Detection of Neural Activities in FMRI Using Jensen-Shannon Divergence

Jayanta Basak
IBM India Research Lab, New Delhi, India
Email: bjayanta@in.ibm.com, basakjayanta@yahoo.com

Abstract

In this paper, we present a statistical technique based on Jensen-Shannon divergence for detecting the regions of activity in fMRI images. The method is model free and we exploit the metric property of the square root of Jensen-Shannon divergence to accumulate the variations between successive time frames of fMRI images. Experimentally we show the effectiveness of our algorithm.

1. Introduction

Automated and robust detection of the activated brain regions from the fMRI image sequences is a challenging task [6] due to very low signal-to-noise ratio and relatively low spatial resolution for adequately high temporal resolution. Due to the difficulty of applying traditional image processing methods [2] are used to make statistical inferences about the regions of activity in fMRI images. One commonly used approach is detecting active regions by the computation and subsequent thresholding of a statistical parameter map subjected to the t-test based on the assumption of Gaussian temporal noise [9]. Various other methods in the literature for fMRI data analysis include correlation analysis, non-parametric Kolmogorov-Smirnoff test, wavelet transform, principal component analysis, independent component analysis, subspace modeling and clustering, a comprehensive list of the reference articles of which are available in [8].

In this article, we introduce a statistical method for detecting the regions of activity in fMRI images based on the Jensen-Shannon divergence [3]. This particular method differs from the conventional t-test or Anova techniques in the sense that it does not depend on the general linear model. Due to the robustness and insensitivity to noise, Jensen-Shannon divergence has been successfully applied in image segmentation [1] earlier. However, the possibility of using the Jensen-Shannon divergence in detecting activity regions in fMRI images has not been explored. Here we provide a method for detecting the activities in fMRI images using the Jensen-Shannon divergence.

2. Algorithm

2.1. Description of JS Divergence

Jensen-Shannon divergence measures the difference between two discrete distributions \( p = [p_1, p_2, \ldots, p_n] \) and \( q = [q_1, q_2, \ldots, q_n] \) where \( p_i \) denotes the probability of a random variable \( X \) taking the \( i \)th value. For example, for two different coins, probability distributions of ‘Head’ and ‘Tail’ can be represented as \([p_1, p_2]\) and \([q_1, q_2]\). The divergence is given as

\[
JS(p, q) = -\alpha_p H(p) - \alpha_q H(q) + H(\alpha_p p + \alpha_q q)
\]  

(1)

where \( \alpha_p, \alpha_q \in [0,1] \) are two positive constants indicating the respective weights for the distributions subject to \( \alpha_p + \alpha_q = 1 \). \( H(.) \) denotes the Shannon entropy, \( H(p) = -\sum_i p_i \log p_i \). For \( \alpha_p = \alpha_q = 0.5 \), \( JS(p, q) \) is symmetric unlike the Kullback-Leibler divergence. Although Jensen-Shannon divergence does not guarantee the triangular inequality of a metric, the square root of the divergence follows the metric property [3].

2.2. Application of JS divergence to neural activity detection

The four dimensional fMRI images \( (x, y, z, t) \) can be considered as the spatio-temporal signals, where in each time frame, the activation occurs over a few voxels, and it propagates over a sequence of time frames depending on the hemodynamic response function. Since \( \sqrt{JS} \) is a metric,

\[
\sqrt{JS(w_i(t_i), w_j(t_j))} \leq \sqrt{JS(w_i(t_j), w_j(t_k))}
\]  

(2)

for any \( t_i < t_j < t_k \). \( w_i(t) \) represents the voxel statistics over a chosen window at a certain location \( i \) at a time frame \( t \). For example, we can chose a \( 7 \times 7 \times 5 \) window at a specific location \( (x, y, z) \) at different time frames. Equation (2) reveals that

\[
\sqrt{JS(w_i(t_1), w_j(t_n))} \leq \sqrt{JS(w_i(t_1), w_j(t_2))} + \sqrt{JS(w_i(t_2), w_j(t_3))} + \cdots + \sqrt{JS(w_i(t_{n-1}), w_j(t_n))}
\]  

