ANATOMICALLY ADAPTED WAVELETS FOR INTEGRATED STATISTICAL ANALYSIS OF FMRI DATA

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ABSTRACT

Wavelets have been successfully used in statistical analysis of fMRI data as a spatial transform providing a compact representation of brain activation maps. However, conventional (tensor-product) wavelet transforms assume a rectangular domain, while the essential brain activity takes place in the convoluted gray-matter layer. We use the lifting scheme to design wavelet bases for more arbitrary domains which do not have a group structure. In particular, we have considered the grey-matter cortical layer as the domain. We then applied the new transform to fMRI data using the wavelet-based SPM (WSPM) framework. Preliminary results show that the adapted wavelets have superior performance in terms of sensitivity than the standard tensor-product wavelets, while having the same control over type-I error rate (specificity).

***Index Terms*—** fMRI, statistical analysis, wavelet design, lifting scheme

1. INTRODUCTION

Functional magnetic resonance imaging (fMRI) is a key modality in current neuroscience research. The detection of neuronal-related activity in data contaminated with high amounts of noise requires effective statistical methods. One of the widely used and recognized methods for fMRI analysis is statistical parametric mapping (SPM) [1]. In SPM, a key step is spatial prefiltering with a Gaussian window, as a means of reducing noise. Wavelet-based alternatives have been proposed, basically replacing the Gaussian filtering step with the spatial wavelet transform. The integrated wavelet-based framework (WSPM) involves thresholding in the wavelet domain, as a denoising step, followed by a thresholding in the spatial domain [2, 3, 4, 5]. Standard wavelets used in these methods are defined on rectangular domains, typically a square in two dimensions and a cube in three dimensions. On the other hand, the natural domain of the neural activity is the brain cortex, which is an intricately convoluted three dimensional domain. In this work, we will use the integrated wavelet based framework with a new kind of wavelet bases that are built to have the brain cortex as their natural domain [6].

Anatomically, the cortical surface is highly convoluted with the grey-matter layer being 2 – 4 mm thick in humans. The precise folding pattern is unique to every individual. Functionally, the neocortex is the seat of cerebral activity. Using the blood-oxygen-level-dependent (BOLD) response as a proxy for neuronal activity, fMRI is able to measure brain function at the gray-matter layer.

Adaptive lifting wavelets have been successful in capturing shape variations of the cortex and in tracking cortical folding changes in newborns [7]. This success, together with the localization and multiscale analysis properties of lifting wavelets, suggested that using adapted domains to perform wavelet transforms on functional data would allow us to achieve improved performance in a variety of fMRI analyses.

Our proposed approach is to use the wavelet lifting scheme to build an efficient in-place algorithm to construct second generation wavelets (these may not be translates and dilates of one fixed "mother wavelet" function [8]). Such wavelets can be adapted to arbitrary domains such as cerebral cortex [9, 10]. The transform coefficients are obtained through a simple subsampling scheme followed by in-place "lifting" updates based on spatial filtering. As these spatial filters may be considered integrands of particular interpolation functions over a localized neighborhood (for example, interpolating polynomials or splines), we adapt the wavelet transform to "mold" itself to cortex by weighting the integrand with a measure defined on the volume.

2. THEORY

2.1. Statistical Parametric Mapping

Statistical parametric mapping (SPM) is a method to detect voxels with stimulus-related activity in fMRI data. A key point in the procedure is spatial prefiltering with a Gaussian

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window, which smooths the data and destroys fine spatial details.

WSPM is a modification of SPM where the denoising step is performed by thresholding in the spatial wavelet domain. This makes the typical advantage of wavelets apparent in the results. The underlying theorem guarantees control over the false-positive rate by a bound of the null-hypothesis rejection probability. Moreover, empirical results show similar sensitivity than SPM with improved spatial detail. The resulting map of active voxels can be seen to align with the cortex, as a demonstration of preserving the detail information.

2.2. Classical Wavelet-Based Analysis

We briefly summarize the classical wavelet-based method [11]. Let us denote an fMRI data set with $v_{\mathbf{n}}(t)$, where $\mathbf{n} \in \mathbb{Z}^3$ is the spatial index, and $t \in \mathbb{Z}$ is the temporal index. With a simplified notation, the wavelet transform corresponds to representing the data under the form

$$v_{\mathbf{n}}(t) = \sum_{\mathbf{k}} w_{\mathbf{k}}(t) \psi_{\mathbf{k}}(\mathbf{n}),$$

where $\{\psi_{\mathbf{k}}\}$ is the wavelet basis. Each basis function is a translated and dilated version of some prototype in the standard wavelets case, but they take more arbitrary forms in the adapted case [6].

