International Journal of Computer Applications (0975 8887)
Volume 115 - No. 15, April 2015

Decoding Multiple Subject fMRI Data using Manifold Based Representation of Cognitive State Neural Signatures

Accamma I. V
Research Scholar
Visvesvaraya Technological University

Suma H. N
Department of Medical Electronics
BMS College of Engineering

Dakshayini M
Department of Information Science
BMS College of Engineering

ABSTRACT

Mind reading or thought prediction is a promising application of functional neuroimaging studies. The emergence of functional magnetic resonance imaging (fMRI) has, in the last two decades given a boost to these studies. In order to improve the accuracy, predictability and repeatability of thought prediction, it is important to have a representation that can capture the nuances of fMRI activations with respect to a particular cognitive state. In this paper, the process of creating a geometrical representation of the activations using non-linear manifolds is described. Manifold learning brings out the geometry of the activated voxels in the fMRI image. It is shown that this kind of representation is able to give high accuracy in classification studies as compared to using activation profiles.

General Terms:

classification, neuroimaging

Keywords:

fMRI, classification, multiple-subject, manifold learning

1. INTRODUCTION

The brain imaging technique of fMRI has several advantages, including, but not limited to, being a non-invasive, non-radiation technique. FMRI has excellent spatial resolution and is a popular tool for imaging brain function. Over the last decade it has provided new insight to understanding cognition ([1]), emotion ([10], [30]) and in being able to understand and predict thoughts, ([26]) to name but a few areas of research.

Conventional statistical analysis of fMRI data focuses on finding regions of brain that are involved in specific mental activities, which is a correlation based process. More recently, there have been efforts made using machine-learning tools to identify signals, which can predict mental states or behaviour directly from neuroimaging data ([31], [14], [29]). Pattern classifiers are first trained on a part of the fMRI data and then used to classify the remaining data, based on the learning. Research in the area indicates that it is indeed possible to predict the underlying thought using an fMRI scan. This has been done both with single subjects as well as multiple subjects. Classification of multiple-subject data is a difficult task given the difference in the size of individual brains and low signal-to-noise-ratio of the activation profiles. Therefore, getting good prediction accuracy is a huge challenge. Progress in the areas of cognitive science and in diagnoses of mental processes, combined with good prediction accuracy, can help to improve prediction in applications such as lie detection and in cognitive control of artefacts.

In cognitive and brain sciences, representation is a key concept. Neuronal activity is understood to represent content. This content could be sensory input or mental activity. In this paper, the underlying spatial structure of the neuronal activity is used as a representation for classification studies. A new method for feature extraction using manifold learning of the spatial structure is proposed to improve the classification accuracy of fMRI data in multiple subjects. The problem of prediction using the entire brain is decomposed to prediction using relevant ROIs only. The most informative voxels from ROIs are extracted and represented by their low-dimensional manifold. These abstractions when used for inter-subject classification yield accuracy above chance levels.

2. RELATED WORK

The majority of classification studies have used fMRI activation to classify sensory input, such as the category of visual stimuli ([13], [16], [25], [17]) or natural images ([19]) or movies ([27], [28]). Additional studies have used fMRI activation to classify lying versus telling the truth ([6]), or recall different object categories ([20]).

Many tasks have been considered for the classification of multiple subject fMRI data. From coarse grained visual, motor, auditory tasks ([43], [42], [40], [25]), reward distinction ([4]), to fine grained categories of objects ([12], [35], [39]) and also very fine-grained category like concrete noun distinction ([26], [15], [36]) have been used to demonstrate the feasibility of classifying a subject's thought based on training from other subjects.

Multiple-subject classification algorithms must take into account the differences that exist between subjects. Functional images from all subjects must be transformed into co-ordinates of a standard brain. Transforming into Talairach Tournoux co-ordinates ([25], [46]) anatomically defined regions using AAL atlas ([26]) or creation of a whole brain mask based on all participants ([4]) are some approaches to standardising.