(3)

for any \( n \). Thus we can add the square root of the divergence \( \sqrt{JS} \) between every consecutive pair of time frames and
the resulting summation between time-frame 1 and time-frame n is always greater than or equal to the $\sqrt{JS}$ measure between time-frame 1 and time-frame n. Therefore, we accumulate the statistical difference (in terms of $\sqrt{JS}$) over consecutive frames, and finally threshold the accumulated value. It is also possible to perform certain kind of clustering in the accumulated value in order to detect the regions.

Figure 1 describes the overall algorithm. First we define an accumulator array $A(x, y, z)$ and initialize $A = 0$ for every $(x, y, z)$. Then for every $t \in \{1, \ldots, n - 1\}$ (assuming that there are $n$ time frames available) and for every location $(x, y, z)$, we consider a window of a specified size centered at $(x, y, z)$. We then obtain the discretized distribution $p(x, y, z, t)$ over every such window centered at $(x, y, z)$ in the time frame $t$. We then compute the Jensen-Shannon divergence in terms of $\sqrt{JS}(p(x, y, z, t), p(x, y, z, t + 1))$ for every $t$ and accumulate in the array $A(x, y, z)$ for every $(x, y, z)$. Finally we threshold the accumulator array with certain user defined threshold and obtain the regions of activity. Note that, it is also possible to recover the time frames where exactly the stimulus has started by adding one more dimension to the accumulator $A$.

**Input :** L slices of $M \times N$ MRI images at each time frame.

**Output :** L slices of $M \times N$ output image.

begin
Initialize an accumulator array $A(x, y, z) = 0$
$x \in \{1, \ldots, M\}, y \in \{1, \ldots, N\}, z \in \{1, \ldots, L\}$
Define a window size $(2m + 1, 2n + 1, 2l + 1)$ where $m, n, l \geq 1$.
for every $(x, y, z) \in \{(m, n, l), \ldots, (M-m, N-n, L-l)\}$
begin
get window $w(x, y, z)(t)$ [center: $(x, y, z)$; time frame: $t$];
compute $p \leftarrow$ normalized histogram of $w(x, y, z)(t)$;
get window $w(x, y, z)(t + 1)$ [center: $(x, y, z)$; time frame: $t + 1$];
compute $q \leftarrow$ normalized histogram of $w(x, y, z)(t)$;
Update $A(x, y, z) \leftarrow A(x, y, z) + \sqrt{JS}(p, q)$;
end
Threshold $A$ with a user defined threshold; output thresholded $A$.
end

**Figure 1.** Overall algorithm

2.3. Analysis of the proposed method

We empirically analyze the effectiveness of the proposed method. We approximate the distribution over a window volume by a histogram. It is necessary because by definition, JS-divergence considers only the discrete distribution. Let the distribution in the original window be $p = \{p_1, p_2, \ldots, p_n\}$ subject to $\sum p_i = 1$ where $p_i$ is the fraction of voxels with $i^{th}$ intensity level. After stimulation, let a fraction of voxels be moved from the $i^{th}$ intensity level to the $j^{th}$ intensity level. Thus the modified discrete distribution after stimulation is

$$q = \{p_1, p_2, \ldots, p_i - \Delta, p_{i+1}, \ldots, p_j + \Delta, p_{j+1}, \ldots, p_n\}$$

where $\Delta$ represents the change in the density of the $i^{th}$ intensity level. We assume that due to the stimulus, some of the voxels having $i^{th}$ intensity level are pushed to the $j^{th}$ intensity level. The effect of stimulus can span over more than one neighboring bin, however, we restrict our analysis to one bin only. The symmetric Jensen-Shannon divergence between $p$ and $q$ is given as

$$JS = \frac{1}{2} \left( p_i \log p_i + p_j \log p_j \right) + \frac{1}{2} \left( \log(p_i - \Delta) + \log(p_i - \Delta) \right)$$

$$\left( \log(p_j + \Delta) + \log(p_j + \Delta) \right) - (p_i - \Delta/2) \log(p_i - \Delta/2) - (p_j + \Delta/2) \log(p_j + \Delta/2)$$

