Utilizing Baseline and Differential Information to Improve FMRI Brain Activation

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Abstract

The practice in fMRI brain imaging is to determine brain activation within a voxel by way of a statistically significant increase in the BOLD signal from baseline due to task performance. This practice ignores valuable information at hand within the voxel about the tissue type contained in the same data. The baseline signal intensity within a voxel indicates the tissue type contained within it. In this work, methods will be explored to utilize both baseline anatomical and differential functional information to determine brain activation.

Key Words: FMRI, Bayesian, activation, baseline

1. Introduction

In fMRI, a subject is placed in the MRI machine and volume images of their brain is scanned at n time points while they are generally performing a experimentally designed cognitive task. In the early 1990's, fMRI (functional magnetic resonance imaging) was developed as a technique to noninvasively observe the human brain in action (1). FMRI is based upon the BOLD (blood oxygen level dependent contrast) in which blood oxygenation changes in the local vicinity of firing neurons (2). The practice in fMRI brain imaging is to determine brain activation within a voxel by way of a statistically significant increase in the BOLD signal.

Typically a general linear model is fit to each time series with independent variable being the expected voxel response from the experimental stimulus paradigm. From this general linear model, every voxel has an estimate of the contribution from the stimulus β_1 along with a corresponding t-statistic describing the degree of activation (change from baseline) within it. The t-statistics are thresholded (3,4) to separate true (biological) signal from noise (random variation/signal not of interest). Voxels with t-statistics above this threshold are superimposed upon a gray scale anatomical image to visualize their physical location.

However, it may be difficult to determine a useful threshold (3,4). If this threshold is determined to be too low, there are often many voxels retained that visually appear to be noise and not of biological origin. If this threshold is determined to be too low, then noise is eliminated, but true biologically active voxels may also be eliminated. From the general linear model, we also have an estimate of the baseline intensity level in β_0. We can have two voxels that have the same activation level, but different baselines. For this reason, the baseline voxel intensity level will be useful in determining voxels that are

active or statistically significantly related to the expected task response and contains grey matter within the voxel as indicated by β_0. Hence the need to utilize the bivariate *t*-distribution for the two coefficients and a wedge of it for significance.

2. Differential Activation

In each voxel, we observe n, data points, $(x_1,y_1),\ldots,(x_n,y_n)$ and determine a statistically significant relationship between x (task design) an y (observed voxel value) as

$$y_t = \beta_0 + \beta_1 x_t + \varepsilon_t \,, \qquad [1]$$

where the errors have been specified to be independent normally distributed with a mean of zero and constant variance, $\varepsilon_t \sim N(0,\sigma^2)$ for $t=1,\ldots,n$. In each voxel, regression coefficients of Equation 1 are estimated as

$$\hat{\beta} = (X'X)^{-1}X'y \,. \qquad [2]$$

In Equation 2, X is the $n\times q$ design matrix with first column of n ones and second column of the n x_t values, y is a column vector of the n y_t values, and β is a 2×1 vector containing the baseline (y-intercept) and activation (slope) coefficients.

The practice in fMRI brain imaging is to determine brain activation within a voxel by way of a statistically significant increase in the BOLD signal from baseline using Equation 3. The *t*-statistic for the activation coefficient is computed,

$$t_1 = \frac{\hat{\beta}_1}{SE(\hat{\beta}_1)} \qquad [3]$$

where $SE(\hat{\beta}_1)=s\sqrt{w_{22}}$ and $W=(X'X)^{-1}=[\, w_{11},\ w_{12};\ w_{21},\ w_{22}]$. Smilarly, a *t*-statistic for β_0, t_0 can also be calculated.

Data from a technology development fMRI study (5) is used to illustrate the practice. The data uses a unilateral right hand finger tapping experiment in which $n_z=7$ axial slices are measured, each slice is an $n_y\times n_x$ array, where $n_y=n_x=96$ and there were $n=490$ time points used for analysis. An example time series (blue) from a task related voxel along with the task on/off timing (dashed grey) and design matrix second column (red) is presented in Figure 1.

