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Matched-filter acquisition for BOLD fMRI

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ABSTRACT

We introduce matched-filter fMRI, which improves BOLD (blood oxygen level dependent) sensitivity by variable-density image acquisition tailored to subsequent image smoothing. Image smoothing is an established post-processing technique used in the vast majority of fMRI studies. Here we show that the signal-to-noise ratio of the resulting smoothed data can be substantially increased by acquisition weighting with a weighting function that matches the k-space filter imposed by the smoothing operation. We derive the theoretical SNR advantage of this strategy and propose a practical implementation of 2D echo-planar acquisition matched to common Gaussian smoothing. To reliably perform the involved variable-speed trajectories, concurrent magnetic field monitoring with NMR probes is used. Using this technique, phantom and in vivo measurements confirm reliable SNR improvement in the order of 30% in a "resting-state" condition and prove robust in different regimes of physiological noise. Furthermore, a preliminary task-based visual fMRI experiment equally suggests a consistent BOLD sensitivity increase in terms of statistical sensitivity (average *t*-value increase of about 35%). In summary, our study suggests that matched-filter acquisition is an effective means of improving BOLD SNR in studies that rely on image smoothing at the post-processing level.

Introduction

Spatial smoothing of imaging volumes is ubiquitous in fMRI (Carp, 2012; Poldrack et al., 2008). Its routine use before statistical analysis aims at improving the sensitivity and interpretability of blood oxygen level dependent (BOLD) contrast in three ways, i.e., from the perspective of (1) signal processing, (2) statistical inference at the single-subject level and (3) group level inference (Friston, 2007).

Firstly, with respect to the signal processing perspective, smoothing the data with a filter that resembles the spatially extended hemodynamic response is considered optimal to detect activation of this particular shape and scale, according to the *matched-filter theorem* (Worsley et al., 1996a, b). Secondly, regarding single-subject inference, image smoothing facilitates the application of multiple comparison correction using random field theory (Worsley et al., 1996a, b) since it ensures spatial smoothness of the residual error distribution. Thirdly, at the group level, spatial smoothing helps to absorb anatomical variability between subjects.

Image smoothing is commonly performed with a filtering operation in k-space that attenuates signal content at high spatial frequencies. In doing so it alters the effective point spread function (PSF) such as to broaden its main peak and suppress far-range contamination. However, importantly, variable k-space attenuation not only affects the PSF but also the propagation of noise from raw data into smoothed images. The noise content of the raw data undergoes the same k-space weighting such that the relative impact of noise increases towards the center of k-space. As a consequence, to maximize the SNR of the smoothed data, the raw data should be acquired with variable sensitivity by corresponding k-space weighting at the acquisition level. As will be detailed in the theory part, optimal net SNR is achieved by acquisition weighting that exactly matches the eventual smoothing filter. The underlying mathematics correspond closely to the matched-filter rationale (North, 1963) of the smoothing operation. It is important, however, to distinguish the different filter-matching rationales. Aiming to match the hemodynamic response by smoothing is common practice today and serves for the purposes summarized initially. The utility of also matching data acquisition is a consequence of the smoothing strategy

Abbreviations: BOLD, Blood oxygen level dependent; EPI, Echo-planar imaging; EPSI, Echo-planar spectroscopic imaging; fMRI, Functional magnetic resonance imaging; FWHM, Full width at half maximum; PSF, Point spread function; SENSE, Sensitivity encoding; SFNR, Signal-to-fluctuation-noise ratio; TLS, Total least squares.

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and serves exclusively for SNR optimization given a chosen smoothing kernel. Importantly, through appropriate image reconstruction including density correction, the matched-filter acquisition does not change the PSF and thus allows for image post-processing that is identical to standard acquisition.

Acquisition weighting has previously been used to improve the sensitivity of MR spectroscopic imaging and non-proton MRI, summarized under the theme of density-weighted phase encoding (Greiser and von Kienlin, 2003; Greiser et al., 2005; Stobbe and Beaulieu, 2008). In this work, we introduce matched-filter acquisition for fMRI with single-shot echo-planar readouts, which is challenging in that it cannot be accomplished merely by altered phase encoding, but requires 2D trajectory design with complex modulation of k-space velocity. Such trajectories are particularly susceptible to common imperfections of gradient systems such as bandwidth limitations and eddy currents. To gauge and address this issue, we incorporate concurrent magnetic field monitoring (Barmet et al., 2008, 2009, 2010) with NMR probes (Barmet et al., 2010; De Zanche et al., 2008), which permits accounting for imperfections in magnetic field evolution at the image reconstruction stage.

The SNR benefit expected from filter matching relies on the incoherence of noise. In particular, the exact form of the matched-filter acquisition rule proposed here refers to the assumption of independent and identically distributed white noise. Thermal noise, which is prevalent in MR, exhibits this property (Johnson, 1928; Nyquist, 1928). For this noise regime, we show analytically that the distribution of acquisition time should indeed exhibit the same weighting in k-space as the target PSF, to achieve maximum SNR. However, BOLD fMRI is also subject to noise related to physiological processes with non-white statistics (Bianciardi et al., 2009; Krüger and Glover, 2001), including inherent neurophysiological fluctuations as well as respiratory and cardiovascular dynamics (Birn et al., 2008; Chang et al., 2009; Dagli et al., 1999; Glover et al., 2000; Shmueli et al., 2007). Therefore, the experimental validation of matched-filter fMRI in this work comprises signal-to-fluctuation-noise ratio (SFNR) measurements of phantom and in vivo time series, in which we vary the degree of signal-mediated fluctuations and evaluate their influence on the observed SFNR gain. Finally, we perform a proof-of-principle experiment showing the feasibility of matched-filter acquisition also for task-based fMRI. Using a visual paradigm in a preliminary group of four subjects, robust t-value increases are reported over standard EPI acquisition.