(5)

Considering that $\Delta = \alpha p_i = \beta p_j$,

$$JS = \frac{p_i}{2} \log \left( \frac{1}{\frac{1}{1+\alpha^2}} \right) + \frac{p_j}{2} \log \left( \frac{1}{\frac{1}{1+\beta^2}} \right)$$

$$+ \frac{\alpha p_i}{2} \log \left( \frac{1}{1+\alpha^2} \right) + \frac{\beta p_j}{2} \log \left( \frac{1}{1+\beta^2} \right)$$

(6)

where $\alpha$ represents the fractional decrease in the number of voxels having $i^{th}$ intensity and $\beta$ is the fractional gain in the number of voxels having the $j^{th}$ intensity value. Considering that $\alpha < 1$ for all $i$, we neglect the higher order terms in $\alpha$ such that

$$JS = \frac{\alpha p_i}{2} + \frac{p_j}{2} \left( \log \left( \frac{1 + \beta}{(1 + \beta/2)^2} \right) + \beta \log \left( \frac{1 + \beta}{1 + \beta/2} \right) \right)$$

(7)

The Jensen-Shannon divergence (Equation 7) behaves in two different ways in two cases for (i) $\beta < 1$ and (ii) $\beta > 1$.

Let us analyze these two cases separately.

Case I : For $\beta < 1$, we neglect the higher order terms in $\beta$ such that $JS = \alpha^2 p_i/4 + \beta^2 p_j/4$.

Simplifying,

$$\sqrt{JS} = \frac{1}{p_i} + \frac{1}{p_j} \frac{\Delta}{\beta}$$

(8)

which shows that for given $p_i$ and $p_j$, $\sqrt{JS}$ varies linearly with $\Delta$ independent of the condition that $i < j$ or $i > j$.

Case II : For $\beta \geq 1$, we approximate Equation 7 as

$$JS = \frac{\alpha^2 p_i}{4} + (\beta - \log \beta + 2 \log 2) \frac{p_j}{2}$$

(9)

If $\beta >> 1$, we have $JS = (1 + \frac{\Delta}{2}) \frac{\Delta}{\beta}$ which reveals that the $JS$ measure varies linearly with $\Delta$ ($= \beta p_j$), and it is independent of the condition whether $i < j$ or $i > j$.

In both the cases (case I and case II), $\sqrt{JS}$ behave symmetrically to the rising and falling part of the hemodynamic response curve (i.e., independent of the condition that $i < j$ or $i > j$). The accumulation with respect to $\sqrt{JS}$ rises linearly with $\Delta$ when $\beta$ is small and linearly with $\sqrt{\Delta}$ for a relatively large $\beta$ for a small $\alpha$. The behavior of the divergence is also independent of any assumption on the distribution.
3. Results

**Synthetic Images:** In order to establish the effectiveness of Jensen-Shannon divergence, we first considered synthetically generated random data. A random noise of amplitude in the range $[50 - 110]$ has been generated over a sequence of $80 \times 80$ images of sequence length 25 (thus the synthetic images are three dimensional $(x, y, t)$ instead of four-dimensional images in the fMRI). We then added synthetic activation to the random noisy images. Synthetic activation is generated by convolving a synthetic stimulus (which is a step function) with a hemodynamic response function (Figure 2) given as [5]

$$h(t) = \frac{(t/t_1)^{d_1} \exp(-(d_1/t_1)(t - t_1))}{c(t/t_2)^{d_2} \exp(-(d_2/t_2)(t - t_2))}$$

with five parameters $t_1, t_2, d_1, d_2,$ and $c.$

![Figure 2. Hemodynamic response in Equation (10).](image)

