Exploring New Methodologies for the Analysis of Functional Magnetic Resonance Imaging (fMRI) Following Closed-Head Injuries

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Abstract. An increasing amount of research has focused on the use of newer and alternative data analytic approaches to multi-dimensional data sets. The primary aim of this paper is to introduce two data analytic approaches as they have been applied to image scans from functional Magnetic Resonance Imaging (fMRI). The first approach involves loading data from fMRI scans into multi-dimensional cubes and performing tensor decomposition. In addition, we introduce a second approach involving the use of network modeling that attempts to identify stable networks in fMRI scans across time. Discussion will be focused on the application of these approaches to the modeling and rehabilitation following closed-head injury.

Keywords: fMRI, Tensor Decomposition, Graph/Network Modeling.

1 Introduction

There has been an increasing need over the past twenty years for the military services to develop research programs dedicated to the understanding and application of neurosciences in operational settings. This "revolution" in the neurosciences, now known as Operational Neuroscience, has resulted in the emergence of an entire discipline dedicated to the application of those principles to warfighters in the field [1, 2]. However, as research programs continue to seek to integrate both basic and applied sciences to maximize the effectiveness of these warfighters, there continues to be a need to explore new and/or alternative approaches to analyze human performance and physiological data more effectively.

Recently, there has been a great deal of interest in the application of exploratory data analysis techniques such as Singular Value Decomposition (SVD) and Principle Components Analysis (PCA) to the analysis of data from functional imaging studies such as functional Magnetic Resonance Imaging (fMRI). Data analytic approaches such as SVD and PCA, when applied to fMRI, are limited in that they are based on matrix calculations where the data may be defined in only two dimensions (i.e., time and location) [3, 4]. However, this form of data analysis, by making the data two dimensional, abstracts out important details such as the identification of activation patterns over time.

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Techniques such as SVD and PCA attempt to portray the data from a single imaging study as a two dimensional data matrix (*X*). Accordingly, data matrix *X* can be further decomposed into a sum of R outer products of individual factors by:

$$X = \sum_{r}^{R} a_r \otimes b_r + E. \tag{1}$$

During the decomposition of this data matrix, spatiotemporal properties from the fMRI scan are encoded as vectors a_r (spatial properties) and b_r (temporal properties). Noise from the functional image is represented as a constant E. The relationships between spatio and temporal data from the fMRI scan can be discovered using a variable number of data analytic processes. Regardless of the data analytic process implemented, both SVD and PCA apply matrix computations and factorize a single two-dimensional data matrix into time courses and spatial maps [3].

A more thorough explanation of a particular dataset might require the simultaneous analysis of three or more dimensions of data (i.e., time, location, and stimulus). Within the past ten years, there has been a proliferation of research attempting to explore newer and alternative data analytic approaches to multi-dimensional data [5, 6, 7]. With respect to Operational Neuroscience, these approaches offer a great deal of promise due to their ability to efficiently identify patterns in very dense data sets.

A promising new approach for the analysis of multi-dimensional data involves the use of tensors. For example, the use of tensors allows the analysis of the fMRI data, without compromise, by representing the data as a four dimensional object (x y z locations on a fMRI scan over time). Simply put, a tensor is a generalization of a matrix (or scalar or vector) to more than two dimensions. Multi-dimensional data can be viewed such that each dimension of a particular dataset might represent a different aspect or characteristic. In the case of the fMRI of a single person: the four dimensions correspond to location and time, or in the case of more than one person, five dimensions and so forth. Figure 1 shows a simple order-three tensor where location has been simplified to be viewed in three dimensions.

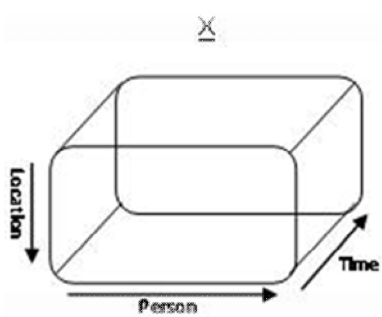

Fig. 1. Order-three tensor illustrating a functional image. This figure illustrates how data from an fMRI scan can be extended to an order-3 (or greater) tensor. Dimensions on the tensor include dimensions for (i) individuals, (j) locations, and (k) activation over time.

