
slice11	643					192.04	91.61			
slice12	1119		1385			190.8		83.01		
slice13	1283			1581		196.16			91.26	
slice14	1150	36	1638			195.21	167.69	90.43		
slice15	1085		1373	128		195.6		93.54	99.01	
slice16	993	83	2179			197.99	193.33	100.77		
slice17	3206					149.03				

3. Expermentation

All study subjects comprising of both normal and patients were imaged using Siemens Magnetom Vision 1.5 T MRI in the department of NIIR, NIMHANS using the same paradigm (described below). BOLD fMRI data was acquired using standard quadrature head coil. All the subjects were explained about the visual task and the MRI acquisition procedures. The stimulus was projected on a screen and coils was equipped with mirror that allowed subjects and patients to see the projection without image distortion. For each subject MPRAGE (magnetization prepared rapid acquisition gradient echo) sequence was used to provide detailed anatomical information. Following this Echo Planar Imaging (EPI) fMRI was performed in 16 contiguous 8 mm axial slices.

4. Paradigm

Memory tasks procedure-Memory tasks included visual memory encoding and retrieval tasks. A sequential task-activation paradigm was employed alternating between an experimental condition and a baseline condition. Baseline condition was the same for all the experiments and consist of the fixation of the '+' sign of different colors in different locations on an off-white background. Scanning was performed over a 400 sec block. Each block included 10 baseline conditions and 10 experimental conditions beginning with the baseline condition.

Two memory experimental blocks was performed —

a) The encoding experimental block consist of 50 scenes (25 outdoor and 25 indoors) arranged in a random order. In one block one scene was presented once for 4 sec. Subjects were instructed to memorize the scenes silently for later recall and press the bulb whenever they see outdoor scenes.
b) The retrieval block consist of 50 scenes (25 outdoor and 25 indoors) arranged in a random order with 25 of them from encoding block and 25 new scenes. Subjects were instructed to press the bulb whenever they see scenes shown already to them in encoding block.

The data points are projected in the space of the principal components and the components representing the area and the centroids of the activity regions (Table-2) is obtained.

Table -2: The principle components for activity region areas (PC_A) and centroids (PC_C) over multiple slices

	PC1_C	PC2_C	PC3_C	PC4_C	PC1_A	PC2_A	PC3_A	PC4_A
SLICE1	.928	-.261	.234	-.110	0.962457	-0.26723	-0.04756	3.21E-09
SLICE2	.918	.349	7.174E-02	5.465E-02	0.166288	0.959647	0.226774	-2.5E-09
SLICE3	.934	-.294	.191	-5.467E-02	0.962457	-0.26723	-0.04756	-1.5E-08
SLICE4	.949	1.686E-02	-.306	-4.950E-02	0.988446	0.150339	-0.01932	1.64E-09
SLICE5	.933	-.335	.130	2.020E-02	0.962457	-0.26723	-0.04756	7.76E-09
SLICE6	.914	9.693E-02	-.381	-7.141E-02	0.962457	-0.26723	-0.04756	1.82E-08
SLICE7	.931	-.342	.120	3.312E-02	0.962457	-0.26723	-0.04756	7.2E-09
SLICE8	.927	-.359	9.191E-02	6.669E-02	0.962457	-0.26723	-0.04756	-1.9E-08
SLICE9	.895	.421	-.104	-1.194E-02	-0.15391	-0.52745	0.83553	1.96E-08
SLICE10	.601	.615	.181	.398	-0.10736	-0.41978	-0.90125	1.03E-08
SLICE11	.957	-.154	-.236	6.525E-02	0.962457	-0.26723	-0.04756	1.45E-09
SLICE12	.971	-1.144E-02	4.241E-03	-.214	0.673718	0.738338	0.031019	1.78E-08
SLICE13	.877	.446	-.147	-8.642E-02	0.338252	-0.603	0.722484	-8.9E-09
SLICE14	.979	-1.549E-02	-6.928E-02	-.168	0.601802	0.797773	0.037315	1.12E-08
SLICE15	.936	.220	.250	-7.336E-02	0.65623	0.746697	0.108652	-9.2E-09
SLICE16	.933	.254	.202	2.870E-02	0.391413	0.918741	0.052059	-5.4E-09
SLICE17	.728	-.485	-.220	.415	0.962457	-0.26723	-0.04756	-9.2E-09

