Detecting fMRI activation allowing for unknown latency of the hemodynamic response⋆

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Several authors have suggested allowing for unknown latency of the hemodynamic response by incorporation of hemodynamic derivative terms into the linear model for the statistical analysis of fMRI data [1,2]. We use random field theory to provide a P-value for local maxima of two test statistics that have been recently proposed for detecting activation based on this analysis [3,4].

Methods

Let $Y(t)$ be the pre-whitened fMRI data at time t, with pre-whitened stimulus $s(t)$, pre-whitened drift and other covariates $z(t)$, and hrf $h(t)$ with unknown delay or latency shift δ, modeled as

$$Y(t) = (s \star h)(t-\delta)\beta + z(t)\gamma + \epsilon(t) \approx x_1(t)\beta_1 + x_2(t)\beta_2 + z(t)\gamma + \epsilon(t)$$

where $x_1 = (s \star h)$, $x_2 = -(s \star \dot{h})$, $\star$ is convolution, dot is derivative, $\beta_1 = \beta$, $\beta_2 = \beta\delta$ and $\epsilon(t) \sim \mathrm{N}(0, \sigma^2)$ independently [1,2].

To detect activation allowing for unknown delay, the T statistic T_1 for β_1 is the best if there is no delay shift, but if there is delay shift then we will lose sensitivity. The F statistic F for both β_1 and β_2 is sensitive to any linear combination of the hrf and its derivative, but it will waste sensitivity on unrealistic linear combinations such as negative BOLD responses to the stimulus.

To overcome this, two alternatives have been proposed: a 'one-sided' F statistic F' that equals the usual F statistic F but which takes the value zero if the estimated β_1 is negative [3], and the cone T statistic T' for testing the regressor $x_1(t) + x_2(t)\delta$ for fixed δ, maximized over all values of $|\delta| < \Delta$ [4]. Approximate P-values of local maxima of these two test statistics, based on random field theory, are given below [5].

One-sided F statistic of Calhoun *et al.* (2004)

[3] considered the more general one-sided F statistic F' which equals the usual F statistic F with p, ν degrees of freedom but which takes the value zero if one of the p contrasts is negative. Let $Resels_d(S)$ be the d-dimensional resels of the search region S in D dimensions, and let $Resels_d^0(S)$ be the expected resels of the boundary where the contrast is zero, given by

$$Resels_d^0(S) = \sum_{i=0}^{\lfloor (D-d-1)/2 \rfloor} \frac{(-1)^i (4\log 2)^{i+\frac{1}{2}} \Gamma(i+\frac{1}{2}) \Gamma(\frac{d}{2}+i+1)}{2\pi^{i+1}\Gamma(i+1)\Gamma(\frac{d+1}{2})} \times Resels_{d+2i+1}(S).$$

The approximate P-value of local maxima of F' is

$$\mathrm{P}(\max_S F' \geq t) \approx \sum_{d=0}^{D} [\tfrac{1}{2} Resels_d(S)\ EC_d^p(t) + Resels_d^0(S)\ EC_d^{p-1}(tp/(p-1))],$$

where $EC_d^p(t)$ is the d-dimensional EC density of the F statistic F with p, ν degrees of freedom.

Cone T statistic of Friman *et al.* (2003)

The T statistic for β_j is $T_j = \widehat{\beta}_j / \widehat{\sigma}_j$, $j = 1, 2$, which has ν degrees of freedom. If c is the correlation between $\widehat{\beta}_1$ and $\widehat{\beta}_2$ then the cone angles are

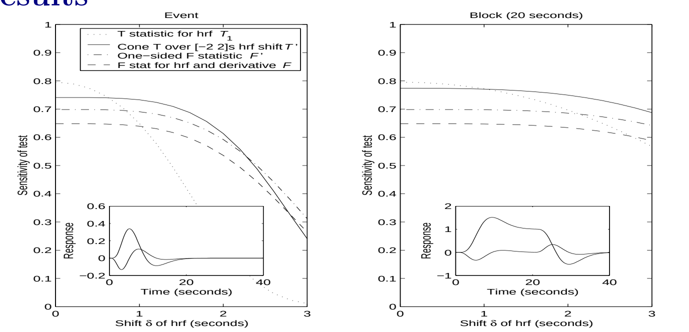
$$\Theta_1 = \arctan(\frac{-\Delta\widehat{\sigma}_2/\widehat{\sigma}_1 - c}{\sqrt{1-c^2}}), \qquad \Theta_2 = \arctan(\frac{\Delta\widehat{\sigma}_2/\widehat{\sigma}_1 - c}{\sqrt{1-c^2}}).$$