Now let $\mathbf{w_k}$ be the vector of wavelet coefficients corresponding to ψ_k; i.e., $\mathbf{w_k} = [w_{\mathbf{k}}(1) \ \cdots \ w_{\mathbf{k}}(N_t)]^T$, where N_t is the total number of time samples. Due to linearity of the wavelet transform, we can write the (same) general linear model as in the spatial domain: $\mathbf{w_k} = \mathbf{X}\mathbf{y_k} + \mathbf{e_k}$, where $\mathbf{X}$ is the $N_t \times L$ design matrix, $\mathbf{y_k}$ is the $N \times 1$ vector of unknown parameters, and $\mathbf{e_k}$ is the residual error. In a simple block based experiment, $\mathbf{X}$ could be a two-column matrix, one representing the on-off stimulus while the other column representing the background. Assuming the noise to be independent and identically distributed Gaussian, the unbiased estimate of $\mathbf{y_k}$ is given by $\hat{\mathbf{y}}_{\mathbf{k}} = (\mathbf{X}^{\mathrm{T}}\mathbf{X})^{-1}\mathbf{X}^{\mathrm{T}}\mathbf{w_k}$. Usually some linear combination of the parameter vector entries is of interest, which is obtained by multiplication with a so called contrast vector $\mathbf{c}$. In our example, the contrast vector could be $\mathbf{c} = [1 \ 0]^{\mathrm{T}}$. Corresponding to each index $\mathbf{k}$ of the wavelet basis, we obtain two scalar values:

$$g_{\mathbf{k}} = \mathbf{c}^{\mathrm{T}} \hat{\mathbf{y}}_{\mathbf{k}},$$
$$s_{\mathbf{k}}^2 = \hat{\mathbf{e}}_{\mathbf{k}}^{\mathrm{T}} \hat{\mathbf{e}}_{\mathbf{k}} \mathbf{c}^{\mathrm{T}} (\mathbf{X}^{\mathrm{T}}\mathbf{X})^{-1} \mathbf{c},$$

where $\mathbf{g_k}$ and $\mathbf{s_k}$ follow a Gaussian and Chi-squared distribution, respectively. From these one can obtain a t value for each wavelet coefficient $\mathbf{k}$:

$$t_{\mathbf{k}} = \frac{g_{\mathbf{k}}}{\sqrt{s_{\mathbf{k}}^2 / J}}, \ \text{ with } J = N_t - \mathrm{rank}(\mathbf{X}),$$

which can be tested against a threshold τ_w, which is chosen in accordance with the desired significance level. After testing, the detected coefficients are reconstructed as

$$\mathbf{r_n} = \sum_{\mathbf{k}} T_{\tau_w}(t_{\mathbf{k}}) g_{\mathbf{k}} \psi_{\mathbf{k}}(\mathbf{n}), \tag{1}$$

where T is the thresholding function corresponding to the two sided t test; i.e., $T(t_{\mathbf{k}}) = 1$ if $|t_{\mathbf{k}}| \geq \tau_w$, and zero otherwise. The volume $r_{\mathbf{n}}$ contains many nonzero voxels, each of which is a function of many voxels from the original data. One must rely on heuristic thresholds on $r_{\mathbf{n}}$ to obtain acceptable detection maps. Moreover, $r_{\mathbf{n}}$ does not have a direct statistical interpretation. These disadvantages are overcome with the WSPM, as explained in the next section.

2.3. Joint Spatio-Wavelet Statistical Analysis

The main idea in the joint spatio-wavelet statistical analysis is to perform two consecutive thresholding operations: first in the wavelet domain and then in the spatial domain. There are two corresponding threshold parameters, τ_w and τ_s, to be determined [3, 4]. A spatial map is obtained after the first thresholding as in (1). Then $r_{\mathbf{n}}$ is weighted by $1/\sum_{\mathbf{k}} \sigma_{\mathbf{k}} |\psi(\mathbf{n})|$ and thresholded by τ_s. That is, the set of voxels that are declared to be active would be

$$\left\{ \mathbf{n} \colon \frac{|\sum_{\mathbf{k}} T_{\tau_w}(t_{\mathbf{k}}) g_{\mathbf{k}} \psi_{\mathbf{k}}(\mathbf{n})|}{\sum_{\mathbf{k}} \sigma_{\mathbf{k}} |\psi(\mathbf{n})|} \geq \tau_s \right\}$$

Given the desired significance level α, an optimal choice for τ_s and τ_w, which minimizes the approximation error between the reconstruction from the fitted parameters and two times thresholded reconstruction, can be computed to be

$$\tau_w = \sqrt{-W_{-1}\left(-\frac{\alpha^2 \pi}{2}\right)}, \quad \tau_s = 1/\tau_w,$$

where W_{-1} is the -1-branch of the Lambert-W function [3].