Feature selection/extraction plays a crucial role in obtaining the commonalities that are comparable across subjects. Most active voxels ([25]), most discriminating voxels ([40], [39]), most stable voxels ([15], parcellation ([42]), searchlight ([4]) are the common techniques. Conversions into an intermediate form like canonical correlates([36]), similarity relations ([35]) or factors ([15]) try to extract the latent variables that underlie the activations.

In all the work so far, the representation used for classification has been the neural activation levels of the fMRI images acquired. In this paper a representation that is based on their geometrical co-ordinates is presented. This representation results in better accuracy in inter-subject decoding of cognitive states. Though there have been many efforts to perform classification of multiple-subjects in an experiment, there is still a requirement for a repeatable, robust technique. The proposed algorithm is generic and could easily be extended to combine multiple studies.

3. DATA AND PREPROCESSING

To describe the methodology the visual object recognition dataset publicly made available by haxby et al is used. This dataset consists of fMRI activation profiles from a block design experiment with 8 different stimuli shown to 6 subjects. The stimuli are face, scissors, chair, cat, bottle, shoe, house and scrambled image. It is known that response in ventral temporal cortex has information enough to distinguish the stimulus categories. The data is pre-processed using FSL fMRI analysis package ([41]) for motion correction and temporal filtering. The original voxel size is maintained and smoothing is not performed to preserve information of each voxel. The functional image is co registered with the anatomical image of the subject.

4. INTER-SUBJECT ALIGNMENT

In this work, the task is to compare fMRI data from multiple subjects. Since individual brains are highly variable in shape and size, they have to be transformed into a common space for analysis. This could be achieved by using anatomical landmarks or functional patterns. An atlas marks the location of anatomical features. The representation of an atlas is given by a template and to this the individual images can be aligned. Talairach atlas ([44]) and templates by Montreal Neurological Institute(MNI) ([9]) are most commonly used. Other approaches are based on correlation between functional patterns ([37]) or by aligning patterns of cortical functional connectivity ([5]). Here the MNI template ICBM-152(International Consortium for Brain Mapping) is used. It is the average of 152 normal MRI scans that have been matched to the original MNI template using a 9 parameter affine transform ([34]).

As mentioned previously, most of the fMRI classification studies use the activation profiles of the selected voxels for training classifiers. Once the voxels are chosen, their activation levels are not important. The voxel numbers are also not consistent across subjects. Therefore, the position of the voxels is used as features for training classifiers.

5. FMRI CO-ORDINATE SYSTEM

When an MRI image is captured, the direction that it is taken is important. The view may be sagittal, coronal or transverse. It is represented in the three-dimensional Cartesian co-ordinate system which provides the physical dimensions of space- depth, width and height. After inter-subject alignment, co-ordinates of voxels are transformed into MNI co-ordinates. There cannot be a one-to-one correspondence between the voxels in different subjects. Therefore, comparing them is not possible. Therefore, their positions are approximated by learning the manifolds formed by the important voxels. The shapes of the manifolds are compared to classify the data.

6. GEOMETRICAL REPRESENTATION

The representation used for classification consists of the following steps.

(1) Extraction of Region of Interest
(2) Feature Selection
(3) Manifold learning

These steps are explained in detail below.

6.1 Extraction of Region of Interest

Harvard-Oxford cortical atlas ([7]) is used to extract the anatomically defined ROIs from the data. Here, only some ROIs that are proven from previous studies on this dataset as having some information about the stimulus ([2], [18], [24], [47]) are considered. Representational distinctions among complex visual stimuli are embedded in VT cortex. Coarse categorical differences like animate vs. inanimate categories manifest in lateral to medial VT cortex ([2], [3], [11], [22]). Faces versus objects and body parts versus objects distinctions can be seen in the fusiform face and body-parts areas(FFA and FBA) ([18], [21], [32]), and places versus objects in the parahippocampal place area (PPA)([8]).