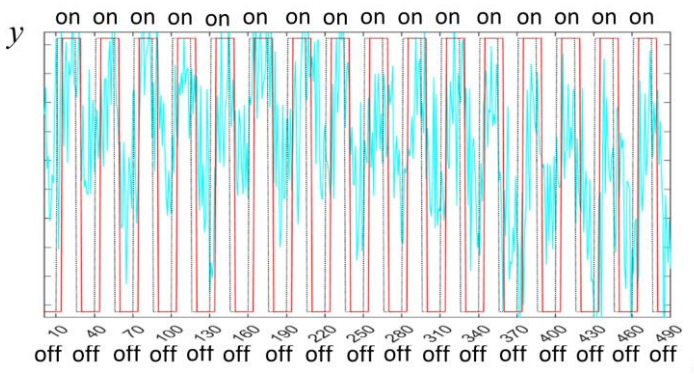

Figure 1: Example voxel time series with task timing and task design.

The *t*-statistic for each voxel within the slices is presented voxels are numbered from 1 to 7 in Figure 1 in superior to inferior order from left to right and top to bottom. Every voxel has a *t*-statistic describing the degree of activation (change from baseline) in it. With every voxel colored according to its *t*-statistic activation level, it is difficult to see detailed locations of activation.

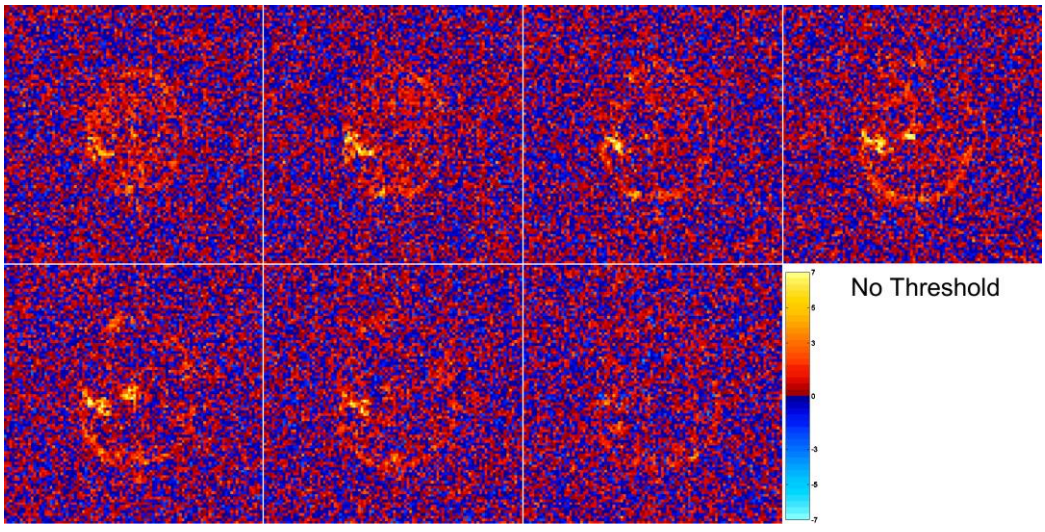

Figure 2: Task activation *t*-statistics in each voxel from β_1.

A histogram of these t_0 and t_1 statistics can be formed as illustrated in Figure 3 (left). The practice is to set a critical *t*-statistics level t_{1c} for t_1, as illustrated in Figure 3 (middle), such that those voxels with *t*-statistics above this level (and below $-t_{1c}$) are retained and those voxels with *t*-statistics below are assigned the anatomical grey value. We threshold to separate true (biological) signal from noise (random variation/signal not of interest). As can be seen in Figure 3 (right),

an additional dimension is available to select voxels using t_0. This additional dimension for t_0 will be utilized later.