Tensors Defined. As mentioned previously, tensors can be viewed as a data cube whereby each dimension of the cube represents some aspect or characteristic of the dataset. For functional imaging scans, a 3rd order tensor can be used to represent three aspects of the dataset: individual, location of activation, and how the activation pattern has changed over time (see Figure 1). A single entry (i, j, k) in the tensor then, corresponds to a single individual (i), location of activation for that individual (j), and the change in activation of that individual's scan over time (k).

2 BOLD Analysis

Brain imaging techniques such as MRI and, more recently, fMRI have been used in a variety of experimental and clinical studies to investigate phenomena ranging from working memory to traumatic brain injury [5]. The most likely explanation for the continued use of these imaging approaches is the ability of these paradigms to portray information processing in the brain as it occurs in real time.

Perhaps the most common approach to measuring brain activity is through the use of fMRI and Blood Oxygen Level Dependence (BOLD). Measurement of BOLD level assumes that increased neuronal activity requires more glucose and oxygen to be rapidly delivered through the blood stream. The ratio of oxygenated and deoxygenated blood in a particular area is therefore presumed to represent brain activation during a specific task. Functional Magnetic Resonance Imaging has revolutionized the behavioral sciences by offering spatial and temporal resolutions far exceeding brain imaging techniques available in the past. Since its introduction during the early 1990s, thousands of studies have been conducted examining a range of issues including structure, pathology, and processing.

While BOLD measurements are commonly viewed as the 'gold standard' in neuroscience today, there are growing concerns over the reliability of fMRI findings and the interpretation of their results. For example, BOLD fMRI is often referred to as a relative technique in that it attempts to compare images taken during one mental state to different scans of the same individual in another state. Series of fMRI scans are aggregated to measure the relative differences between two states to perform a statistical analysis within a single individual.

Similarly, neuroimaging studies usually involve the analysis of scans from several individuals taken from several different sessions. For analysis techniques such as SVD and PCA, this results in the aggregate of data across individuals and/or time. Therefore, these types of data analytic approaches may result in the inability to identify specific individual differences across different imaging scans. Therefore, for the purposes of identifying individual differences across scans, a more suitable data analytic approach is one that involves the analysis of multiple data sources all at once [3].

3 Tensor Applications to fMRI Analysis

Due to many of the aforementioned limitations in fMRI, there has been an increased interest in the application of multi-dimensional data analytic tools for functional imaging analysis. Here, we describe the application of PARAFAC decomposition to fMRI. Other more complex decompositions exists but we shall use this simplest of decompositions to illustrate our points.

3.1 PARAFAC Decomposition

Our primary criticism to previous approaches to the analysis of fMRI data is the aggregation across various data sources to limit the data to two dimensions. However, often times it is more meaningful to identify patterns in the dataset across more than two dimensions. For example, suppose that there is a group of functional images that identify a pattern of activation for a specific cognitive task (i.e., spatial rotation task). In addition, there may be one or more patients in that population that performs poorly on that task due to some preexisting trauma. One goal of the data analytic approach might be to then identify those individuals that performed poorly on the cognitive task and those that performed equivalent to the normal group. Moreover, we might be interested in identifying how the pattern of activation for the two groups different across time.

The approach we outline here, constrained PARAFAC decomposition, overcomes many of the aforementioned limitations by using a Low-rank tensor approximation. This process involves loading images from an fMRI scan into a multi-dimensional tensor. After the image is loaded into the tensor, a PARAFAC decomposition (see Figure 2) is performed such that each slice may be analyzed independently at separate locations and at different times [7, 8].

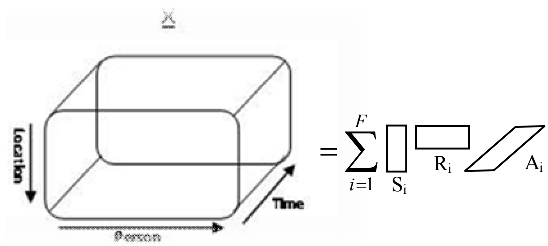

Fig. 2. PARAFAC Decomposition of FMRI. This figure illustrates the decomposition of F factors (i), each of which describes a time, individual, and location of activation. The decomposition of the tensor varies depending upon the relationship between the different dimensions in the data cube.

The PARAFAC decomposition is accomplished by representing three (or more dimensions) of data by a trilinear combination of three outer products:

$$X = \sum_{r}^{R} a_r \otimes b_r \otimes c_r ... \otimes i_r + E. \tag{2}$$

For the purposes of fMRI, properties such as spatial location (a_r), the individual (b_r), and/or the activation pattern as it occurs over time (c_r) are each encoded as vectors.