We added two synthetic activation at the $(x, y)$ locations $(30, 30)$ and $(50, 50).$ The starting and stopping time of the stimuli are $(3, 10)$ and $(10, 20)$ respectively. We considered two different types of hemodynamic response functions, one for the auditory cortex and the other for the motor cortex. The parameter values for auditory cortex are $t_1 = 5.4,$ $d_1 = 6,$ $t_2 = 10.8,$ $d_2 = 12,$ and $c = 0.35,$ and for motor cortex, $t_1 = 5.5,$ $d_1 = 5,$ $t_2 = 10.8,$ $d_2 = 12,$ and $c = 0.4$ [5]. Figure 3(a) - (d) illustrate the regions detected using the auditory cortex hemodynamic response function with stimulus amplitude 30, 40, 50, and 60 respectively. Figure 3(e) - (h) illustrate the same for motor cortex hemodynamic response function with same stimuli amplitude. Note that, in all cases we consider the stimulus amplitude to be much less than the noise amplitude in order to make a low signal-to-noise ratio.

**fMRI Images:** We considered the fMRI data from the fMRI data center [4] particularly the dataset used by Hirsch, Rodriguez, and Kim [7]. Each data set in this experiment, consists of sequences of $128 \times 128$ images with sequence length 21 over 36 time frames. In the experiment by Hirsch et al. [7], subjects performed three cognitive tasks namely, object naming, integer computation and same-different discrimination. We considered fMRI images for the first task i.e., object naming. As mentioned by Hirsch et al. [7], the brain areas involved in the object-naming task (object-naming subsystem) are left inferior frontal gyrus (Brodmann’s areas 44 and 45), left superior temporal gyrus (Brodmann area 22) and left medial frontal gyrus (Brodmann Area 6). Figure 4 illustrates the results obtained by our algorithm using the Jensen-Shannon divergence (with an window size $7 \times 7 \times 5$). The left panel of each pair ((a1), (b1), (c1), (d1), (e1), and (f1)) shows the regions of activity detected by our algorithm, and the right panel ((a2), (b2), (c2), (d2), (e2), and (f2)) shows that by t-test as provided in [4]. We observe that our algorithm is more effective in localizing the areas of neural activities as compared to the t-test. We compute the difference in gray value distribution over successive time frames based on the window location. Therefore, due to the effect of blocking, certain activities are detected outside the brain region (liquor and the CSF around the brain). This can be eliminated by restricting the activity to be detected within the brain region. The brain region can be obtained by segmenting the brain images.

**4. Discussion and Scope of Future Study**

We presented a statistical technique based on Jensen-Shannon divergence for detecting the regions of activity in fMRI images. We exploited the metric property of the square root of Jensen-Shannon divergence to accumulate the variations between successive time frames of fMRI images. Use of Jensen-Shannon divergence makes our algorithm independent of the assumption of any statistical distribution. Jensen-Shannon divergence has been used in the context of image segmentation [1] before, but the use of the same in spatio-temporal data analysis has not been explored, and fMRI is one such example. In the proposed method, we consider a window around each voxel in a $M \times N \times L$ (say) image and compute statistics over $T$ such time frames. Since the computation of $\sqrt{JS}$ metric is linear in time with the number of voxels (considering a fixed number of bins in the histogram) in a window, the overall computation requires $O(MNLTW^2h)$ time where the size of the window is $W \times W \times h.$ Using a sliding window computation of
the histograms, the overall complexity can be reduced to $O(MNLT_w^2)$ time. We do not address the issues of false activity detection due to the improper registration in this article. This can be pursued as one of the future work. We compared our results with that of t-test (as a statistical significance test). There are more elegant techniques for neural activity detection in fMRI, such as clustering. In clustering based techniques, often the detection of regions is fine tuned after identifying the activated voxels (detecting changes in the intensity level). The performance of the present algorithm can also be improved by performing clustering on the accumulator values [9] instead of just thresholding with a pre-defined threshold.

References