Lateral Occipital Cortex (LOC), Fusiform Gyrus (FG), Parahippocampal Gyrus (PG) and Inferior Temporal Gyrus (ITG) are the ROIs considered for this analysis. The ROIs are extracted from the functional image based on the atlas. (Figure 1). Each ROI image is converted to time series data format $D = x_1, x_2, x_3.....x_n$ where each voxel x_i is a column vector representing the activation values in a time series of a run. The ROI in time series format is used as input for the next step.

6.2 Feature selection

In each ROI, not all voxels carry information about a particular stimulus. Some voxels have neurons that are activated as a response to the stimulus. The voxels are filtered to extract only those that can help to distinguish between the stimuli. Among them again some are more important than others. Therefore, a feature selection algorithm is run over the ROI to extract the most informative n voxels.

6.2.1 Finding the most discriminative features:. Let D = $\{x_1, x_2, x_3.....x_n\}$ be the fMRI dataset from an ROI containing N voxels. Here each x_i is a time series column vector containing a voxel's response to a stimulus. Class C_1 to which the dataset belongs is known. The maximum relevance minimum redundancy

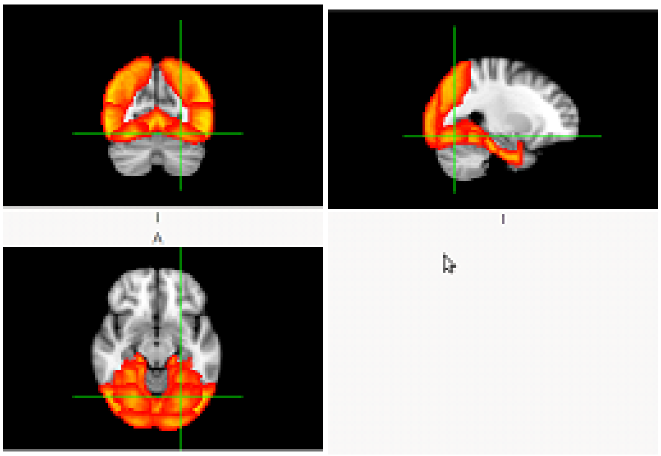

Fig. 1: ROIs selected from the atlas

technique (MRMR) ([33]) is used to select the voxels. Only those n voxels that have high mutual information shared with a stimulus of class C_1 are filtered. Therefore, if in an fMRI experiment C_1 and C_2 are two classes of stimulus, those voxels that help to best discriminate C_1 from C_2 are selected. Here each of the seven stimulus categories is considered as C_1 and it is discriminated from scrambled input considered as the class C_2. Therefore, the voxels that maximize the mutual information between their activation profiles and the class are chosen while also making sure that the mutual information between the selected voxel i and all the other voxels are minimized. This reduces the redundancy.

6.3 Manifold representation

The discriminating voxels are chosen based on their magnitude of activation. Once they are selected, the magnitude is not taken into consideration but their geometrical co-ordinates are. For classification, the fMRI activation profiles are not compared between subjects, but the geometry of the selected voxels is. It is not the magnitude of neuronal activation that represents a cognitive state, but it is the location of the neuron than can characterize the cognitive state. Since the neurons cannot be identified, the smallest available unit in an fMRI image i.e. a voxel is used to identify which location is activated. The selected voxels constitute the neural signatures that represent a cognitive state.

The locations of the activated voxels cannot be directly compared between subjects or different runs of the same subject. Therefore, manifold learning is used to reduce the data into lower dimensions. Manifold learning is the process of uncovering the intrinsic manifold structure in a data set. Manifold learning is a popular approach to non-linear dimensionality reduction. The algorithms that perform manifold learning work with the assumption that data points from a low-dimensional manifold are embedded in a high dimensional space. The manifolds of the selected voxels are extracted in the next step. For each of the selected voxels the three geometrical co-ordinates are considered. This 3-dimensional representation is reduced to 2-dimensional manifold representation.

