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Reprint of 'Noise contributions to the fMRI signal: An Overview'

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ABSTRACT

The ability to discriminate signal from noise plays a key role in the analysis and interpretation of functional magnetic resonance imaging (fMRI) measures of brain activity. Over the past two decades, a number of major sources of noise have been identified, including system-related instabilities, subject motion, and physiological fluctuations. This article reviews the characteristics of the various noise sources as well as the mechanisms through which they affect the fMRI signal. Approaches for distinguishing signal from noise and the associated challenges are also reviewed. These challenges reflect the fact that some noise sources, such as respiratory activity, are generated by the same underlying brain networks that give rise to functional signals that are of interest.

1. Introduction

In a functional magnetic resonance imaging (fMRI) experiment, a time series of images is acquired with a temporal resolution (ranging from several hundred milliseconds to several seconds) that depends on the experimental design and the parameters of the MRI acquisition. The acquisition is designed to reflect changes in the apparent transverse relaxation rate, an MRI parameter that is sensitive to the amount of deoxyhemoglobin in the blood and exhibits a complex dependence on cerebral blood flow, metabolism, and volume (Buxton et al., 2004). This dependence forms the basis for blood oxygenation level dependent (BOLD) fMRI. The acquired time series data contain contributions from BOLD-weighted signal changes related to brain activity. In addition, there are a variety of undesired noise components (both BOLD and non-BOLD weighted) whose magnitude is often comparable or even greater than the signal of interest.

Over the past two decades, efforts to characterize and mitigate the effects of noise in BOLD fMRI time series have played an integral role in the development of fMRI acquisition and analysis approaches (Murphy et al., 2013; Greve et al., 2013; Birn, 2012). Advances in methods to distinguish signal from noise have led to improvements in the ability to detect and estimate brain activity. In this paper, we will review the primary sources of noise in fMRI, with a focus on the noise components that appear in fMRI time series signals. In-depth treatments of the various noise sources are provided elsewhere in this special issue. In the analysis of fMRI studies, there are additional sources of noise, such as inter-scan, inter-subject, and inter-site variability (Greve et al., 2013), but these sources will not be considered here.

We will begin by reviewing a basic signal model for BOLD fMRI and considering the various ways in which noise affects the elements of the model. This will be followed by an examination of the mechanisms through which various processes, such as cardiac and respiratory activity, can act as noise sources. We will conclude with an overview of approaches for separating signal from noise in fMRI.

As we consider the sources of noise in the fMRI time series, we will find that the line between signal and noise is not always clear. Whether a component is considered to be signal or noise depends on our current perspective and understanding of the underlying physiology and biophysics. Indeed, over the course of the history of fMRI, there have been several instances when a component that was originally considered to be noise has become a signal of great interest.

2. Signal and noise components

In order to understand the role of noise in BOLD fMRI, it useful to start with a basic signal model of the form

$$S(t) = S_0(t)\cdot\exp\left(-R_2^*(t)\cdot\mathrm{TE}\right) + n(t) \tag{1}$$

where $S(t)$ denotes the signal acquired at time t, $R_2^*(t)$ is the apparent transverse relaxation rate, TE denotes the echo time, $S_0(t)$

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denotes the magnetization at zero echo time $TE = 0$, and $n(t)$ represents additive background noise.

For most fMRI experiments, it is the relative change $\Delta S/S$ in the measured signal that is typically of interest. To derive a simplified expression for this quantity, we first approximate the absolute change in the measured signal as

$$\begin{aligned}\Delta S(t) &\approx \Delta S_0(t)\cdot\frac{\partial S}{\partial S_0}\bigg|_{t=0} + \Delta R_2^*(t)\cdot\frac{\partial S}{\partial R_2^*}\bigg|_{t=0} + \Delta n(t)\\ &= \Delta S_0(t)\cdot\exp\left(-R_2^*(0)\cdot TE\right)\\ &\quad - \Delta R_2^*(t)\cdot S_0(0)\cdot\exp\left(-R_2^*(0)\cdot TE\right)\cdot TE + \Delta n(t)\\ &\approx S(0)\cdot\frac{\Delta S_0(t)}{S_0(0)} - S(0)\cdot TE\cdot\Delta R_2^*(t) + \Delta n(t)\end{aligned} \tag{2}$$

Dividing the final expression by the initial signal value $S(0)$ yields an expression for the relative change

$$\frac{\Delta S(t)}{S(0)} \approx \frac{\Delta S_0(t)}{S_0(0)} - TE\cdot\Delta R_2^*(t) + \frac{\Delta n(t)}{S(0)} \tag{3}$$

as the sum of three terms: (1) the relative change in the magnetization at zero echo time $\frac{\Delta S_0(t)}{S_0(0)}$, (2) a term $TE\cdot\Delta R_2^*(t)$ proportional to the change in relaxation rate, and (3) the relative change in the background noise term $\frac{\Delta n(t)}{S(0)}$. We are typically most interested in the $TE\cdot\Delta R_2^*(t)$ term, as it is the change in the relaxation rate $R_2^*(t)$ that most directly reflects functional changes in blood oxygenation, flow, and volume. This term is sometimes referred to as the BOLD-like component, whereas the magnetization term is referred to as the non-BOLD component. In the sections below, we examine the role of noise in each of the terms.

