Assessing fMRI activation using maximum convolved correlation

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Overview

Common traditional approach:
Form a statistical map, estimate p-values based on standard general linear model/correlation.

For fMRI with faster sampling rates, it is sometimes necessary to model the haemodynamic response with various filters [1]. Usually the filter parameters are estimated *on the same data*, hence an optimistic bias.

The test statistic is artificially high because the parameters are identified such that the corresponding filter correlates well with the data!

$\Longrightarrow$ increased false positives.
Bias increases even more when parameters are estimated locally (eg in each voxel).

> 1. We propose to investigate the correlation over a whole range of parameter values.

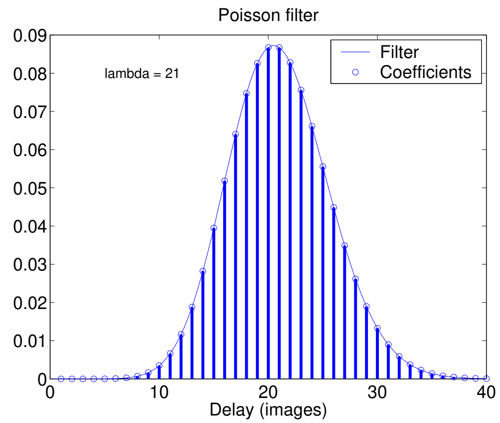
> 2. The distribution under the null hypothesis is estimated using Monte Carlo sampling.

- ⋆ Parameters can be estimated locally,
- ⋆ Significance levels stay correct,
- ⋆ Extends to filters with many parameters.

We evaluate and compare the methods on data containing noise, and on a fMRI experiment involving visual stimulation.

Convolution and correlation

Stimulus $p(t)$, T images $1 < t < T$.
Signal $f(t, x, y, z)$ measured in (x, y, z).
Filter $h_w(t)$ parameterised by w.
Eg: Poisson (λ), Delay (d), Gaussian(μ, σ), Gamma (α, β), FIR (w_i) ...



Convolution of the stimulus:

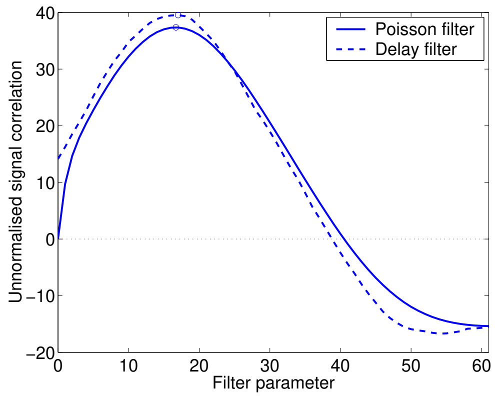
$$r_w(t) = \sum_{\tau=0}^{+\infty} p(t-\tau) h_w(\tau)$$

Un-normalised signal correlation:

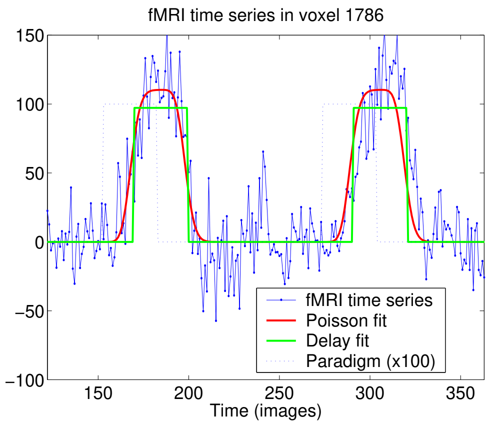
$$c_w(x, y, z) = \frac{1}{T} \sum_{t=1}^{T} f(t, x, y, z) r_w(t)$$

Note: $c_w(x, y, z)$ *not* correlation coefficient.

For each value of $w \to$ corresponding c_w.



The maximum correlation (o) corresponds to the best fit:



Usually: use best fit to identify parameters. Reference and correlation come from *same data*
$\Longrightarrow$ correlation biased upwards.

Estimating the p-value

Statistic: the maximum correlation M

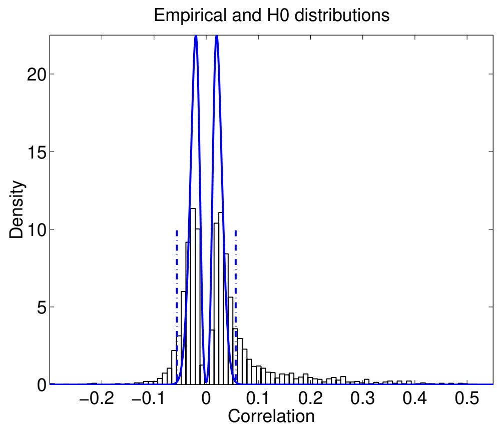
$$M(x, y, z) = \max_w c_w(x, y, z)$$

H0: no signal, only zero mean Gaussian noise.

When noise is Gaussian $\mathcal{N}(0, \mathbf{\Sigma})$, the convolved signal is also Gaussian, with covariance $\mathbf{R\Sigma R}^\top$, ($\mathbf{R}$ contains h_w's, see [2]).
$\Longrightarrow$ The distribution under H0 can be estimated using Monte Carlo.

