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Intensity / Correlation Thresholding of FMRI Data: Data-driven Regions of Interest using Bridge Voxels

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Abstract-**Analysis of functional magnetic resonance imaging data considers temporal correlation of hemodynamic intensity patterns to a known activation paradigm as well as spatial regions of similar responses. Default regions of interest are often obtained by analyst-directed thresholding of intensity or correlation values. This paper presents a method to determine data-driven regions of interest using image erosion to identify structurally significant components in the default regions, namely bridge voxels.**

I. Introduction

Challenges in functional magnetic resonance imaging (FMRI) data analysis [1] revolve around the detection, extraction, and transformation of information from a large set of complex data. Many unsupervised learning techniques such as fuzzy C-Means (FCM) [2] are used to elicit intrinsic data structure, to discover novelty, and to make robust statements about the data in the presence of noise. Use of such data-driven techniques are critical and serve to complement evolving, possibly idiosyncratic, hemodynamic response models.

FMRI analysis often begins by examining a set of user-defined intensity (correlation) thresholds that define volume elements, or voxels, in the dataset. A voxel consists of spatial coordinates and a series of blood flow intensities acquired in the study. Ideally, these voxels correspond to functional areas stimulated in the study, for example, the visual cortex in a neural activation study with a visual stimulus. The mean temporal blood flow, or time course (TC), intensity is a common threshold used to generate initial regions of interest (ROI) for subsequent analysis. Candidate ROI are also generated by thresholding Pearson correlation coefficients of the TCs with respect to the activation paradigm in the study. However, the general validity of such methods may suffer from the variety of conditions under which FMRI data is acquired [3].

This paper examines a process of determining data-driven intensity and correlation thresholds by identifying structurally significant voxels in the initial ROI. Structural significance is characterized by interior voxels which persist through repeated erosion of the ROI and, having been eroded, fundamentally change the region properties, such as splitting or fragmenting the ROI. Voxels holding these properties with respect to mathematical morphological [4] [5] erosion are denoted bridge voxels [6].

II. Bridge Voxels

The process for discovering data-driven ROI in FMRI datasets occurs in two stages. First, a user-specified set of intensity or correlation thresholds is used to define initial ROI. A set of thresholds is used to make the process robust against idiosyncratic patient hemodynamic responses and to allow targeting of the functional area over the series of regions that result from a gradient of thresholds. Initial regions are eroded until they split, fragment or vanish, revealing structure and identifying bridge voxels. Successive erosions decrease the ROI area or shatter the ROI into multiple, dis-connected sub-regions. When an ROI shatters, a bridge voxel is said to have been eroded. [A special case occurs when ROI erosion leaves a single voxel.] That is, bridge voxels are the structurally significant voxels that connect the erosion-susceptible components of the initial ROI. Erosion continues until all ROI are completely eroded or shattered.

Second, bridge voxel intensity or correlation values are used to generate a second set of thresholds, which in turn, highlight a set of data-driven ROI. Thus, the steps are:

1. Identify Bridge Voxels: User-defined thresholds determine initial ROI. ROI are eroded until they fragment or vanish. Bridge voxels (or last remaining voxels) determine a second set of thresholds.

2. Identify Data-driven ROI: The second set of thresholds are used to elicit ROI revealing more intrinsic structure.

This second set of thresholds defines the data-driven ROI. The two sets of ROI, user-defined and those derived from bridge voxels, may be compared in terms of voxel intersection, and average intensity and correlation values.

A. FMRI Spatio-Temporal Methods

Goals of FMRI analysis include reducing the impact of outlier TCs, determining ROI that relate to the functional activity, and focusing the researcher's attention on novelty by limiting false positive rates. Robust data interpretation begins by considering all sample features within a spartan data model. Bridge voxels meet this criterion in their spatio-temporal approach to FMRI data and by examining ROI fragmentation. Other methods, for example FCM derivatives such as FCMP [7], combine spatial and temporal distances to generate ROI with both high temporal similarity and spatial proximity. This process was shown to significantly reduce the false positive rate. FMRI analysis of neural activations found by FCM in studies often detects distinct yet proximal areas with similar centroid *TC*s. Other algorithms of interest are fuzzy region growing [8] and EROICA®, an ROI cluster analysis algorithm [9].

III. Data

S05 is an *in vivo* neural activation study acquired at IBD. The activation paradigm is based on a checkered visual stimulation presented to the subject. Neuron activations for a single z-plane, or slice, were recorded at 42 distinct time instants. The dataset is composed of TCs with (X,Y,Z,T) dimension of (128, 256, 1, 42). A mean intensity image is shown in Fig. 1.

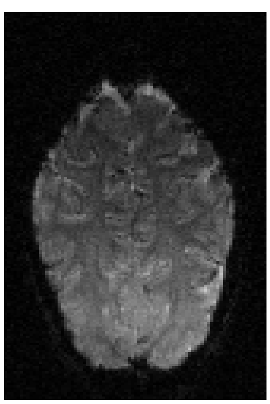

Figure 1. Mean intensity image for S05.

