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Structural adaptive smoothing methods for fMRI and its implementation in R

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Functional Magnetic Resonance Imaging (fMRI) has become the most informative tool for in-vivo examination of human brain function on small spatial scales. As fMRI suffers from low signal to noise ratio (SNR) noise reduction forms an inherent step in the analysis of fMRI experiments. Smoothing by Gaussian filter increases SNR, reduces the number of independent decisions, relaxes the severe multiple test problem and leads to a situation where critical values for signal detection can be assigned using Random Field Theory (RFT). The inherent blurring effect can be ignored as long as the precise shape and extent of the activation area is not important. However, as experiments become more and more sophisticated and explore e.g. columnar functional structures in the brain or functions near brain lesions, adaptive noise reduction methods become essential.

Preprocessing

- Registration
- Normalization

GLM

- Pre-whitening
- $Y = X\beta + \varepsilon$

Smoothing

- Gaussian filter
- Adaptive!

Signal detection

- RFT
- FDR

- In GLM approach, smoothing has twofold effect: increasing SNR and reducing the number of independent tests for the multiple test problem. Gaussian filter and GLM can be interchanged.
- For adaptive approaches described here, smoothing is not considered a preprocessing step, but the GLM a dimension reduction step for the high-dimensional data.
- Alternative approaches (without GLM): CCA, ARF, ICA, ...

Structural adaptive smoothing

Workflow:

- Linear modeling / parameter estimation
- Structural adaptive smoothing of parameters or contrasts
- Signal detection / thresholding by Random Field Theory
- Under Null hypotheses (no activation) the smoothing creates approximately a Gaussian Random Field

Algorithm:

- Initialization: $\theta_i = \gamma_i$ - contrast from linear model, scale $h_1, k = 1$.
- Generate weighting scheme $\forall i, j$

$$w_{ij} = K_s\left(\frac{\mathscr{K}(\theta_j, \theta_i)}{\lambda \sigma_i^2}\right) K_l\left(\frac{|i-j|}{h_k}\right)$$

- Compute new (smoothed) parameter estimates

$$\theta_i = \frac{\sum_j w_{ij}\gamma_i}{\sum_j w_{ij}}$$

- Iterate: $k := k+1$, $h_k = c_h h_{k-1}$.
  If $h_k > h_{max}$ stop, else continue with second step.

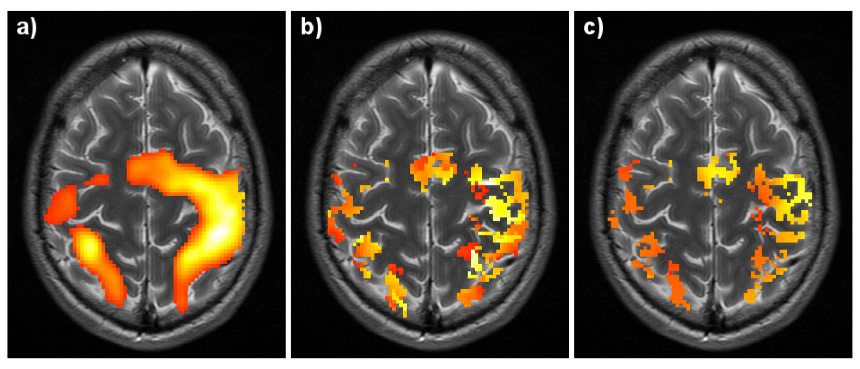

Figure 1: *Signal detection in the package fmri using different smoothing methods (multiple test corrected $p = 0.05$): a) signal detection using Gaussian smoothing, b) signal detection using structural adaptive smoothing with signal detection by random field theory, c) results using structural adaptive segmentation. Since the algorithm provides only two segments (activation/no-activation) additional information can be overlayed in color (here estimated BOLD)*

Structural adaptive segmentation

Advantages

- combines smoothing and signal detection in one step
- provides sequential multiscale test for signals exceeding a minimal size
- does not rely on a local constant assumption under the alternative
- provides a multiscale test

$$T(\Gamma) = \max_{h \in \mathscr{H}} \max_{i \in V} \frac{\theta_i^{(h)} - \delta}{a_{n(h)}\sqrt{\mathbf{D}\theta_i^{(h)}}} - \frac{b_{n(h)}}{a_{n(h)}}$$