2.4. Anatomically Adapted Wavelets

In the mentioned methods, the wavelet transforms are either performed slice by slice as two dimensional wavelet transforms, or are appplied to the whole volume as a three dimensional wavelet transform. In either case, the domain of the signals are assumed to be the rectangular. However, in reality the activity takes place in a subset corresponding to the brain cortex, which is a highly convoluted three dimensional structure. Therefore we used the lifting scheme to build customized wavelet bases, whose natural domains are the brain cortex. Lifting scheme is a simple and powerful framework for building customized wavelets, with the help of an interpolation scheme [12].

A key point in the procedure is to obtain a nested family of partitions on the domain. When we have a regular domain, like a rectangular subset of $\mathbb{R}^n$, there are obvious choices for the nested family of partitions. However, an irregular domain is harder to partition in a natural way. We propose a randomized method [6], as illustrated in Fig. 1, which starts by declaring the individual voxels as the sets of the finest level partition, and then continues by merging them with their neighbors in a random fashion to form the coarser levels. Each distinct realization of a random partitioning yields a distinct wavelet basis. The randomized merge algorithm can be summarized as follows:

1. Declare each voxel as a set belonging to the finest partition.
2. Randomly select at most 3 neighboring sets and merge them, to form a set in the next level of partition.
3. Calculate the center of mass of each set. For the next level, repeat Step 2. with probability of merge among multiple neighbors proportional to the closeness of the center of masses.

The random choices in the algorithm results in a different family of partitions for the same domain after each run. This in turn will lead to a different wavelet basis for each realization. We can repeat any signal processing algorithm involving these wavelets over many realizations and average the results.

After the nested sequence of partitions is defined, first step is to simply define Haar-like wavelets that are piecewise constant on the member sets of the partitions. After this step, these non-smooth Haar-like wavelets can be turned into more smooth wavelets in lifting updates [6, 9, 10, 12].

3. EXPERIMENTAL RESULTS

3.1. Simulated Data

We generated smooth function over a domain consisting of concentric circles, to represent the fine layered structure of the gray-matter cortical layer with different widths. We contaminated the data with white Gaussian noise, whose magnitude is decreasing from left to right, as shown in Fig. 2. The adapted wavelets showed an improvement in the sensitivity, while keeping the specificity within the theoretical limits. Also as the level of the wavelet decomposition increased, the sensitivity kept increasing with the adapted wavelets, while it remained unchanged with the standard wavelets. See Fig. 3 for the comparison of sensitivities obtained with standard and adapted wavelets.

3.2. Real Data

We tested the proposed method with data obtained from a visual stimulation experiment, with 16 slices of 128×128 voxels, whose size is 1.8 mm $\times$ 1.8 mm $\times$ 5 mm. We performed segmentation with SPM, and generated the adaptive wavelets using the domain corresponding to the gray-matter layer. With the standard orthogonal wavelets, the analysis

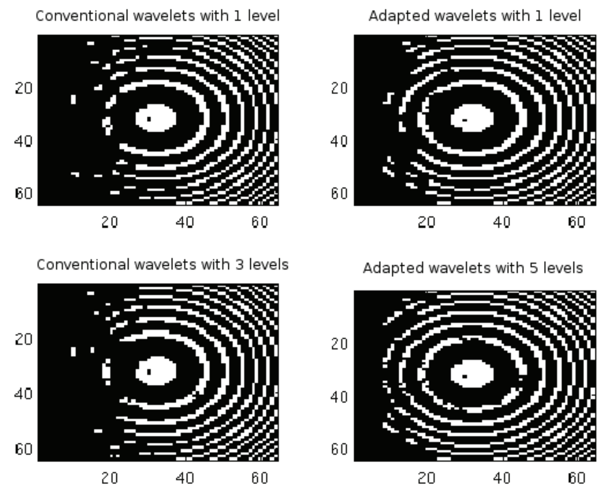

Fig. 2. The detected map of active voxels. Left column shows with standard orthogonal wavelets, and the right column shows the result with the anatomically adapted wavelets. In the second row the level of wavelet decomposition is increased, and the performance of adapted wavelets have also increased while the performance of standard wavelets remain unchanged.

resulted in 1032 detected voxels, while with the adapted wavelets it resulted in 1214 active voxels. In both cases the sensitivity parameter α is taken to be 0.001. This suggests an improved sensitivity, with a detection of larger number of voxels, as shown in Fig. 4.