The average linkage clustering algorithm applied to this one-dimensional set would yield clusters represented by the dendogram for area (Fig-2) and for centroids (Fig-3).The cluster of principle components with highest variance represents the prime activity. The clusters with next lesser value of variance represent the most prominent accompanying activity. The number of principle components can be decided upon by considering the details of accompanying activities to be considered for any specific task.

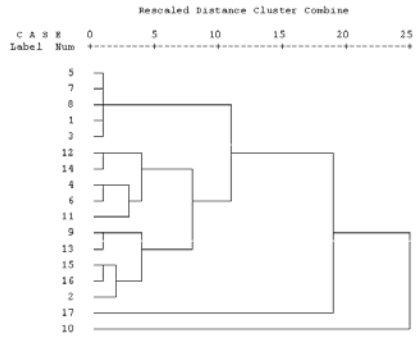

Fig-2: Dendogram obtained by average linkage clustering of principal components for Area data

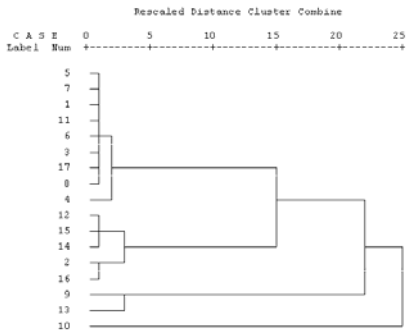

Fig-3:Dendogram obtained by average linkage clustering of principal components for centroid data

The fine representation of the clusters can be done by plotting (Fig-4) the principle component verses the next prominent component. The grouping is done for components representing the area and centroid. These clusters are similar to the grouping made by the average linkage clustering. The clusters formed in fig-3 endorse the grouping done by the average linkage clustering.

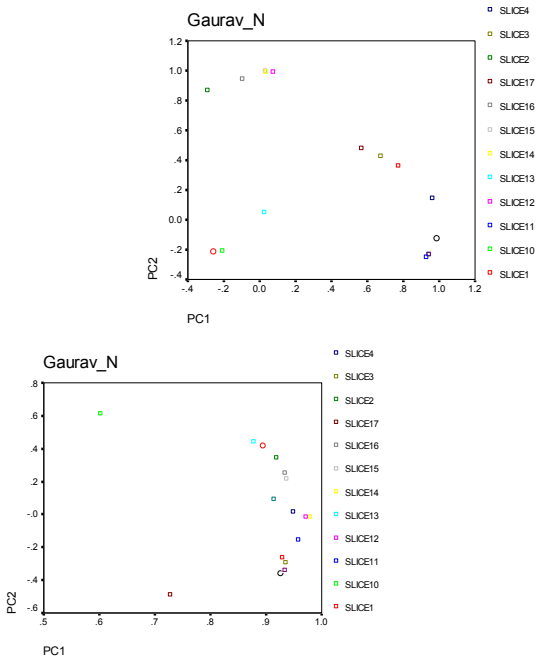

Fig-4 : clusters formed by mapping PC1 verses PC2 for area and centroid

5. Classification[4]

fMRI enables scientists to determine with greater precision when brain regions become active and how long they remain active. As a result, they can see whether brain activity occurs simultaneously or sequentially in different brain regions [9] as a subject thinks, feels, or reacts to experimental conditions. An fMRI scan can also produce high-quality images that can pinpoint exactly which areas of the brain are being activated.

Using multivariate analysis [10] approach the extent to which global and local signals could be used to decode subjects' subsequent behavioral choice can be determined based on their brain activity during a defined trial. It is found that subjects' decisions could be decoded to a high level of accuracy on the basis of both local and global signals even before they were required to make a choice, and even before they knew which physical action would be required. Furthermore, the combined signals from three specific brain areas (anterior cingulate cortex, medial prefrontal cortex, and ventral striatum) are found to provide all of the information sufficient to decode subjects' decisions out of all of the regions studied. These findings implicate a specific network of regions in encoding information relevant to subsequent behavioral choice.