IsoMap, Locally Linear Embedding, Laplacian eigenmaps and Diffusion Maps are the algorithms used for learning the nonlinear manifolds. These algorithms are able to recover the intrinsic

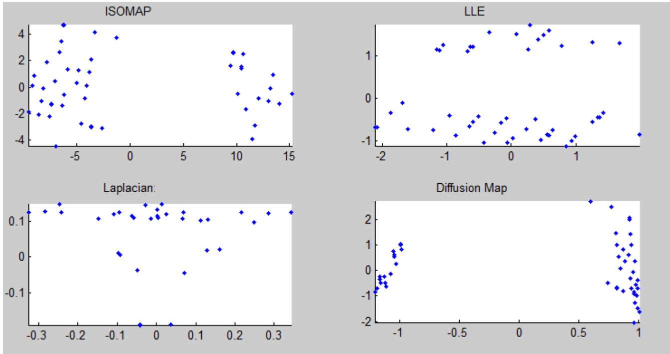

Fig. 2: Two-dimensional manifolds of the selected voxels for 'face' stimulus in the TOFC region of interest for subject 1

geometric structure of the non-linearly embedded data manifolds. Isomap algorithm estimates the geodesic distances between points in the input using shortest-path distances in the k-nearest neighbour graph. It then finds points in low-dimensional Euclidian space whose interpoint distances match the shortest path distances. Locally linear embedding represents each point as a weighted combination of its nearest neighbours. It then finds a configuration in reduced dimensions whose local geometry is characterized well by the weights. In Laplacian eigenmaps , a local similarity matrix is created to capture the degree to which the points are near to one another. The low-dimensional representation is found that matches the degree of similarity. In Diffusion maps, a measure of proximity of data points called diffusion distance is calculated. When representing the data in low-dimensions, this diffusion distance is maintained. LLE ([23]), Laplacian Eigenmaps ([45]) and Diffusion maps ([38]) have previously been used to find task-related components and resting-state networks in fMRI data.

The 2-dimensional manifolds for the Temporal Occipital Fusiform Cortex region of interest for different algorithms for the presentation of a 'face' stimulus to subject 1 show a clear structure (Figure 2).

7. CLASSIFICATION

Classification is done locally for each of the ROI. For each ROI, for each of the subjects, for each stimulus the most discriminating voxels are selected. It is important to note that the voxels are chosen based on their activation levels. Once the voxels are selected, geometrical information of the selected voxels is used.

Data is derived from 6 subjects for 8 different stimuli. A leave-out-one subject cross-validation is used to validate the results. 5 subjects are used as training data and 1 subject as test data. The scrambled image stimulus is left out. For a leave-one-subject out validation for binary classification, there are 142 cases. With 2-class classification problem the chance level is accuracy is 50%. There are 8 stimuli. They belong to two categories, animate and inanimate. For comparing animate vs. inanimate, face vs. house is considered. For within category distinctions, face vs. cat is used from animate category and house vs. scissors, house vs. bottle and shoe vs. chair from inanimate category.

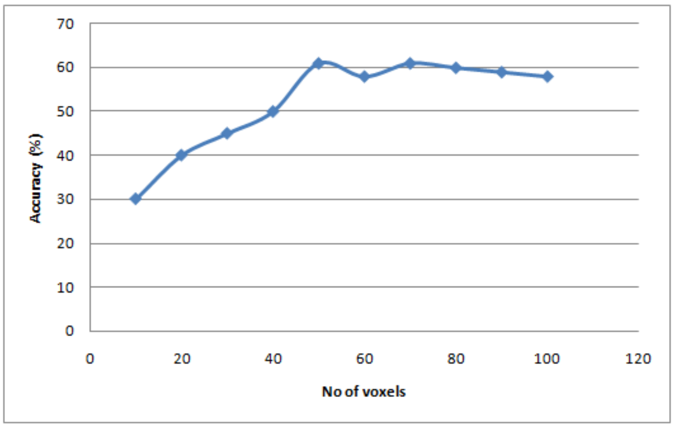

Fig. 3: The number of voxels considered vs. the accuracy

8. IMPLEMENTATION AND RESULTS

It is known from previous studies that specific regions of the brain get activated for specific type of response. Here the ventral temporal cortex that handles the perception of complex visual stimuli is considered. In the relevant ROI, the voxels that are important for distinguishing the specific stimulus are identified.