However, other properties of the functional image may also be projected within the multi-dimensional data cube. Regardless of the number of dimensions, decomposition of the tensor allows for the identification of specific relationships between any or all vectors of the tensor.

A novel computation of our work is to explore constrained tensor decomposition. Regular decompositions will find the mathematical optimal decomposition but this may yield non-actionable results. For example, the outer product of a_i and b_i may yield a non-contiguous activation area or the activation level (the t dimension) may be non-smooth or multi-modal. In our work we explore constraining the decomposition so that these and other issues which may make the decomposition difficult to interpret are constrained not to occur

3.2 fMRI Interpretation

For the present study, we used a rank 10 tensor to approximate the original tensor. The tensor approximation allows us to view brain activation as a multi-dimensional process. In the case presented below, we are representing BOLD activation in a three dimensional space as it unfolds over time. However, the tensor decomposition approach allows us to model activation for any number of dimensions.

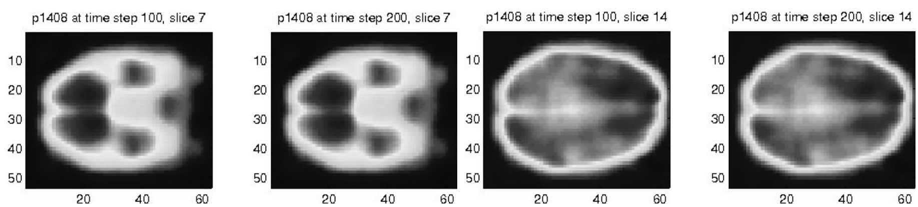

Fig. 3. Visualization of functional images from the same patient at different time steps. Note that similar activation patterns are clearly identified for different time series.

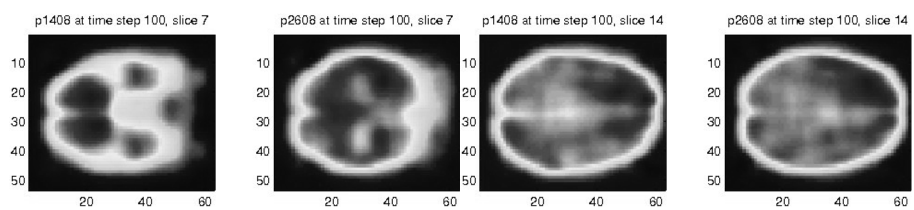

Fig. 4. Visualization of functional images from different patients at the same time steps. Note that very different activation patterns are clearly identified for different image slices.

To further illustrate this process, the tensor decomposition process was applied to several fMRI images from patients while at rest. Since a 53×63×28×235 tensor can also be considered as 53×63×28 tensors over 235 time steps, we compared these tensors (from the same patient) over time. Not surprisingly, when this process was applied to the same patient at rest we found that the tensors do not differ much. However, when comparisons from two tensors from two different patients were made, the resulting tensors were quite noticeably different (see Figures 3and 4). These conclusions were consistent for both the original tensor and its approximation. Together, these results provide converging evidence that the decomposition approach does provide an alternative analytic approach to brain imaging techniques.

4 Network/Graph Analysis of fMRI

Though PARAFAC analysis has many advantages, it is limited in that it does not (in its basic form) consider the spatial relationships between the different locations from an fMRI scan. When searching for interactions, PARAFAC treats different but adjacent locations from the functional scan the same as locations that are far apart. This can, in turn, lead to the inability to identify factors which are spatially diverse and not contiguous. Furthermore, tensor analysis also has other inherent limitations such as requiring a symmetrical distance which is implicitly defined. A symmetrical distance function requires the distance from a to b to be the same as b to a and this is not often the case. Therefore, we have also applied principles of network/graph analysis to fMRI data in an attempt to overcome some of these limitations. The benefit of a network/graph analysis of fMRI data is that these spatial relationships and preferences can be directly encoded.

Network/graph analysis attempts to identify both symmetrical and asymmetrical relationships between discrete objects. A graph can be viewed as an abstract representation of a network consisting of nodes and a set of edges (or connections). An edge that connects two nodes suggests there is a relationship between both nodes in the graph (see Figure 5) and the weight of the edge indicates a measure of distance or similarity between the nodes.