Fuzzy sets and fuzzy logic have been applied in various domains, including medicine, and shown to be an alternative method to both the Artificial Neural Networks and statistical methods [11],[12]. The fuzzy –nearest neighbor (FK-NN) algorithm, which is one of the widely used fuzzy-based pattern classification methods, has been shown to be a powerful soft pattern classifier. This method gives not only a class to which the pattern is assigned, but also the class membership degree that provides information about the certainty of the classification decision. As far as we can ascertain, most applications involving fuzzy logic in oncological research have so far been mainly centered on image analyses for diagnostic purposes.

The Region Of Interest (ROI) represent the activity regions. These activity regions are localized by identifying their exact location in all three directions. The presence of the activity over multiple slices in all, AXIAL, SAGITTAL and CORONAL directions are found. This forms the statistical data for recognition of the specific activity in whole.

The fMRI data is obtained through experimentation performed on nine different normal subjects performing different defined tasks as described in the experimentation section. In this paper three tasks are considered. Motor task involves a procedure where subjects are asked to move their left hand thumb during active period. They are cautioned as to not to let their thumb touch their palm which if done would result in additional sensory (touch) task. They are asked not to move their thumb during rest period. Vision task involved a procedure where subjects were asked to view a checker board during active period and a blank screen during rest period. The activity for visio-memory task is different for the two different phases. The encoding phase which involves only visualization has the activity in occipital lobe and the retrieval phase involves both visualization and memory retrieval. The activity is therefore found both in occipital lobe and the parietal lobe which is responsible for memory related activity.

Dimensionality reduction of high dimensional data is useful for three general reasons [13]: it reduces computational requirements for subsequent operations on the data, it eliminates redundancies in the data, and, in cases where the feature data set dimensionality doesn't match then a common dimension is to be arrived at with the available data. All three reasons apply here, and motivate the use of PCA, a standard method for creating

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uncorrelated variables from best-fitting linear combinations of the variables in the raw data. This approach is equivalent to finding an orthogonal basis such that the projection onto each successive vector (or "principal component") is of maximal variance (and uncorrelated with each previous vector). Since all activation maps are normalized to a template brain, they have voxels in register. Let the number of subjects in a training set be n, and let the length m column vectors $\boldsymbol{v_i}$, **i = 1,…, n,** represent the activation maps. The matrix **E** is defined as all the $\boldsymbol{v_i}$, that is a matrix with one subject per row and one activation map per column. Let $\hat{\mathbf{E}}$ be **E** with the mean of each column subtracted. The principal components are then defined as the eigenvectors, $\mathbf{e_i}$, of the covariance matrix $\mathbf{C} = \hat{\mathbf{E}}^{\mathbf{T}}\hat{\mathbf{E}}$; that is, $\mathbf{Ce_i} = \boldsymbol{\lambda_i}\mathbf{e_i}$, where each eigenvalue $\boldsymbol{\lambda_i}$ is proportional to the variance in the original data represented by the ith principal component ei. This allows calculation of the eigenvectors of the **m x m** covariance matrix **C** to be replaced with calculation of the eigenvectors of the smaller **n x n** matrix **C'**. Typically, many principal components account for only small fractions of the total variance. Dimensionality reduction in addition to the above can be accomplished by sorting components by decreasing eigenvalue and then discarding some of the trailing components. The selected principal components form the columns of a matrix **P**, which is a basis for representing activation data. Projection of the activation matrix **E** onto this basis is carried out as $\tilde{\mathbf{E}} = \mathbf{EP}$. Following projection, the reduced representations $\tilde{\mathbf{E}}$ can be used to build a classifier.