The resels of the cone C are $Resels_0(C) = 1$ and $Resels_1(C) = (4\log 2)^{-1/2}(\Theta_2 - \Theta_1)$. An approximate P-value of local maxima of the cone T statistic T' is

$$\mathrm{P}(\max_S T' \geq t) \approx \sum_{d=0}^{D} Resels_d(S) \sum_{k=0}^{1} Resels_k(C)(1+t^2/\nu)^{-k/2} EC_{d+k}(t),$$

where $EC_d(t)$ is the d-dimensional EC density of the T statistic T_1 with ν degrees of freedom.

Results

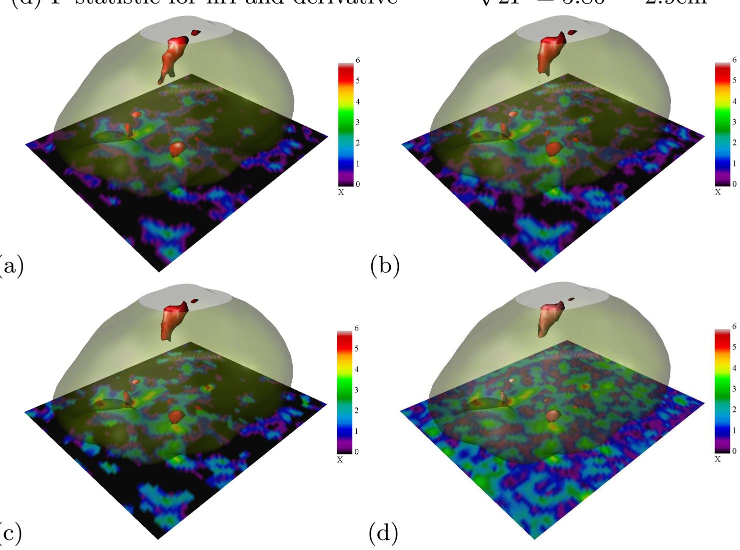


Sensitivities of the four tests at $P = 0.05$ as a function of the shift δ of the hrf for an event related design (left) and a block design (right). The responses and their derivatives are shown in the lower panels. For shifts less than ∼1s, the simple T statistic is the most sensitive, but for larger shifts the cone T statistic is the most sensitive. For very large shifts the one-sided F statistic is the most sensitive, but the simple F statistic is always the least sensitive. The same holds for the block design but the differences are less pronounced. Our overall recommendation is to use the simple T statistic if the shift in the hrf is less than 1s, and the cone T statistic if not.

Application

We applied the above test statistics to detecting a hot stimulus in a pain perception experiment with blocks of 9s hot and 9s warm stimuli, interspersed with 9s rest [6]. For a whole brain search of 1184cm^3 with an estimated 8.78mm FWHM average smoothing, the P=0.05 thresholds for the test statistics are (for a $\Delta = 2$s hrf shift range, the cone angle $\Theta_2 - \Theta_1$ was $60.9 \pm 1.7°$):

Statistic, transformed to equal expected	Threshold	Volume
(a) T statistic for hrf	$T_1 = 5.15$	4.0cm^3
(b) Cone T statistic	$T' = 5.44$	4.3cm^3
(c) One-sided F statistic	$\sqrt{2F'} = 5.63$	3.8cm^3
(d) F statistic for hrf and derivative	$\sqrt{2F} = 5.80$	2.9cm^3



(a) (b) (c) (d)

The four statistics thresholded inside the search region S are shown above. The volume of detected activation is roughly the same (Table, third column) but the cone T statistic T' in (b) detects the most activation (left primary somatosensory area and left and right thalamus).

References

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