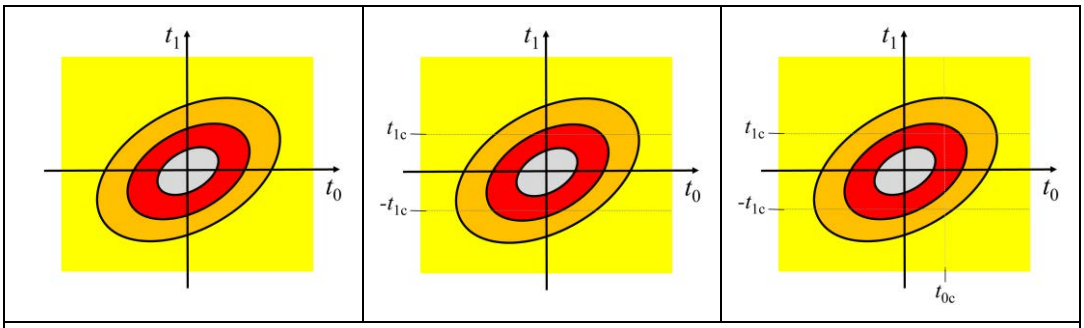

Figure 3: Joint contour illustration of t_0 and t_1 statistics.

The voxels for the n_z=7 slices in Figure 2 are again presented in Figure 4 but with an α=0.05 voxel threshold of t_{1c}=1.96. We can se in Figure 4 that there are many colored voxels being displayed, though mostly scattered throughout the image indicating the noise level. (Note that in Figure 4 only one dimension of *t*-statistics is being utilized in determining active voxels.)

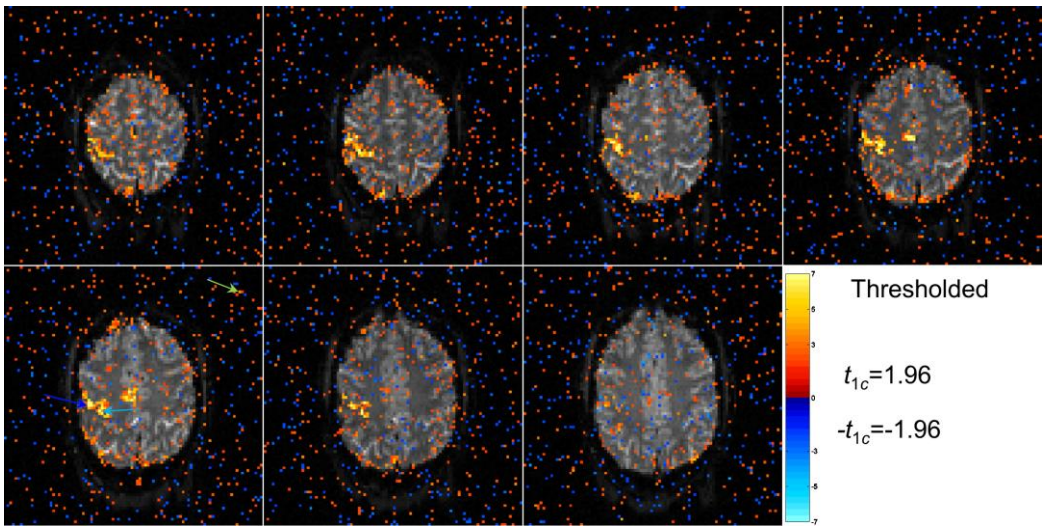

Figure 4: Thresholded task activation *t*-statistics in each voxel from β_1.

3. Baseline Information

If a low threshold is determined in Figure 4 based upon t_1 statistics, then there are often too many voxels displayed, or if a high threshold is determined, it may eliminate good voxels. It can be extremely difficult to determine a threshold and many researchers have spent years on the topic. Upon a more detailed examination of voxel statistics, we can see that there are voxels with large t_1 statistics, but extremely small t_0 statistics. An example of this phenomenon are the

green and blue voxels in slice 5 of Figure 4 indicated with arrows. The both indicated voxels are active, but the green one is outside the subject's brain and the blue one is inside. The time series for these two voxels are displayed in Figure 5 along with their statistics [$\hat{\beta}_0$, $\hat{\beta}_1$,SE($\hat{\beta}_1$),t_1]. Note that the two voxels have very similar t_1 activation statistics for $\hat{\beta}_1$, but drastically different $\hat{\beta}_0$ coefficients.