In each case, results with varying numbers of principal components are calculated. Because overtraining can occur when the number of classification features is high, simply using all the principal components is generally not advisable. In a practical classifier, a heuristic selection of the number of principal components is generally used. In this paper an attempt is made towards implementing different number of principal components. The results are indicative (Table-3) of the fact that the decision on the number of components is heuristic. The graph (Fig-5) shows the classification errors while incorporating three, five and seven principal components. The graph indicates that the classification error is less for five components as compared to three components. The change in error values for five and seven components is very minimal. We therefore fix the number of principal components to seven for creating the template for recognition/classification.

The same way the number of epochs considered is also a prime feature for neural network training. The network traces different paths for different epochs (Fig-6). The successful training with minimum epochs is the need of the design. We consider the minimum value of epoch for the training process.

6. Conclusions

The analysis of scattered patterns through clustering of principle components mainly aids in identification of prime activity. The advantage of this analysis is that it also gives details of the accompanying activities which aid the execution of the main task. We can also decide on the number of accompanying activities to be considered for analysis and consider only that many components. Devising principle components obtained from area and centroid values helps in delineating two prime activities in case of scattered patterns with bilateral tasks. The same method works effectively for non-bilateral tasks in which case we can consider only principle components obtained from the area data. The analysis involves clustering of principal components and also plotting the two prime principal components which mainly helps in endorsing the clusters that are formed.

An attempt is made towards implementation of a technique for classifying spatial patterns in brain activation maps. Our method consists of selecting appropriate activation maps obtained through SPM in all the three brain imaging orientations, reducing the dimensionality of depth values using PCA, and creating a classifier using back propagation neural network and a training set of labeled activation maps. An attempt is made towards implementing different number of principal components and in lieu with the classification error that the network arrives at, an appropriate number of components is selected. The classification procedure is tested for three trained tasks and the classification with low error is achieved. As fMRI data has a low signal to noise ratio, activation patterns may not be completely consistent even across the healthy control subjects. Given these factors, the size of the datasets used here is probably minimal, and better prediction will likely result with larger collections of brain activation maps.

Table – 3 : The classification error for 3,5 and 7 principal components.

	MOTOR			VISION			VISIO_ MEMORY		
	3-comp	**5-Comp**	**7-comp**	**3-comp**	**5-Comp**	**7-comp**	**3-comp**	**5-Comp**	**7-comp**
Subject1	-0.0474	-0.0097	-0.0018	-0.0116	-0.0054	-0.0069	0.0151	-0.0027	0.0088
Subject2	-0.0274	-0.0025	0	-0.0086	-0.006	0.002	0.0065	-0.0012	0.0063
Subject3	-0.0171	-0.0062	-0.0026	0.0192	-0.0011	0.0023	-0.0048	0.0023	0.0075
Subject4	-0.0474	-0.0095	-0.0029	-0.0101	0.0013	0.0065	-0.0043	0.0006	-0.0048
Subject5	0.0047	-0.0374	0.0069	-0.0696	0.0058	0.0081	1E-04	0.0014	0.0079
Subject6	0.0027	-0.0028	0	0.0076	-0.0024	0.0004	-0.0058	-0.0038	0.008
Subject7	-0.0204	-0.0021	0.0036	0.0047	-0.0022	0.0121	0.0015	-0.0013	0.0156
Subject8	0	-0.0315	0.0015	0.0061	-0.0029	0.0125	-0.0025	0.0009	0.007
Subject9	0.1037	-0.0096	-0.0022	-0.0118	-0.0028	0.0043	0.0292	0.0013	0.0063