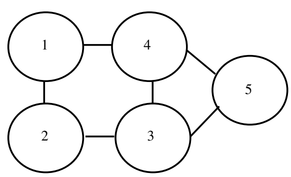

Fig. 5. Visualization of a graph or network. Each node in the network may refer to the activation of a particular area during functional imaging. Edges connecting various nodes in the network suggest that different locations may have a similar pattern of activation.

Formally, graphs can be represented as an adjacency matrix A. Edges that connect two nodes in the graph are represented in the adjacency matrix as $A_{i,j} = 1$. However, if no relationship exists between the two nodes, then the adjacency matrix represents that relationship as $A_{i,j} = 0$. Furthermore, the number of edges connecting to a particular node is described as the degree k. Therefore, the probability P(k) that a randomly chosen node will have degree k is given by the degree distribution [9].

The edges in any particular network can be represented as either nondirectional, where the relationship between each node is homogenous, or directional, where the relationship between the nodes may be heterogeneous (one node influences the other). This concept is important with regard to modeling fMRI activation. Specifically, this allows us to model patterns of activation such that some areas of activation may facilitate the activation of other areas in the brain. However, that relationship need not be reciprocal.

The network model we use is an example of an enhanced 2-Graph. In this network/graph, each voxel from an fMRI scan is treated as a separate node in the network. Similarly, there exist edge weights between nodes indicative of their spatial distance or some other measure of similarity. However, the analyst can set these edge weights to reflect what-ever relationship they wish the analysis to emphasize. At each node/voxel is the behavior of that node over time as given by the fMRI scan. In this way, the network analysis can be viewed as a tensor with encoded spatial (or other) information in the form of edge weights.

The benefits of edge weights as a tool to allow analysts to emphasize their domain expertise cannot be over-emphasized. The relationship between voxels need not be symmetrical for a pair of voxels or even provided if it is not known. Furthermore, graphs are a more natural interpretation (extension) of the way in which we theorize processing to occur in the brain. That is, it is common to view the brain as being composed of very discrete structures separated by geographic boundaries within the brain. Therefore, it would seem apparent of the need to apply a discrete modeling process. Similarly, this discrete modeling process takes into account many of the spatial properties that were alluded to earlier.

The study of graph theory and its application to neuroscience is an important area of focus. For example, it has been suggested that this approach can be used as a methodology for identifying functional clusters of brain activity during experimental tasks. However, it is critical to first identify under what boundary conditions this form of data analytic approach might be used.

The analysis of such a complex graph is an area of ongoing research. Recently, Davidson and collaborators showed how to analyze such graphs so as to segment them [10], project them into lower dimensional space [11] and perform multilabel prediction [12]. However, very little research has been conducted to examine the application of these approaches to fMRI data [13, 14].

5 Diagnosis and Rehabilitation Following Closed-Head Trauma

FMRI is commonly recognized as a premier modality for imaging brain physiology and tracking neural correlates of plasticity. The increase in popularity of functional imaging paradigms is due to the ability of these imaging technologies to view the activated brain during specific tasks. However, functional imaging modalities are not immune to their own criticisms. As discussed previously, these imaging techniques are often limited to very coarse data analytic techniques. The techniques outlined in this paper are an attempt to formalize alternative data analytic techniques that might identify more granular patterns in the data set. Specifically, the use of tensor decomposition or network/graph analysis is able to efficiently analyze interactions in the data that might occur across individuals, localized activation from the scan, or activation patterns across time.

However, there has been little progress in the use of imaging technology on patients following closed head trauma [15]. Unfortunately, it is these types of functional imaging modalities that offer the most promise with respect to the diagnosis and rehabilitation of patients following closed-head trauma. Ultimately, it is our hope to establish a paradigm for the diagnosis of and eventual rehabilitation of patients following traumatic brain injury. Specifically, it is believed that the approaches highlighted above can be used to identify intact neural pathways for patients following traumatic brain injury. In addition, these approaches may also allow for the identification of those neural pathways that might bypass neural pathways affected by cortical injury or strengthen those pathways that promote neural plasticity.

6 Concluding Remarks

Currently, there is a gap that exists between the basic science of brain imaging technology and the implementation of that science in the operational environment. Operational Neuroscience, to be effective, must continue to utilize recent innovations in both basic and applied research. Ultimately, operational neuroscience should continue to challenge the boundaries that define the limits of human performance. The primary aim of this paper was to introduce alternative data analytic approaches to fMRI. These approaches, if proven to be efficient and scalable, might be used to supplement the use of neuroimaging tools in operational settings.

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