4. SUMMARY AND CONCLUSION

We have used a new class of wavelets that are adapted to the anatomy of the brain cortex, within the wavelet-based SPM framework. We have observed an improved sensitivity, while retaining the same amount control over type-I errors. As opposed to the standard wavelet transform, the adapted wavelets show clear improvement as the decomposition level increases. The influence of redundancy in the wavelet transform, and the performance of the adapted wavelets in multi-subject studies will be explored in future works.

5. REFERENCES

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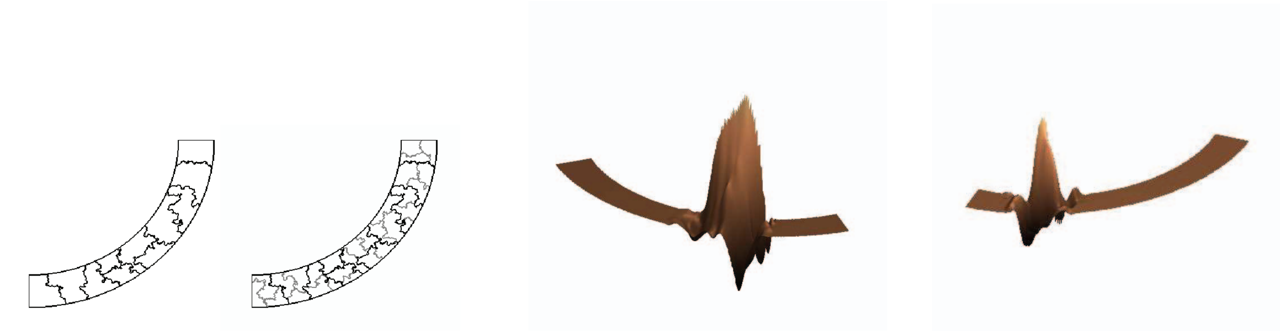

(a) Sample random partitioning of two levels (b) Scaling function (c) Wavelet

Fig. 1. Illustration of partitioning and adapted wavelets on an annular shaped domain.

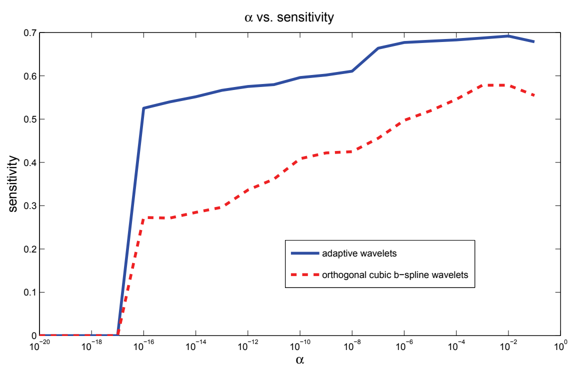

Fig. 3. The ROC curves with standard (tensor-product orthogonal cubic B-spline wavelets) and anatomically adapted wavelets. The α-value represents the type-I error control rate that is input to the algorithm.

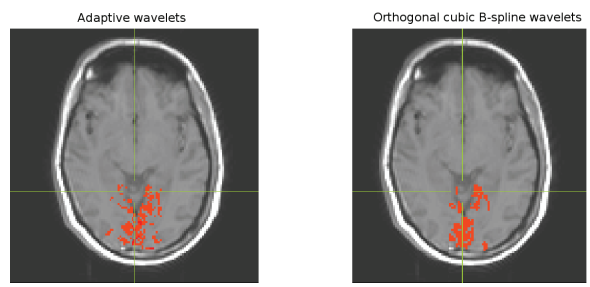

Fig. 4. Slices from detected activation maps with real visual stimulation data. Left image is obtained with adaptive wavelets, and right image is obtained with orthogonal cubic B-spline wavelets.

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