Monte Carlo:

1. sample N data from $\mathcal{N}(0, \mathbf{R\Sigma R}^\top)$
2. estimate the relevant quantiles of M under H0 (eg $q_{.99}$ for 1% significance)
3. assess significance of measured M



Experiments

We compare:

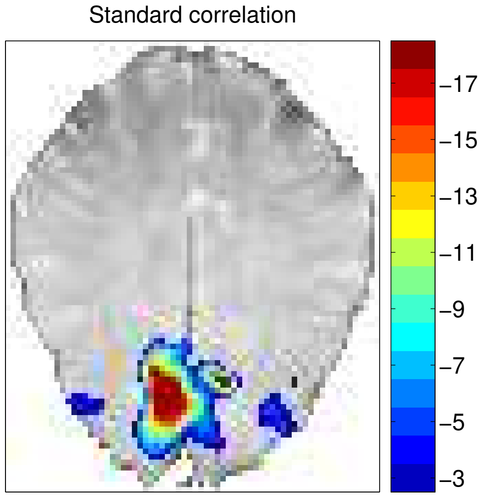
1. Standard correlation analysis,
2. Correlation analysis with a global filter estimated on the data,
3. Correlation analysis with local filters estimated in each voxel,
4. The maximum convolved correlation with Monte Carlo estimation of p.

Test: a brain template with Gaussian noise.
Amount of false positives:
(with (D)elay or (P)oisson filter)

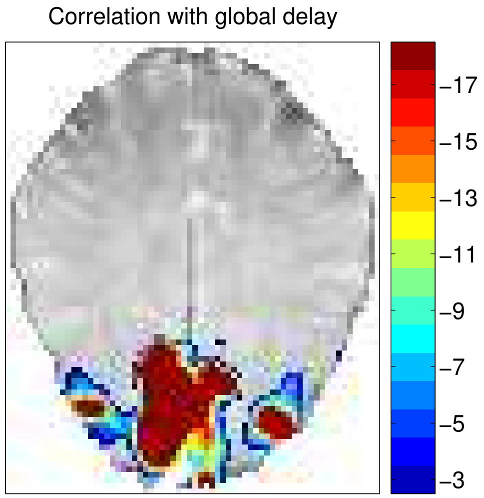
	$p < .01$	$p < .001$
Theory	39 ± 12	4 ± 3
Standard	48	3
Global(D)	38	3
Global(P)	48	3
Local(D)	308	39
Local(P)	155	16
Max C.C.	40	3

Global method gives roughly right amount as bias is very small.
Local estimation grossly exaggerates the activation.
The p-values estimated using Monte Carlo on the maximum convolved correlation yield the expected amount of false positives.
When the statistical map is smoothed, no false positive remains.

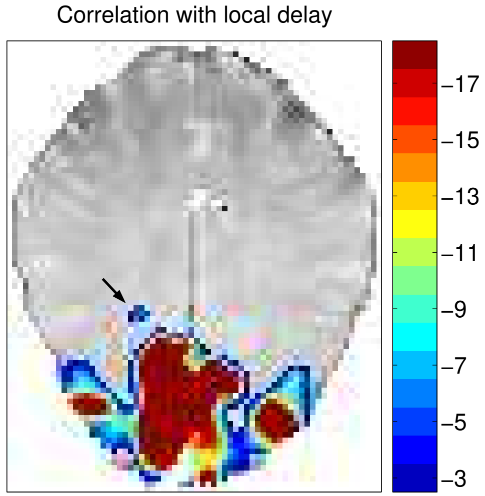
Comparison on real data:
Statistical maps are smoothed with a Gaussian kernel of bandwidth 1 voxel.



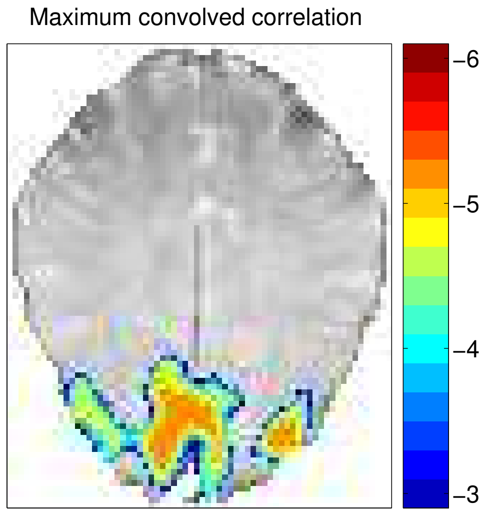
Map of (log) probabilities obtained from standard correlation analysis (or equivalent t-test).
Delay $\Longrightarrow$ underestimates the activation.



Map of (log) probabilities obtained from correlation analysis with delayed paradigm.
The global delay of 15 images (5s) is common to all voxels.



When the delay is estimated for each voxel, the optimistic bias increases. The activated region is overestimated and some artifactual clusters of activation can appear by chance (arrow), *even when the statistical map is smooothed.*



Note different scale because of size of Monte Carlo sample, but same threshold: $p < 10^{-3}$.
We use $N = 100000$ Monte Carlo sample, so $p_{min} = 5.10^{-6}$.

Data

The data has been acquired at Hvidovre Hospital on a 1.5T Magnetom Vision MR scanner:

subjects : single subject.
task : visual stimulation with a full-field checker board reversing at 8 Hz during activation.
modality : 1.5T EPI ($T2^*$ weighted)
paradigm : 60-30-60 images (first 29 removed).
 # runs : 10.
frequency : 3 images/second.
location : para-axial orientation parallel to calcarine sulcus.
slice : 128x128 voxels.
FOV : 230 mm.
ROI : 82x68 voxels.
voxel size : 1.8x1.8x8mm.

References

1. Friston, Jezzard, Turner, *Human Brain Mapping*, 1:153-174, 1994.
2. Goutte, Toft et al., *NeuroImage*, 9:298-310, 1999.