A Signal Processing Model for Arterial Spin Labeling Perfusion fMRI

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Introduction

In perfusion based functional magnetic resonance imaging (fMRI) experiments with arterial spin labeling (ASL), a series of control images and tag images, in which arterial blood is either fully relaxed or magnetically inverted, respectively, is acquired. Typically, the control and tag images are acquired in an interleaved fashion, and a perfusion time series can be formed from either a simple pair-wise or surround subtraction of the control and tag images [1] or from a subtraction of sinc interpolated images [2]. Recent experimental and simulation studies [2,3] have demonstrated that the ASL subtraction process tends to whiten the 1/f noise typically observed in fMRI experiments contrast, where the degree of whitening depended on the subtraction method used. In addition the choice of subtraction method has been shown to have an effect on the contamination of the perfusion signal by blood oxygenation level dependent (BOLD) weighting of the acquired images. A qualitative description of the noise whitening process and BOLD contamination effects has been provided in [2,3]. Here we present a model of the perfusion fMRI signal processing chain that allows for an analytical evaluation of the various subtraction methods.

Signal Model

A signal model of the ASL subtraction process is shown in Figure 1. The measured time series $y[n]$ is the sum of the interleaved BOLD weighted tag and control images plus an additive noise term $e[n]$ with autocorrelation function $\rho[n]$. The BOLD weighted tag images $b[n](M[n]-q[n])$ occur at even indices, while the BOLD weighted control images $b[n]M[n]$ occur at odd indices, where *b[n]* represents the BOLD weighting, *M[n]* is the in-slice magnetization, and *q[n]* is proportional to the difference in magnetization between fully relaxed and inverted arterial spins that are delivered to the imaging slice. An estimate of the perfusion is obtained as $\hat{q}[n]=\left[(-1)^{n+1}y[n]\right]*g[n]$ where *g[n]* is a low-pass interpolation filter that depends on the subtraction method used [5]. For pair-wise subtraction, $g[n]=[1\ 1]$; for surround subtraction, $g[n]=[1\ 2\ 1]/2$; and for sinc subtraction $g[n]=\text{sinc}[n/2]$ [2,4].

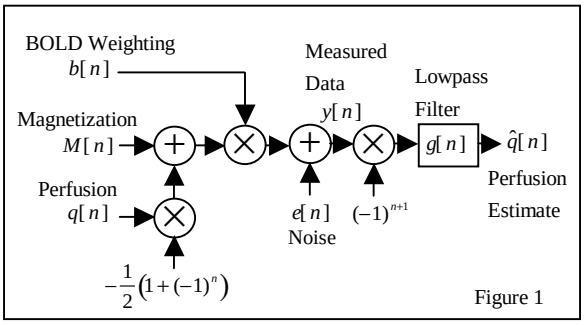
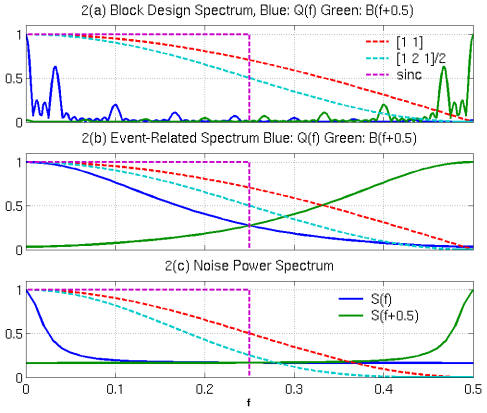


Figure 1

Expanding the expression for the perfusion estimate yields a sum $\hat{q}[n]=q_1[n]+q_2[n]+q_e[n]$ of three components. These are a BOLD-weighted, low-pass filtered perfusion component $q_1[n]=(b[n]q[n]/2)*g[n]$, a high-frequency spurious component $q_2[n]=-\left[(-1)^n b[n](M[n]-q[n]/2)\right]*g[n]$, and an output noise component $q_e[n]=-\left[(-1)^n e[n]\right]*g[n]$. For most perfusion fMRI experiments, a reasonable approximation is that the in-slice magnetization is constant $M[n]\approx M_0$, and in the absence of background suppression is much greater than the perfusion component ($M_0 >> q[n]$), so that the spurious component $q_2[n]\approx-\left[(-1)^n b[n]M_0\right]*g[n]$ is approximately the BOLD signal modulated at the Nyquist frequency and then low-pass filtered. In addition, if the percent change in perfusion is much greater than the percent change in BOLD, an additional approximation is $b[n]q[n]=(1+\Delta b[n])(q_0+\Delta q[n])\approx q[n]$, which yields $q_1[n]\approx q[n]/2*g[n]$.

Lowpass Filter

The impact of the lowpass filter is most easily appreciated in the frequency domain. The discrete-time Fourier transforms of the perfusion and spurious components are $Q_1(f)=G(f)[B(f)*Q(f)/2]\approx G(f)Q(f)/2$ and $Q_2(f)=-G(f)[B(f+0.5)*(M(f)-Q(f)/2)]\approx -M_0G(f)B(f+0.5)$ where f denotes normalized frequency. An optimal lowpass filter will minimally attenuate the perfusion spectrum $Q(f)$ while maximally attenuating the modulated BOLD spectrum $B(f+0.5)$. Figure 2a shows an example of the normalized spectra $Q(f)$ and $B(f+0.5)$ for a block design (4 cycles of 30 seconds on/off) convolved with a gamma density function. Also shown are the spectra $G(f)$ for $g[n]=[1\ 1]$, $g[n]=[1\ 2\ 1]/2$, and $g[n]=\text{sinc}[n/2]$. Consistent with the findings of [2], it is clear that the sinc filter provides minimal attenuation of $Q(f)$ and maximal attenuation of $B(f+0.5)$. Figure 2b show the spectra assuming a randomized event-related design convolved with the gamma density spectrum. In this case, both $Q(f)$ and $B(f+0.5)$ have relatively broad bandwidths, and the sinc filter significantly reduces the bandwidth of the desired perfusion spectrum. Thus, if BOLD weighting can be minimized (e.g. with a short echo-time spiral acquisition [4]), a filter with a large bandwidth (e.g. $g[n]=[1\ 1]$) is preferable. The power spectrum of the output noise is $\hat{S}_e(f)=S(f+0.5)|G(f)|^2$ where $S(f)$ is the Fourier transform of $\rho[n]$. Figure 2c shows $S(f)$ and $S(f+0.5)$ when the input noise is the weighted sum of a white noise process and a first order auto-regressive process [5]. Note that the 1/f portion of $S(f)$ is moved to the Nyquist frequency due to the modulation inherent in ASL processing. Also shown is $|G(f)|^2$ for the various lowpass filters. Consistent with the findings in [3], the sinc filter yields the flattest noise spectra at low frequencies, while the $g[n]=[1\ 1]$ filter provides reasonable performance over the entire frequency range.



Conclusion: We have presented a signal processing model for the ASL subtraction process which is useful for assessing the relative performance of various subtraction methods. For block designs, a sinc filter is optimal, while for randomized event-related designs a $g[n]=[1\ 1]$ filter is preferable if there is minimal BOLD weighting.

References: [1] EC Wong et al., *NMR in Biomed*. 10:237-249, 1997 [2] GK Aguirre et al, *NeuroImage* 15:488-500 (2002). [3] J Wang et al. *NeuroImage* 19:1449-62 (2003). [4] TT Liu et al, *NeuroImage* 16:269-82 (2002). [5] MA Burock, AM Dale, HBM 11:249-60 (2000).