The algorithm is applied over the Lateral Occipital Cortex, Fusiform Gyrus, Parahippocampal Gyrus and Inferior Temporal Gyrus. Lateral Occipital Cortex (LOC) from combining Superior and Inferior divisions, Temporal Occipital Fusiform Gyrus (TOFC), Occipital Fusiform Gyrus (OFG), Occipital pole (OP), Parahippocampal Gyrus (PG) obtained by combining Anterior and Posterior division ROIs and Inferior Temporal Gyrus(ITG) obtained by combining anterior, posterior and temperooccipital parts. The above areas are believed to be involved in processing and storing information about object form.

8.1 Feature selection

The first decision that is to be made is the number of voxels to be selected by the feature selection algorithm. The most discriminating voxels for face and house categories are chosen by comparing against the scrambled category. The raw activation profiles are considered to decode face vs. house using nearest neighbour classification algorithm. Classification using 50 voxels gives the best results (Figure 3). Therefore, 50 voxels are considered for each of the ROIs.

8.2 Comparison of different representation techniques over different regions of interest

The performance of manifold representation is compared against the other common type of representations - one that uses the raw activation profile of the selected voxels. The Fusiform Gyrus is the face area of the brain. Therefore, the representation techniques to decode face vs. house category in the TOFC region of interest are considered. For a simple nearest neighbour classifier the accuracy obtained in predicting face vs. house for single subjects (Figure 4) as well as multiple subjects (Figure 5) are evaluated. As the graph shows, the Manifold representation outperforms raw activation profile format in prediction accuracy in both the cases.

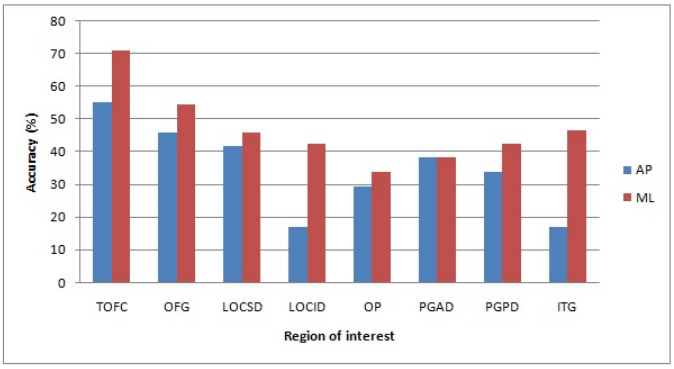

Fig. 4: Accuracy of different representation techniques over Fusiform Gyrus on a single subject

Fig. 5: Accuracy of different representation techniques over Fusiform Gyrus for multiple subjects

8.3 Comparison of Manifold representation across classification algorithms

KNN, SVM and GNB are algorithms that have been successfully used for classification on fMRI data. The prediction accuracies

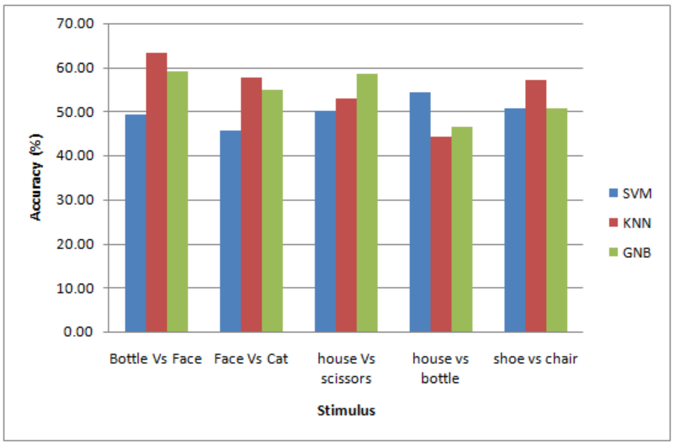

Fig. 6: Comparison of classification algorithms for classification in the TOFC region of interest