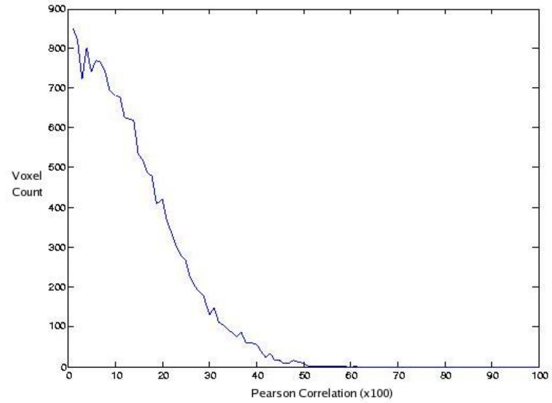

Figure 2. Correlation histogram for S05.

The visual cortex, lower centre, and a lobe in the right hand lower side, show high levels of signal intensity. The activation paradigm is [010110]. The focus of analysis for S05 is the visual cortex and the adjacent lobe.

A correlation histogram for S05, Fig. 2, shows significant correlation values with respect to the activation paradigm. Typical TCs with above average intensity values for S05 are seen in Fig. 3 while Fig. 4 shows TCs with relatively high correlation. Thresholding of the mean intensity and correlation planes (z=0), seen in Figs. 5 and 6, generates ROI that include the functional response area, the visual cortex, but also extend throughout the plane. Noise and spatial outliers are present in the S05 dataset as indicated by significantly correlated TCs well outside of the visual cortex.

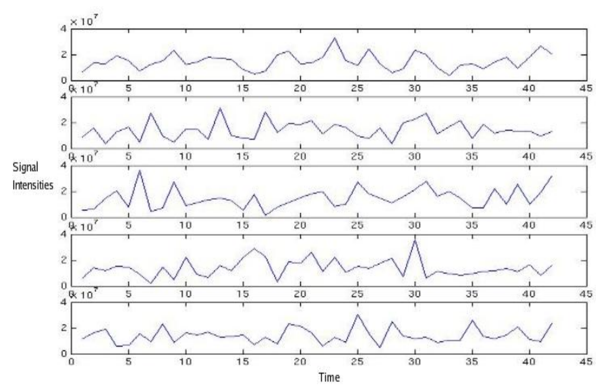

Figure 3. Typical TCs in S05 with greater than average intensity.

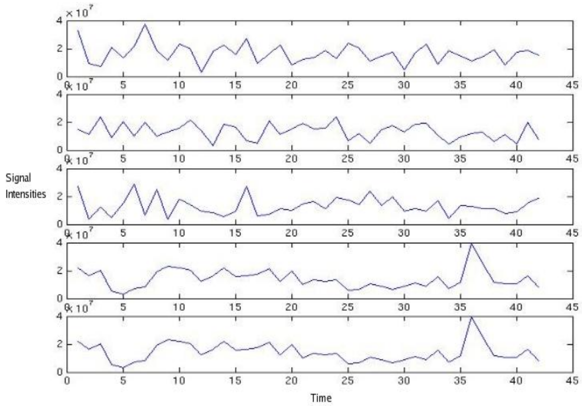

Figure 4: Typical TCs in S05 with above average correlation to paradigm.

Figure 5. Intensity thresholded ROI of S05. Threshold is sixty percent of the maximum intensity.

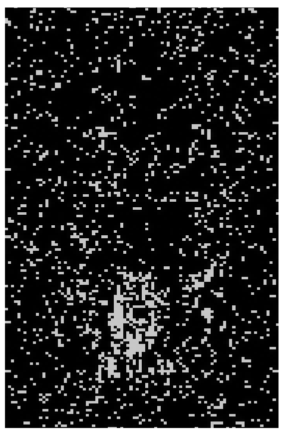

Figure 6. Thresholded correlation plane S05. Pearson Correlation threshold is set at T =0.2.

1. EXPERIMENT

The experiment consisted of the following. To determine initial ROI, intensity thresholds of {0.6, 0.7, 0.8, 0.85, 0.9} of the maximum mean intensity value were used. Correlation thresholds of {0.05, 0.1, 0.15, 0.2, 0.25} were also used. Thresholding often produces multiple ROIs. For each threshold, only the largest four-connected region was examined and bridge voxels were identifued by the noted erosion process. When considering the Pearson correlation of the TCs to the activation paradigm, an ideal activation response is used for the paradigm. ROI erosion used a 3 by 3 structuring element. Implementation was in C++ code as a Scopira™ kit [10].

Figure 7. Initial ROI based on intensity threshold at 60% of maximum.

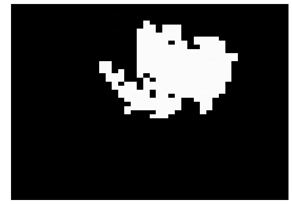

Figure 8. Initial ROI based on intensity threshold at 70% of maximum.

