Wavelet methods for enhanced false discovery rate control in functional brain mapping

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Introduction

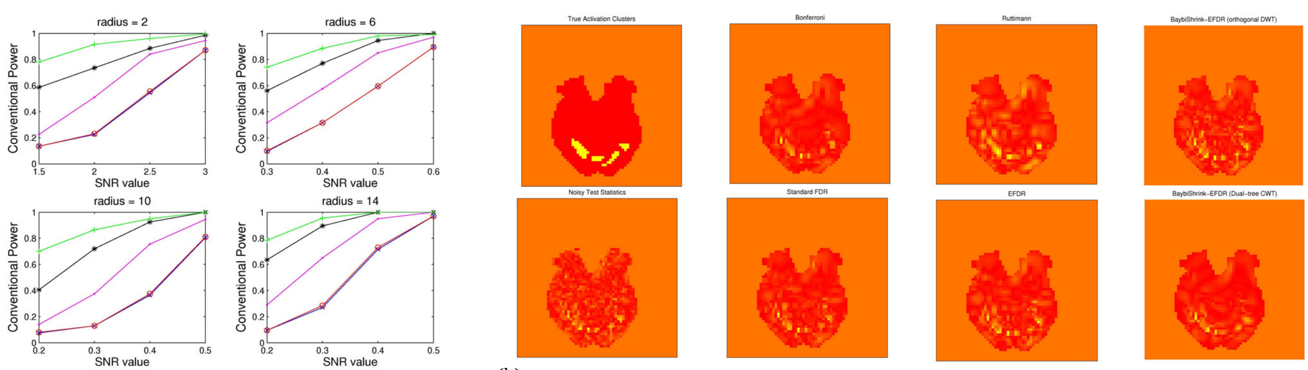
The detection of signals based on noisy observations is a problem common to many real-life image processing situations. Neuroimaging is specifically concerned with the detection of spatially extended brain activation based on two- or three-dimensional maps of statistics estimated by linear modeling of functional magnetic resonance imaging (fMRI) time series. The combination of low signal-to-noise, small numbers of subjects, and stringent criteria for significance is a recipe for type 2 (false negative) error. We can formalise this problem in terms of the number of null hypotheses H_{0i} and alternative hypotheses H_{ai} ($i = 1,2,\ldots,\mathbf{V}$) where the search volume, or number of hypotheses to be tested, **V** is typically in the order of 10^4. In the context of multiple comparisons, the conventional voxel threshold for refuting an individual null hypothesis $\alpha = 0.05$ is liable to yield a large number of false positives. In response to this, we have developed an alternative algorithm for wavelet-based hypothesis testing of fMRI statistic maps that adopt a two-stage approach. Our method improves on previous hypothesis testing procedures [1,2].

Methods

Ruttimann's method [1] can be rewritten more generally as a two-stage testing procedure where the total number of hypotheses tested **V** is first reduced by a preliminary thresholding operation in the wavelet domain; then the smaller subset of surviving coefficients **V*** < **V** is tested in a way which controls the family-wise error rate (FWER) or the false discovery rate (FDR) over all **V*** tests. Finally, the signal is reconstructed in the spatial domain by the inverse wavelet transform using only those coefficients which survive both tests (all other coefficients being set to zero). Shen's method [2], called the *enhanced* false discovery rate (EFDR) algorithm, is another two-stage testing procedure that differs from [1]. In the first stage of Shen's algorithm, generalized degrees of freedom is used to produce a reduced subset of wavelet coefficients. In the second stage, the statistic of interest is influenced by the local neighborhood around each wavelet coefficient rather than treating each coefficient in isolation. The threshold of significance for each test was set such that the FDR was 0.05. We improve on these methods by, first, replacing the orthogonal discrete wavelet transform (DWT) with the dual-tree complex wavelet transform (CWT) [3]. The dual-tree CWT is a wavelet frame obtained by concatenating two wavelet bases. The coefficients of the transform are estimated by two wavelet filter banks or "trees" operating iteratively in parallel; one wavelet basis is approximately the Hilbert transform of the other. Second, bivariate Bayesian shrinkage [4] is used to discard wavelet coefficients prior to implementing formal hypothesis testing. This new shrinkage function, which depends on both the wavelet coefficient and its parent, yields improved results when compared with standard wavelet-based image denoising methods. Our first set of simulated data is identical to that previously reported in [2]. A disc of signal with radius **r** and intensity **h** is embedded in a 64x64 matrix of i.i.d. Gaussian noise; the SNR of the simulations varied as a function of **h**. The second set of data is based on a realistic simulation of both signal and noise structure. A simple periodic signal was placed in geometrically irregular regions of differing size and embedded in a 2D section of real fMRI noise, correlated in time, obtained from an fMRI dataset of a single human subject lying "at rest". The strength of activation was estimated by fitting a general linear model at each voxel, using autoregressive least squares to account for the fMRI noise (Fig. 1b).

Results

Performance of the algorithms in detecting the simulated discs was quantified in terms of conventional power (Fig. 1a); i.e., the number of null hypotheses rejected divided by the number of true positive tests. Increasing SNR was predictably associated with increasing power for signals of all sizes. The Bonferroni and classical FDR algorithms had very similar (relatively low) power to detect signals compared to all two-stage algorithms. Shen's algorithm was consistently more powerful than Ruttiman's algorithm; our new method, incorporating Bayesian bivariate shrinkage (BaybiShrink), was the most sensitive method overall, incrementally more powerful than Shen's algorithm especially at low SNR. Maps of noisy *t*-statistics from the second set of simulated data (Fig. 1b) were tested for significance using the five methods previously mentioned. The BaybiShrink method, using the dual-tree CWT, provides the best balance between sensitivity (similar to that of Ruttiman's method) but at the same time controlling specificity (similar to that of the Bonferroni method).



(a) (b)

Figure 1: *(a) Conventional power curves of noisy signals with variable radius and SNR using Bonferroni (blue), standard FDR (red), Ruttimann's (pink), Shen's (black), and BaybiShrink-FDR (green) algorithms. (b) A set of activated voxels embedded in real fMRI noise, where the signal was recovered by various multiple hypothesis testing algorithms including the BaybiShrink algorithm implemented using the dual-tree CWT (lower right).*

Discussion

The multiple-hypothesis testing procedure for fMRI activation proposed here provides improved power while still controlling the family-wise error rate (or FDR) by reducing the number of hypotheses to test via wavelet denoising. Improvements on previous algorithms are achieved by utilizing the dual-tree complex wavelet transform to represent two-dimensional structures more efficiently and then applying a computationally efficient bivariate Bayesian shrinkage procedure which takes advantage of the interscale dependencies of the wavelet coefficients.

References

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