In discussions of signal and noise in fMRI, a commonly used metric to characterize the performance of an acquisition is the temporal signal-to-noise-ratio (tSNR) (Parrish et al., 2000; Triantafyllou et al., 2005). This is defined as

$$\begin{aligned}\text{tSNR} &= \frac{\text{Mean signal Amplitude}}{\text{Standard Deviation of the Noise Over Time}}\\ &= \frac{S_{mean}}{\sqrt{\sigma_T^2 + \sigma_{NB}^2 + \sigma_B^2}}\end{aligned} \tag{4}$$

where σ_T^2, σ_{NB}^2, σ_B^2 represent the noise variances of the background, non-BOLD, and BOLD-like components, respectively. The tSNR level determines the ability of an acquisition to detect activity-related changes, with smaller percent BOLD changes requiring a larger tSNR value. For example, Parrish et al. (2000) reported that to detect a 0.5% signal change (in a time series of 112 images) with a probability of detection of 0.95 and a probability of false alarm of 0.05, a tSNR of 138 would be required. The required tSNR is inversely proportional to the signal change, so that a 1% change would require a tSNR of 69 at the same probabilities of detection and false alarm.

As noted by Krüger and Glover (2001), it useful to rewrite tSNR as follows

$$\begin{aligned}\text{tSNR} &= \frac{S_{mean}}{\sqrt{\sigma_T^2 + \sigma_p^2}}\\ &= \frac{S_{mean}/\sigma_T}{\sqrt{1 + \sigma_p^2/\sigma_T^2}}\\ &= \frac{\text{SNR}_0}{\sqrt{1 + \lambda^2\text{SNR}_0^2}}\end{aligned} \tag{5}$$

where $\text{SNR}_0 = S_{mean}/\sigma_T$ represents the image SNR, the term $\sigma_p^2 = \sigma_{NB}^2 + \sigma_B^2$ is the sum of the non-BOLD and BOLD-like noise variances, and λ is a scaling factor that relates this term to the mean signal amplitude, such that $\sigma_p = \lambda S_{mean}$. This last relation reflects the fact that both the non-BOLD and BOLD terms in Eq. (2) are proportional to the signal term $S(0)$. For small image SNR values where $\lambda^2\text{SNR}_0^2 \ll 1$, tSNR scales linearly with SNR_0. Since $\text{SNR}_0 = \sigma_p/(\lambda\sigma_T)$, this can also be viewed as the regime in which the signal independent noise term σ_T is much greater than the signal dependent term σ_p. For example, for high resolution scans in which the voxel volume is relatively small, the thermal noise contributions (described in the next section) will tend to dominate the signal-dependent physiological noise terms. As image SNR increases such that $\lambda^2\text{SNR}_0^2 \gg 1$, the dependence of tSNR on image SNR weakens and tSNR eventually saturates at a limiting value of $\text{tSNR} = 1/\lambda$. This is the case that applies for the moderate resolution scans used in most fMRI studies in which the signal dependent term σ_p dominates the signal independent noise term σ_T. When operating in this regime, increases in image SNR (e.g. due to an increase in magnetic field strength) have a diminishing effect on tSNR (Triantafyllou et al., 2005). The dependence of tSNR on voxel volume is discussed further in Section 2.4.

2.1. Background noise

The background noise term $n(t)$ in Eq. (3) reflects the contributions of sources that are independent of the signal of interest. This includes thermal noise arising from the thermal agitation of charge carriers in both the subject and the MRI system electronics. For the modern systems and field strengths used in most fMRI studies, the thermal noise term is typically dominated by the subject noise contribution (Edelstein et al., 1986). The background noise also includes other sources of radiofrequency (RF) noise, such as RF spikes due to intermittent mechanical contacts between metal components and spurious RF noise from the environment (e.g. commercial radio signals that leak through a magnet room's RF shield) (Greve et al., 2011). The background noise term is present even if there is no activity-related signal of interest. Indeed, one way to measure the background noise is to simply acquire the data without exciting any magnetization. This is done by setting the flip angle of the RF excitation pulse to zero, such that $S_0(t) = 0$ and therefore $S(t) = n(t)$.

The presence of RF spikes and interference is considered undesirable for a well operating MRI system and much engineering effort goes into minimizing these noise sources. On the other hand, thermal noise is always present. However, since it is a wideband noise source (i.e. equal power at all temporal frequencies), its effects can be reduced through filtering to eliminate noise from frequencies that are outside of the signal band of interest. This is accomplished in the acquisition process through the use of low-pass filters in the signal processing chain (e.g. by setting the receiver bandwidth to an appropriate value). Further filtering is performed during the processing and reconstruction of images from the acquired raw MRI data. Because MRI acquires data at different spatial frequencies as a function of time, wideband noise in the temporal frequency domain is transformed into wideband noise in the spatial frequency domain (Nishimura, 2010). Noise outside the spatial frequencies of interest can therefore be directly filtered out in the spatial frequency domain (known as k-space filtering) or in the image domain through convolution with a low-pass spatial filter (e.g. smoothing of the images).

2.2. Noise in the magnetization term

The $\frac{\Delta S_0(t)}{S_0(0)}$ term reflect temporal changes in the initial transverse magnetization $S_0(t)$ that is created by the RF excitation pulse at the start of each repetition. Noise sources in this term include both MRI system-related instabilities and physiological noise components. In an ideal MRI system, all of the RF and gradient pulses are