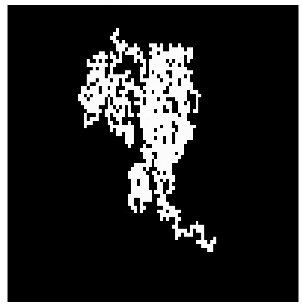

Figure 9. Initial ROI based on correlation value of 0.05.

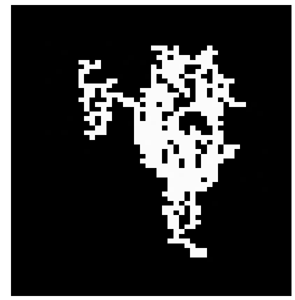

Figure 10: Initial ROI based on correlation value of 0.1.

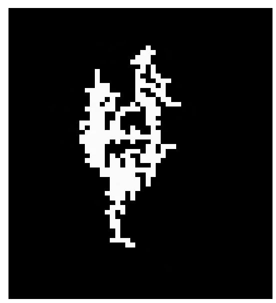

Figure 11. Initial ROI based on correlation value 0.15.

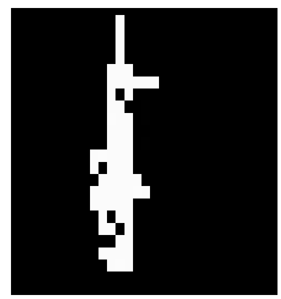

Figure 12: Initial ROI based on correlation value of 0.2.

V. RESULTS

Figures 7-8 show initial ROI generated by intensity thresholds while Figs. 9-12 show ROI for correlation thresholds. Initial ROI exhibit irregular structure, roughly corresponding to anatomical structure of the visual cortex, and often contain holes of low average intensity or low correlation. Of interest was the change in location of the ROI as the gradient increased. Initial ROI for increasing threshold values were not sub-regions of lower thresholded ROI. This may have been due to the selection of the largest four connected region in the process although a previous study [7] showed that similarity of intensity values are not always a good indicator of spatial proximity between voxels.

Regarding region properties, data-driven thresholding produces smaller ROI that have fewer holes. This occurs because the bridge voxels, by being in the interior of the initial ROI, typically have higher intensity and correlation values. Thus, data-driven thresholds are appreciably higher than those which generated the initial ROI.

It was found necessary to introduce the following heuristic: all eroded voxels in the image are designated as candidates for the bridge voxel. The largest two subregions of the shattered initial ROI define a directed line segment, terminating in the centre of mass of each subregion. This line segment is then dilated by a structuring element. Finally, voxels in the intersection of the dilated line segment and the eroded voxels are defined as bridge voxels. When more than one bridge voxel exists, the average intensity (correlation) is used. As a caveat, it is not obvious that voxels in a direct line between ROI sub-regions should be included as candidate brdige voxels due to the actual tissue-type paths, that is gray-white convolutions, found in the brain.

Some ROI, derived from correlation thresholds, eroded without leaving any bridge voxels, that is, they eroded by vanishing rather than shattering. When this occurred, the ROI centre of mass defined the bridge voxel.

Using bridge voxel properties to define global thresholds resulted in ROI that were substantially smaller in area than the ROI used to initiate the process. Reconstructed ROI areas were typically 25% or less of the original areas. Also, although some of the reconstructed areas were fairly small, consisting of 7-29 voxels, the regions often exhibited one or more holes. Considering a single threshold set (the initial threshold and the one defined by the bridge voxel), there are two possibilities for the resultant ROI. If the initial ROI is considered as a mask for the dataset, the data-driven ROI must be a sub-region of the initial ROI. Otherwise, the data-driven ROI has the potential to be in a different spatial location and with no intersection with the initial ROI. This possibility is one way that novelty is discovered by this process.

Thresholding intensity variance does not generally produce insightful ROI.

VI. Conclusions

An investigation into the data-driven derivation of global thresholds for fMRI has been described and comparisons between initial and data-driven ROI provided. Bridge voxel thresholds were consistently higher than user-defined thresholds and the existence of holes in the data-driven ROI was unexpected. Definition and demonstration of data-driven ROI generation for fMRI was detailed using concepts in mathematical morphology. The benefit of data-driven methods for FMRI analysis was discussed and alternate spatio-temporal methods introduced. The use of bridge voxels provides an independent means to generate intensity and correlation thresholds, which in turn, define data-driven ROI in the dataset.

A. Future Work

Of interest is the case where a threshold derived from bridge voxels is less than that of the initial threshold, as this would be an exception to the pattern to date. Also of interest is an extension to the bridge voxel approach that incorporates region growing. Finally, an examination of the interdependence between intensity and correlation values in the bridge voxel process is needed. That is, the relationship between initial intensity (correlation) thresholds and resultant correlation (intensity) values in the data-driven ROI, needs to be examined.

Acknowledgment

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