Non-negative least-squares random field theory⋆

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We model imaging data at a voxel by a linear model with some or all coefficients constrained to be non-negative. The model is fitted by non-negative least-squares (NNLS) separately at every voxel. We wish to detect those voxels where the constrained coefficients are significantly positive. We present new random field theory results for finding the corrected P-value that allows us to detect such points. We apply these results to detecting activation in fMRI using a set of extreme HRF basis functions.

Methods

The linear model for image data at a single voxel is

$$\mathbf{Y} = \mathbf{X}\beta + \mathbf{Z}\gamma + \epsilon, \quad \epsilon \sim \mathrm{N}(0, \mathbf{C}\sigma^2)$$

where $\mathbf{Y}$ is an observation vector, $\mathbf{X}$ and $\mathbf{Z}$ are design matrices common to every voxel, β and γ are vectors of unknown coefficients, and ϵ is an error vector with unknown variance σ^2 but a known correlation structure $\mathbf{C}$ common to every voxel. Without loss of generality, we can assume that $\mathbf{C}$=$\mathbf{I}$, the identity matrix, by pre-whitening the model.

The important point is that $\beta \geq 0$ (component-wise) whereas γ is arbitrary. Fitting the model by NNLS is straightforward [1]:

1. Do all subsets regression on $\mathbf{X}$.
2. Amongst the submodels with $\beta > 0$, select the submodel with the least error sum of squares, SSE_1.

Let SSE_0 be the error sum of squares of the null model $H_0 : \beta = 0$ and let ν be its df. The NNLS test statistic of H_0 is

$$F_{\mathrm{NNLS}} = \frac{SSE_0 - SSE_1}{SSE_1/(\nu - 1)}.$$

The random field theory P-value of the F_{NNLS} SPM is [2]:

$$\mathbb{P}(\max F_{\mathrm{NNLS}} \geq t) = \sum_{j=1}^{\nu-1} p_j \mathbb{P}\left(\max F_{j,\nu-j} \geq t\frac{\nu - j}{j(\nu-1)}\right) + p_\nu.$$

The P-values on the RHS are the usual random field theory P-values for an F-statistic SPM with $(j, \nu - j)$ df. The weights are

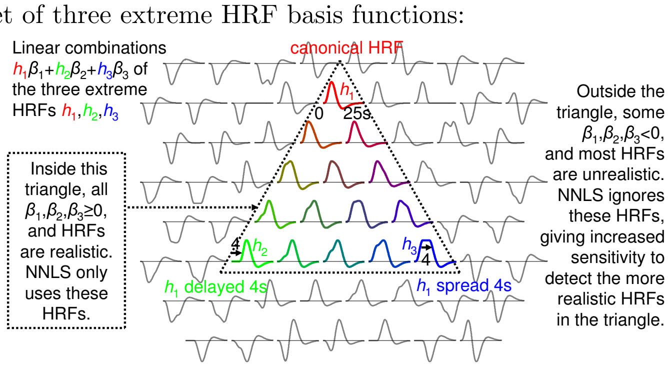
$$p_j = \mathbb{P}\left(\#\{\beta'\mathrm{s} > 0\} = j\right)$$

under H_0. In practice p_j is found by one simulation of Gaussian white noise under H_0, then averaging across voxels.

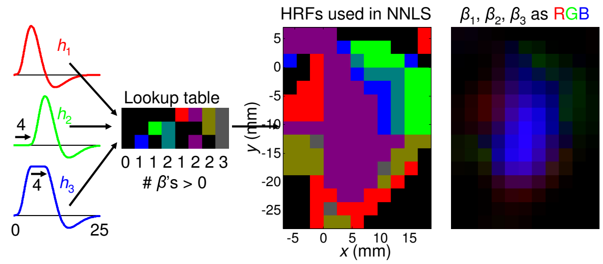
Surprisingly, it is possible to have far more regressors in $\mathbf{X}$ than observations! If these regressors are highly correlated then $\beta \geq 0$ forces $p_j \sim 0$ for large j. An example is the spectral method for fitting compartmental models to PET data.

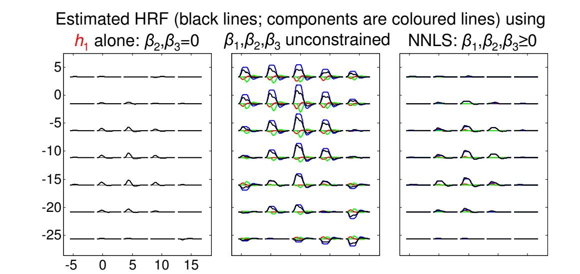
Results

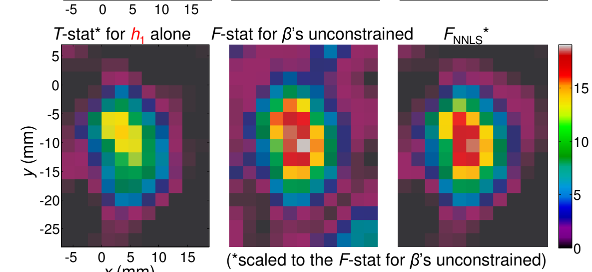
We apply these results to detecting activation in fMRI using a set of three extreme HRF basis functions:

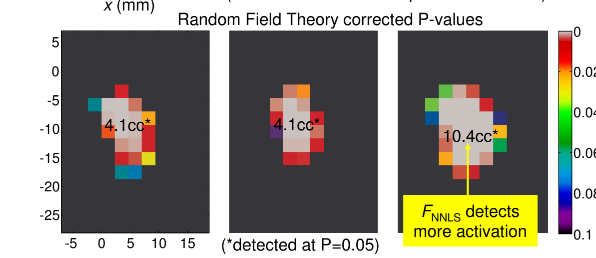


A subject received a 9s painful heat stimulus alternating with a 9s warm stimulus interspersed with 9s rest, repeated 10 times [3]. The three columns of $\mathbf{X}$ are the hot-warm stimuli convolved with the three extreme HRFs. The columns of Z are the hot+warm stimuli convolved with the three extreme HRFs and spline drift regressors. The null degrees of freedom is $\nu = 109$. The weights were: $p_1 = 0.498$, $p_2 = 0.141$, $p_3 = 0.003$. Results in a small part of a slice through the right supplementary motor area are shown in the following figures.









Conclusions

NNLS is more sensitive than either the T-statistic on the canonical HRF, or the F-statistic for the unconstrained model. The reason is that the T-statistic is not flexible enough to detect departures from the canonical HRF, whereas the unconstrained F-statistic is too flexible and wastes sensitivity on unrealistic (negative coefficient) HRFs.

References

[1] Lawson & Hanson (1974). *Solving Least Squares Problems.*

[2] Taylor & Worsley (2007). Detecting sparse cone alternatives for Gaussian random fields... *Annals of Statistics*, submitted.

[3] Worsley et al. (2002). *NeuroImage* **15**:1-15.

⋆#548 T-PM: poster at http://www.math.mcgill.ca/keith/fmristat/poster_nnls.pdf June 17, 2008