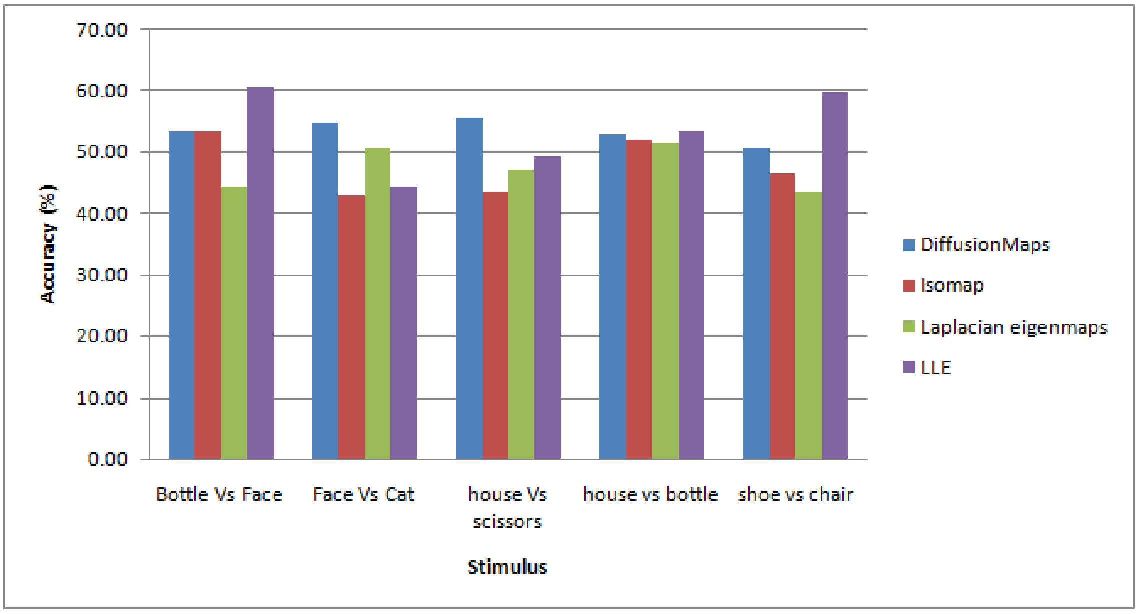

Fig. 7: Comparison of different manifold learning techniques

obtained for manifold representation for classification using all three techniques on the TOFC region of interest for face vs. house decoding are evaluated (Figure 6). As can be seen from the graph k-nearest neighbour classifier with k=5 gives the best accuracy.

8.4 Comparison of different manifold learning techniques

There are many manifold learning techniques available. The most popular non-linear algorithms are considered here. The four techniques that are used are compared for various category distinctions in the TOFC region of interest (Figure 7). LLE and Diffusion maps seem to perform well for most of the category distinctions.

9. CONCLUSION

This paper proposes a new approach to classify multiple subject fMRI data. Instead of a whole brain approach, ROI specific approach is adapted to classify each subject's data as belonging to a category. Each category of cognitive state is represented as manifold of discriminating voxels. The voxels are chosen based on their activation levels and discriminating ability. The manifold is learnt based on the geometrical coordinates of the discriminating voxels. Results indicate that the classification accuracy is higher when using this representation as opposed to using raw activation profiles. If fMRI data has to be shared across subjects and studies then this separation of steps is advantageous. Only binary classification is considered here. Future work will include classification of multiple categories and scaling the algorithm to include multiple studies.

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