Conjunction Inference Using the Bayesian Interpretation of the Positive False Discovery Rate

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Abstract

Many neuroimaging studies use conjunction analyses to find brain regions with effects consistent across tasks. We find that SPM's minimum statistic inferences [1] are often misinterpreted and, in other work, we describe a simple method to make inferences on the "conjunction null" using the minimum statistic ([2] & Poster WE137).

In this work we describe a new method for conjunction inference that doesn't use the minimum statistic. We propose using Bayesian methods to compute the posterior probability of the conjunction null. In lieu of a full Bayesian model, we show how the Positive False Discovery Rate (pFDR) can be used to compute such a posterior probability. We describe the method and apply it to a conjunction analysis from an fMRI study of inhibition.

I. Introduction

Many neuroimaging studies look for brain regions where set of effects are all present, a *conjunction* of effects. For example, researchers may be interested in whether a brain region responds generally to tasks requiring attentional control, or whether the area is only activated in a subset of attentional tasks.

SPM99 and SPM2 use the minimum statistic for conjunction inference [1]. The minimum of, say, K statistics is computed and compared to the null hypothesis distribution of all K effects being absent. When the resulting P-values are significant, they are often misinterpreted to mean that all K effects are real. This is incorrect, as this test simply refutes the **global null** in favor of one or more effects being real. The **conjunction null**, in contrast, is one or more effects being absent, which is rejected in favor of the alternative of all effects being present. In other work, we show that to make inference on the conjunction null, one simply assesses the minimum statistic as if it were a single statistic (See [2] & WE 137).

In this work we propose a new method for conjunction inference *not* based on the minimum statistic. There are two components: First, we propose the use of Bayesian methods to make inference on the conjunction null. Such inference has the form of posterior probabilities, and is easily approximated by summing the K posterior probability maps of the null effects. Second, in lieu of a full Bayesian model, we show how the Positive False Discovery Rate (pFDR) can be used to compute the posterior probability of the conjunction null. We apply the method to a analysis of inhibition to demonstrate its utility.

II. Theory

Before defining the conjunction inference problem and our solution, we first introduce FDR & pFDR for a single statistic image.

II-A. False Discovery Rate (FDR)

Let T_i be the statistic at voxel i, and H_i denote the state of the null hypothesis at voxel i, $i = 1, \ldots, V$. $H_i = 0$ indicates the null is true, $H_i = 1$ that the null is false.

The False Discovery Rate (FDR) [3,4] is the fraction of false positives among suprathreshold voxels. Let $R(u)$ be the number of voxels above a threshold u (the number of rejections), and let $R_0(u)$ be the number of those voxels with true nulls (the number of false rejections). Then $R_0(u)/R(u)$ is the fraction of false positives, and FDR controls the expected value of this quantity:

$$\mathrm{FDR}(u) = \mathsf{E}\left(\frac{R_0(u)}{R(u)} I_{\{R(u)>0\}}\right), \tag{1}$$

where $I_{\{R(u)>0\}}$ defines the fraction as zero when $R(u) = 0$. There is an easy method, using only P-values, for finding a threshold u_α that controls FDR at α [3,4].

II-B. Positive False Discovery Rate (FDR)

The Positive False Discovery Rate (pFDR) [5] is a modified FDR measure. pFDR only considers the case when there is at least one detection. That is, it conditions on $\{R(u) > 0\}$,

$$\mathrm{pFDR}(u) = \mathsf{E}\left(\frac{R_0(u)}{R(u)} \middle| R(u) > 0\right). \tag{2}$$

pFDR has been described as "the rate at which discoveries are false." Note that FDR can also be written

$$\mathrm{FDR}(u) = \mathsf{E}\left(\frac{R_0(u)}{R(u)} \middle| R(u) > 0\right) \mathsf{P}\left(R(u) > 0\right) \tag{3}$$

showing that $\mathrm{pFDR}(u) \leq \mathrm{FDR}(u)$, and that estimates of pFDR can be found by dividing FDR by an estimate of $\mathsf{P}(R(u) > 0)$.

II-C. Bayesian Interpretation of pFDR

In a Bayesian approach the veracity of null hypothesis is a random variable. $\mathsf{P}(H_i = 0)$ is prior probability of the null at voxel i before observing any data, and $\mathsf{P}(H_i = 0|T_i = t_i)$ is the probability after observing t_i, the posterior probability.

pFDR has the following Bayesian interpretation. For voxel i thresholded at u,

$$\mathrm{pFDR}(u) = \mathsf{P}\left(H_i = 0 | T_i \geq u\right) \tag{4}$$

And if we observe statistic value t_i at voxel i, the pFDR P-value or **q-value** is

$$q_i = \mathrm{pFDR}(t_i) = \mathsf{P}\left(H_i = 0 | T_i \geq t_i\right). \tag{5}$$

Note that this is *exactly* the converse of a P-value computation; a P-value is P(Extremity of Data|Null), while the q-value is P(Null|Extremity of Data).