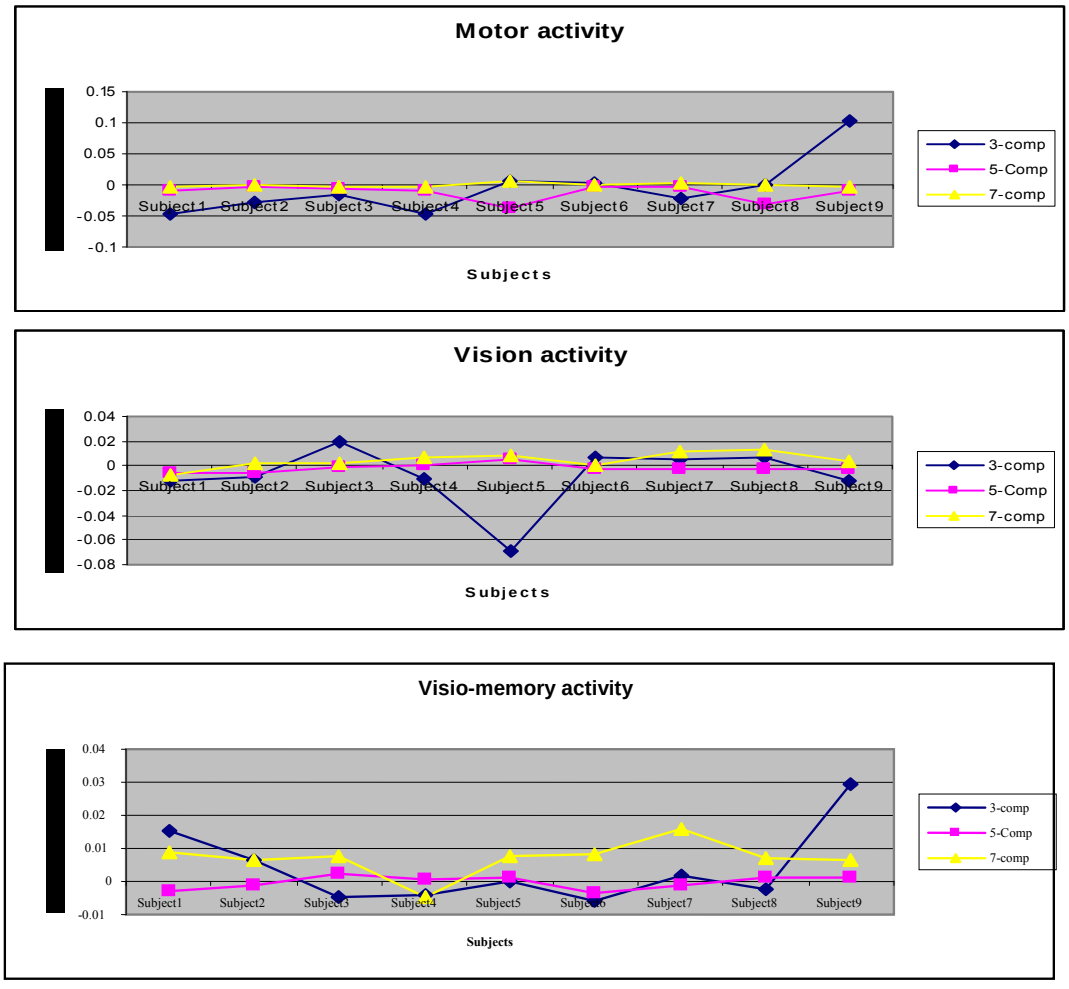

Fig-5: Graphical representation of classification error for 3,5 and 7 principal components.

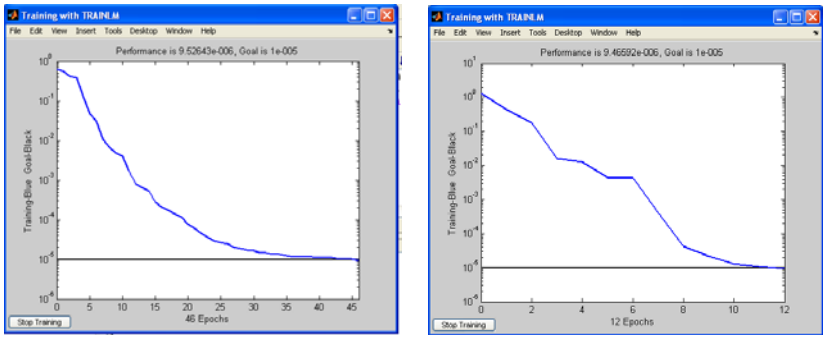

Fig-6: The representation of the training path traced by back propagation NN.

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