Absolute Beginner's Guide to functional MRI

Christina Triantafyllou, Ph.D.
Massachusetts Institute of Technology, Cambridge, MA, USA

Introduction

Over the past fifteen or twenty years functional MRI has extended the boundaries of brain mapping from basic neuroscientific research into more sophisticated applications in neuroscience. More recently fMRI has begun to find further application in clinical science (e.g. neurological or psychiatric disorders) and in drug discovery. Functional MRI (fMRI) detects hemodynamic changes associated with neuronal brain activation during, for example, a visual, motor or cognitive stimuli. This neuronal activity drives local hemodynamic changes, such as increased local blood flow and blood volume, while generating relatively small changes in oxygen consumption. The resulting "endogenous" contrast mechanism (to which the functional MR signal is sensitive) is known as the Blood Oxygenation Level Dependent (BOLD) effect (Ogawa et al. 1990, Turner et al. 1991, Bandettini et al. 1992, Kwong et al. 1992, Ogawa et al. 1992).

Most fMRI studies utilize the BOLD effect as the contrast mechanism of choice to detect brain activity. In the BOLD effect, the magnetic properties of the blood change depending on blood oxygen levels as a consequence of the fact that oxygenated hemoglobin (Hb) molecules are diamagnetic while deoxygenated hemoglobin (dHb) is paramagnetic. The MR visible water, in and around the blood vessels, dephases in the presence of the inhomogeneous field pattern around the paramagnetic dHb. The dHb concentration dependent dephasing is seen in the images as an intensity change in a T_2^*-weighted imaging sequence. Given that increased neuronal activity drives increases in local blood flow and blood volume as well as smaller percentage changes in oxygen consumption, the dHb concentration decreases during activation. Thus, the BOLD effect is connected to a lengthening of the local value of T_2^* in activated tissue (brighter signal in the T_2^* weighted images). Because of the need to be sensitive to T_2^* and insensitive to motion artifacts, most fMRI studies utilize fast, single-shot T_2^*-weighted acquisitions based on gradient echo pulse sequences either using echo planar (Mansfield 1977) or spiral (Glover and Lee 1995) imaging. Given that the changes in image intensity associated with subtle brain activation in the fMRI experiment are relatively small, imaging parameters need to be optimally selected to maximize the fMRI contrast, improve sensitivity and encoding capabilities in functional MRI.

Image Quality and Artifacts

While fast image acquisitions capture sufficiently the BOLD effect, they are accompanied by some drawbacks. Ghosting artifacts in EPI, for example, result from phase differences during the acquisition of odd and even lines in k-space. Even more problematic artifacts arise from the effect of local susceptibility gradients on the EPI or spiral imaging. As discussed, the BOLD effect is based on microscopic alterations of the local magnetic field susceptibility gradients, at the macroscopic level. Thus we must make our sequences sensitive to local field alterations, however, the macroscopic magnetic susceptibility shifts arising at air and tissue interfaces results in image artifacts in fMRI acquisitions: (a) Signal loss due to within voxel dephasing (through plane susceptibility gradients) and (b) geometrical image distortions (e.g. signal compression or expansion in EPI) due to local in-plane susceptibility gradients or image blurring in spiral

acquisitions. We will discuss the origin of these artifacts and practical considerations in mitigating distortions for typical fMRI experiments (Jezzard and Balaban 1995, Merboldt et al. 2000, Andersson et al. 2001, Deichmann et al. 2002, Zaitsev et al. 2004, Weiskopf et al. 2006, Xiang and Ye 2007).

Signal and Noise characteristics in fMRI
Sensitivity in BOLD fMRI is characterized by only two fundamental parameters of the imaging sequence: 1) the sensitivity of the sequence to the T_2 or T_2^* changes produced by the BOLD effect (this is simply determined by optimizing the TE of the acquisition); and 2) the Signal-to-Noise Ratio (SNR) of the time-series (tSNR), which contains fluctuations from thermal (image noise) and physiological noise sources. Alteration of an acquisition parameter that alters the MR signal level can affect the tSNR differently depending on the relative contribution of the physiological and thermal noise. Therefore, knowledge of this ratio is essential for optimizing fMRI acquisitions (Kruger and Glover 2001, Triantafyllou et al. 2005). As the MR signal increases (e.g., from higher field strengths, the use of array coils, or changes in voxel volume), the physiological noise increases proportionally. This is problematic since improving detection sensitivity, for example with array coils, will not translate to improved tSNR for fMRI if the time-series variance is dominated by physiological noise. In this talk, we will discuss how to translate the improved detection sensitivity toward other desirable directions, such as increased spatial resolution or additional parallel imaging acceleration (with reduced susceptibility-induced image distortion)(de Zwart et al. 2002, Triantafyllou et al. 2010).