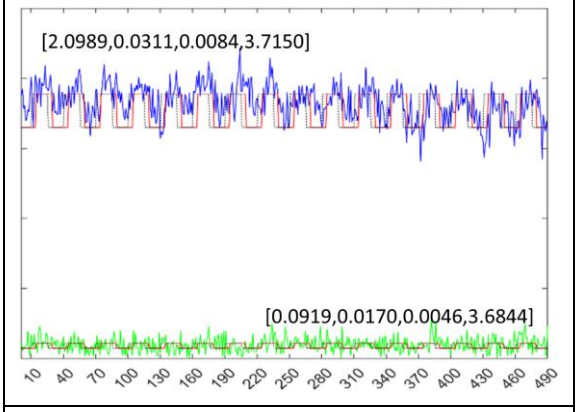

Figure 5: Example of two voxels with similar activation but different baselines.

It only makes sense to consider this baseline information that we already have in determining if a voxel is within the brain and thus should be active.

To visually see the potential information in the β_0 and β_1 regression coefficients, histograms of their estimated values are presented in Figure 6. We can see as indicated by the red ellipse in Figure 6 that there is a region of large β_1 activation

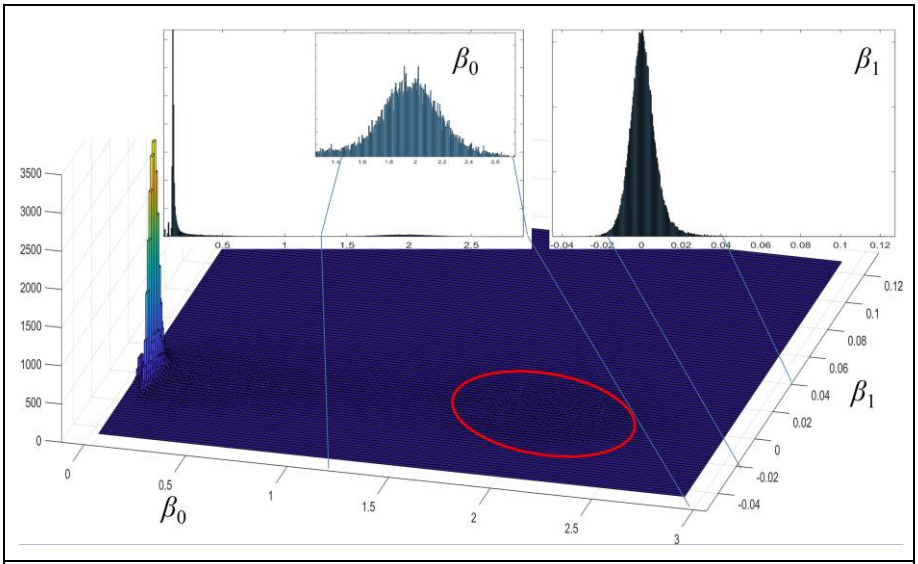

Figure 6: Histograms of estimated β_0 and β_1 coefficients.

coefficients that also have large β_0 baseline coefficients. However, we also need to consider their standard errors. In Figure 7, are histograms of the t_0 and t_1 statistics. It is evident that there is a region as indicated by the red ellipse of large t_1 statistics that also have large t_0 statistics. The large t_0 statistics indicate that the corresponding voxel is within the brain while the large t_1 statistic indicates that it is active.

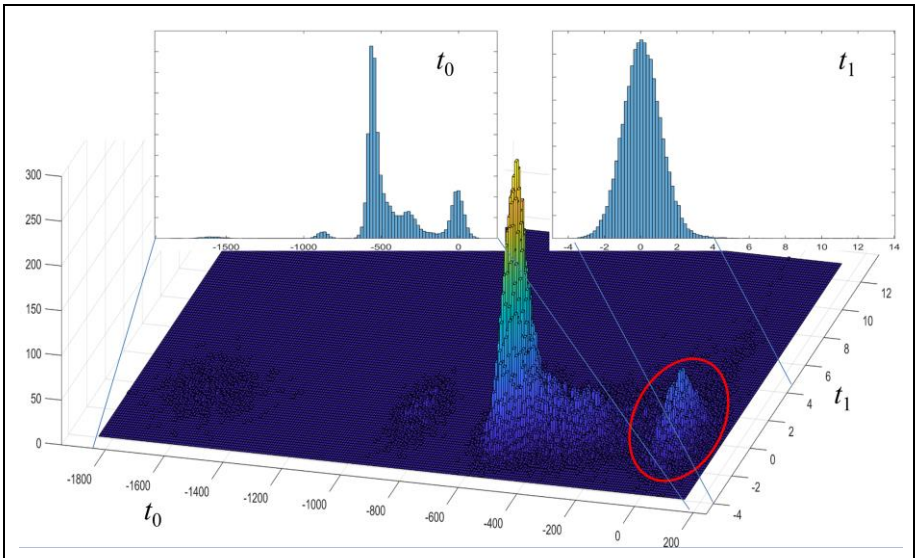

Figure 7: Histograms of estimated t_0 and t_1 statistics.