II-D. Controlling of Conjunction False Positives w/ pFDR

We first extend our notation to account for a set of K test statistics. Let T_i^k and H_i^k denote statistic and null hypothesis for test k, $k = 1, \ldots, K$, voxel i. We assume independence across tests; that is, that test statistics T_i^k and $T_i^{k'}$ are independent for $k \neq k'$. Dependence in space is not assumed.

A conjunction of effects at voxel i is $\cap_k \{H_i^k = 1\}$, and the **conjunction null** hypothesis is its complement $\mathcal{H}_i = \bigcup_k \{H_i^k = 0\}$. Compare this with the **global null** hypothesis $\bigcap_k \{H_i^k = 0\}$, that all K tests are null.

The natural Bayesian approach to conjunction inference is to assess posterior probability of $\mathcal{H}_i$, $\mathsf{P}(\mathcal{H}_i | T_i^k = t_i^k,\ k = 1, \ldots, K)$. If these posterior probabilities are not available, we propose instead controlling the pFDR-equivalent quantity, $\mathsf{P}(\mathcal{H}_i | T_i^k \geq t_i^k,\ k = 1, \ldots, K)$. For either approach, this probability can be conveniently bounded. For pFDR,

$$\begin{aligned}
\mathsf{P}\left(\mathcal{H}_i \middle| \bigcap_{k=1}^K \{T_i^k \geq t_i^k\}\right) &= \mathsf{P}\left(\bigcup_{k=1}^K \{H_i^k = 0\} \middle| \bigcap_{k=1}^K \{T_i^k \geq t_i^k\}\right) \\
&\leq \sum_k \mathsf{P}\left(H_i^k = 0 \middle| \bigcap_{k=1}^K \{T_i^k \geq t_i^k\}\right) \quad (6) \\
&= \sum_k \mathsf{P}\left(H_i^k = 0 \middle| T_i^k \geq t_i^k\right) \quad (7) \\
&= \sum_k q_i^k
\end{aligned}$$

where q_i^k is the pFDR q-value for test k, voxel i. The inequality (6) uses Bonferroni, which should not be so conservative since K is so small, and the subsequent equality (7) uses independence of the K tests.

III. Application

III-A. Real Data Details

From a fMRI study of inhibition we consider two tasks, a Go-No-Go and a Flanker task. In the Flanker task subjects were to respond to a central dot color, while two flanking dots of varying colors provided interference. 14 subjects were scanned and individual models were fit on each subject. The resulting intrasubject contrast images were submitted to two-separate second-level models, one for each task.

We compared the summed q-value method proposed here and the revised minimum statistic method (proposed in [2]) assess with pFDR; these two methods both make inference on the conjunction null with pFDR. The minimum statistic method used consisted of: creating the minimum of the two t statistic images, assessing the minimum as if it was as $t_1 3$ statistic, and finally transforming the resulting P-values into pFDR q-values.

III-B. Real Data Results

Consistent activation is detected in Anterior cingulate and insular regions (Figs. 1& 2), though the summed q-value method is more significant.

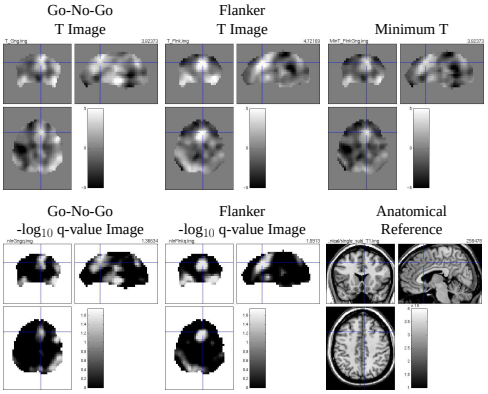

Figure 1: Inhibition data results for each task. The Go-No-Go and Flanker tasks both appeared to recruit anterior cingulate and insular regions.

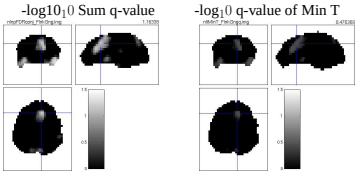

Figure 2: Inhibition data conjunction results. Both methods methods identify similar regions, but the summed q-value method is more sensitive. The summed q-value method had 5 voxels significant at 0.05 and 123 voxels at 0.1; the min statistic had no q-values below 0.1

IV. Conclusions

We have observed how easy conjunction inference is with Bayesian methods. Using pFDR, we can obtain Bayesian inferences without a full Bayesian model. Our one dataset and preliminary simulations (not shown) suggest that the summed q-value method is more sensitive than a corresponding minimum T method. A further challenge remains in how to relate these findings to a classical model, and back to the multiple comparisons framework of FDR.

References: [1] Friston *et al.*. NI 10:385-396, 1999. [2] Nichols *et al.*. Valid Conjunction Inference with the Minimum Statistic. In Preparation; draft available at `http:www.sph.umich.edu/~nichols/Conj`. See also poster WE 137. [3] Benjamini & Hochberg. JRSS-B, 57:289-300, 1995. [4] Genovese *et al.*. NI 15:870-878, 2002. [5] Storey. JRSS-B 64:479-498, 2002. [6] Wager et al. Common and unique components of response inhibition revealed by fMRI. In Submission