Theory and methods

Theory: Matched-density acquisition for image post-processing filters

In the following section, we establish the relationship between variable acquisition speed in k-space, the point-spread function (PSF) and signal-to-noise ratio (SNR) within an MR image. This is contrasted to shaping the PSF by retrospective smoothing only.

To estimate SNR, we consider the different propagation of signal and noise in both stages, focusing on the total thermal noise contribution similar to Pipe and Duerk (1995) and Stobbe and Beaulieu (2008), but treating all quantities in a continuous fashion, which then leads to a variational optimization of SNR.

Accrual of signal and noise in a given k-space region depends on how much acquisition time is spent in that region. If local acquisition time is distributed non-uniformly, it becomes dependent on the k-space position vector $\boldsymbol{k} = (k_x, k_y k_z)$. Hence, we denote the resulting distribution of acquisition time as *acquisition density* $d_{\text{acq}}(\boldsymbol{k})$ Upon gridding reconstruction, d_{acq} becomes effectively smooth on the scale of the Nyquist sampling interval and represents the local density of trajectory segments and their velocity.

Signal accrues coherently over time and thus linearly with $d_{\text{acq}}(\boldsymbol{k})$. Thermal noise, on the other hand, accrues incoherently because it is uncorrelated due to being identically, independently normally distributed (Johnson, 1928; Nyquist, 1928). Hence, the *variance* of the thermal noise increases linearly with local acquisition density:

$$\sigma^2_{\text{acq}}(\boldsymbol{k}) \propto d_{\text{acq}}(\boldsymbol{k}). \tag{1}$$

Let us now consider smoothing during post-processing which is performed to achieve a target PSF. As the combined action of smoothing and acquisition weighting in k-space should yield the target density, we obtain a defining equation for the smoothing filter:

$$d_{\text{smooth}}(\boldsymbol{k}) := \frac{d_{\text{target}}(\boldsymbol{k})}{d_{\text{acq}}(\boldsymbol{k})} \tag{2}$$

with d_{target} and d_{smooth} being the Fourier transform of the PSF and smoothing kernel, respectively.

We now investigate the action of this post-processing filter on the acquired k-space data, which is already a superposition of signal and noise. The application of $d_{\text{smooth}}(\boldsymbol{k})$ is a mere re-weighting of these data. Thus, the signal scales linearly with this density as in the case of acquisition weighting. The noise amplitude, however, is now also proportionally scaled with this density, inducing a quadratic dependency of the noise variance on d_{smooth} in the final, post-processed data,

$$\sigma^2_{\text{final}}(\boldsymbol{k}) = d^2_{\text{smooth}}(\boldsymbol{k}) \cdot \sigma^2_{\text{acq}}(\boldsymbol{k}) \propto d^2_{\text{smooth}}(\boldsymbol{k}) \cdot d_{\text{acq}}(\boldsymbol{k}) = \frac{d^2_{\text{target}}(\boldsymbol{k})}{d_{\text{acq}}(\boldsymbol{k})}, \tag{3}$$

where equality and proportionality arise from Eqs. (1) and (2), respectively.

This equation illustrates that the acquisition density is an additional degree of freedom for an MR experiment with a given target PSF, because the target PSF can always be achieved retrospectively by smoothing with an appropriate image filter K_{smooth}. The choice of the acquisition density, on the other hand, then determines the noise landscape in k-space, σ^2_{final} for the final, reconstructed image, as described in Eq. (3).

Given a specific target PSF, an immediate application of Eq. (3) is to find the acquisition density that maximizes SNR in the image. As long as Nyquist sampling is ensured, the signal level is independent of d_{acq}, because it is determined by the target PSF (which is the same for all acquisition densities). Thus, to maximize SNR, it suffices to minimize the noise variance in each image voxel. As we reconstruct an image from the acquired k-space data of an individual coil through Fourier transformation and the thermal noise accrued in k-space is uncorrelated, the noise landscape in the conjugate image space will be flat according to the Wiener-Khinchin theorem (Weisstein, 2006b), rendering all voxel noise variances in the image equal. Minimizing the noise variance per voxel is therefore equivalent to minimizing the total noise power in the image which, in turn, is equivalent to the noise power in k-space due to Parseval's theorem (Weisstein, 2006a).

Hence, maximizing the SNR per voxel amounts to a constrained minimization of the noise power in the covered k-space volume V_k which we define as

$$|\sigma_{\text{final}}|^2_2 := \int_{V_K} \sigma^2_{\text{final}}(\boldsymbol{k})\, \mathrm{d}\boldsymbol{k}. \tag{4}$$

The optimization constraint is given by a constant total acquisition time T_{acq}, such that the full optimization problem incorporating relation (3) reads

$$|\sigma_{\text{final}}|^2_2 = \int_{V_k} \frac{d^2_{\text{target}}(\boldsymbol{k})}{d_{\text{acq}}(\boldsymbol{k})} \mathrm{d}\boldsymbol{k} \rightarrow \min \text{ with } \int_{V_k} d_{\text{acq}}(\boldsymbol{k})\, \mathrm{d}\boldsymbol{k} = T_{\text{acq}}. \tag{5}$$