Algorithm

- Initialization: $\theta_i = \gamma_i$ - contrast from linear model, scale h_0, $k = 1$,
  $\zeta_i = 0$ - initial segmentation
- Generate weighting scheme w_{ij} $\forall i, j$, adaptive if $any(\zeta_i, \zeta_j) = 0$, else nonadaptive.
- Compute new (smoothed) parameter estimates
- If $\frac{\theta_i^{(h_k)} - \delta}{a_{n(h_k)}\sqrt{\mathbf{D}\theta_i^{(h_k)}}} - \frac{b_{n(h_k)}}{a_{n(h_k)}} > \tau$ set $\zeta_i = 1$.
- Iterate: $k := k+1$, $h_k = c_h h_{k-1}$.
  If $h_k > h_{max}$ stop, else continue with second step.

- Structural adaptive smoothing increases sensitivity, while preserving shape of activation areas.
- 3D method
- Better grey matter alignment of activation area (no cortex based method!!)
- Suited for columnar functional structure (ODC)? Simulations show YES!

Implementation of structural adaptation for fMRI in R

The rapid progress of research in the neuroscience and neuroimaging fields has been accompanied by the development of many excellent analysis software tools. These are implemented in a variety of computer languages and programming environments, such as Matlab, IDL, Python, C/C++ and others. This variety has been developed over time through a combination of user preferences and the strengths/weaknesses of the computing environments. We present our implementation in the R Statistical Language.

R: A Language and Environment for Statistical Computing

Package: fmri

- Open-source, free of charge
- Easy to install
- Easy to use
- Full pipeline: I/O, GLM, structural adaptive smoothing, signal detection, publication images

Example Code for Single Run Blockdesign

```
R> library(fmri)
R> ds <- read.NIFTI("Imagination.nii")
R> scans <- 105
R> onsets <- c(16, 46, 76)
R> duration <- 15
R> tr <- 2
R> hrf <- fmri.stimulus(scans, onsets, duration, tr)
R> x <- fmri.design(hrf)
R> spm <- fmri.lm(ds, x)
R> spm.segment <- fmri.smooth(spm, hmax = 4, adaptation = ßegment")
R> ds.ana <- read.NIFTI("MPRAGEco.nii")
R> plot(spm.segment, ds.ana, slice = 13)
```

Conclusions

- Structural adaptive smoothing may enhance sensitivity of signal detection in fMRI analysis without blurring activation areas.
- The implementation of the methods in the R-package **fmri** allows for an easy analysis from linear modeling to signal detection and publication quality images.
- Growing number of tools written in R to provide more features.

Further reading

Structural adaptive methods in fMRI

- K. Tabelow, J. Polzehl, H.U. Voss, V. Spokoiny (2006), 'Analyzing fMRI experiments with structural adaptive smoothing procedures', *NeuroImage*, vol. 33, pp. 55–62. (Original PS method)
- K. Tabelow, V. Piëch, J. Polzehl, H.U. Voss (2009), 'High-resolution fMRI: Overcoming the signal-to-noise problem', *J. Neurosci. Meth.*, vol. 178, pp. 357–365. (Application to high-resolution fMRI)
- J. Polzehl, H.U. Voss, K. Tabelow (2010), 'Structural adaptive segmentation for statistical parametric mapping', *NeuroImage*, vol. 52, pp. 515–523. (Extended Segmentation method)

Implementation in R: Package **fmri**

- K. Tabelow, J. Polzehl (2010), 'Statistical parametric maps for functional MRI experiments in R: The package fmri', WIAS-Preprint no. 1562. (Explaining the usage of the package)
- Download: `http://cran.r-project.org/web/packages/fmri/index.html`

Medical imaging in R

- K. Tabelow, J.D. Clayden, P. Lafaye DE Micheaux, J. Polzehl, V.J. Schmid, B. Whitcher (2011), 'Image analysis and statistical inference in neuroimaging with R', *NeuroImage*, vol. 55, pp. 1686–1693.
- `http://cran.r-project.org/web/views/MedicalImaging.html`
- Upcoming Special issue of *Journal of Statistical Software* 'Magnetic Resonance Imaging in R', scheduled August 2011, `http://www.jstatsoft.org`
- See poster **#365-WTh** 'Performing tasks in Medical Imaging with R'

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