4. Results

As has been shown, there is useful information that can be applied when determining which voxels are active. In Figure 8 top left are histograms of the β_0 and t_0 statistics with activation map of t_0 statistics t_0>1.96 in lower left. In Figure 8 top middle are histograms of the β_1 and t_1 statistics with activation map of t_1 statistics $|t_1|$>1.96 in lower middle. Information from both statistics can be utilized. In Figure 8 top right is a heatmap of t_0 statistics on the horizontal axis and t_1 statistics on the vertical axis. Upon applying a combined t_0>1.96 and $|t_1|$>1.96 threshold, we can arrive at a much more meaningful activation map as seen in Figure 8 bottom right. Note the activation in the left motor cortex as well as supplementary motor area colored yellow in the lower right of Figure 8.

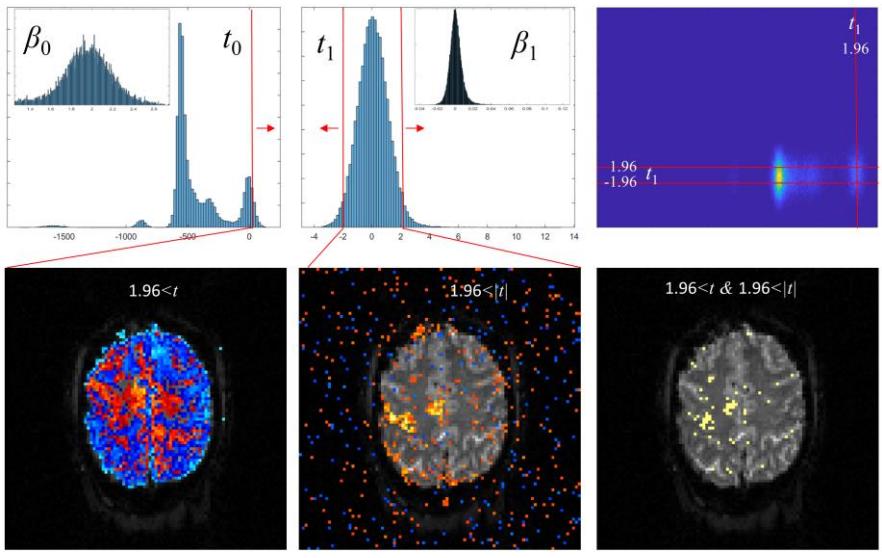

Figure 8: Activation map incorporating both t_0 and t_1 statistics.

5. Discussion

Baseline anatomical information was explored along with differential functional information to determine brain activation. Utilizing the baseline signal intensity which is a strong indicator of tissue type can assist in detecting activation in gray matter tissue and reduce false positives. By utilizing t-statistics for differential activation along with baseline intensity level, more accurate activation maps with less noise and improved interpretability can be derived.

References

1. Bandettini P, Jesmanowicz A, Wong E, Hyde JS. Processing strategies for time-course data sets in functional MRI of the human brain. Magn Reson Med 30:161–173, 1993.
2. Ogawa S, Lee TM, Nayak AS, Glynn P. Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. Magn Reson Med 14(1):68–78, 1990.
3. Logan BR, Rowe DB. An evaluation of thresholding techniques in fMRI analysis. Neuroimage 22(1):95–108, 2004.
4. Logan BR, Geliazkova MP, Rowe DB. An evaluation of spatial thresholding techniques in fMRI analysis. Hum Brain Mapp 29(12):1379–1389, 2008.
5. Karaman MM, Bruce IP, Rowe DB: A statistical fMRI model for differential T_2* contrast incorporating T_1 and T_2* of gray matter. Magn Reson Imaging, 32(1):9–27, 2014.