In this lecture we will describe the physiology of the BOLD effect and need-to-know practical basics of the MR physics to enable brain function imaging at high spatial resolutions. Specifically, we will define common acquisition schemes describing important parameters such as pulse sequence selectivity and image reconstruction techniques. We will outline sources of image artifacts, and discuss corrective procedures regarding how they might affect functional activation maps. Finally, we will describe signal and noise characteristics in fMRI time-series and the limiting effects of spatial and temporal resolution on the SNR.

Books
Buxton RB. Introduction to Functional Magnetic Resonance Imaging: Principles and Techniques. 2nd Edition, Cambridge University Press, 2009.
Huettel SA, Song AW, and McCarthy G. Functional Magnetic Resonance Imaging, Second Edition, Sinauer Associates, Inc., 2009.

References
Andersson JL, Hutton C, Ashburner J, Turner R, Friston K. Modeling geometric deformations in EPI time series. Neuroimage 13: 903-19; 2001.
Bandettini PA, Wong EC, Hinks RS, Tikofsky RS, Hyde JS. Time course EPI of human brain function during task activation. Magn Reson Med 25: 390-7; 1992.
de Zwart JA, van Gelderen P, Kellman P, Duyn JH. Application of sensitivity-encoded echo-planar imaging for blood oxygen level-dependent functional brain imaging. Magn Reson Med 48: 1011-20; 2002.
Deichmann R, Josephs O, Hutton C, Corfield DR, Turner R. Compensation of susceptibility-induced BOLD sensitivity losses in echo-planar fMRI imaging. Neuroimage 15: 120-35; 2002.
Glover GH, Lee AT. Motion artifacts in fMRI: comparison of 2DFT with PR and spiral scan methods. Magn Reson Med 33: 624-35; 1995.

Jezzard P, Balaban RS. Correction for geometric distortion in echo planar images from B0 field variations. Magn Reson Med 34: 65-73; 1995.

Kruger G, Glover GH. Physiological noise in oxygenation-sensitive magnetic resonance imaging. Magn Reson Med 46: 631-7; 2001.

Kwong KK, Belliveau JW, Chesler DA, Goldberg IE, Weisskoff RM, Poncelet BP, Kennedy DN, Hoppel BE, Cohen MS, Turner R, et al. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. Proc Natl Acad Sci U S A 89: 5675-9; 1992.

Mansfield P. Multi-planar imaging formation using NMR spin echoes. J Physics C Solid State Phys 10: L55-L58; 1977.

Merboldt KD, Finsterbusch J, Frahm J. Reducing inhomogeneity artifacts in functional MRI of human brain activation-thin sections vs gradient compensation. J Magn Reson 145: 184-91; 2000.

Ogawa S, Lee TM, Kay AR, Tank DW. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. Proc Natl Acad Sci U S A 87: 9868-72; 1990.

Ogawa S, Tank DW, Menon R, Ellermann JM, Kim SG, Merkle H, Ugurbil K. Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc Natl Acad Sci U S A 89: 5951-5; 1992.

Triantafyllou C, Hoge RD, Krueger G, Wiggins CJ, Potthast A, Wiggins GC, Wald LL. Comparison of physiological noise at 1.5 T, 3 T and 7 T and optimization of fMRI acquisition parameters. Neuroimage 26: 243-50; 2005.

Triantafyllou C, Polimeni JR, Wald LL. Physiological noise and signal-to-noise ratio in fMRI with multi-channel array coils. Neuroimage; 2010.

Turner R, Le Bihan D, Moonen CT, Despres D, Frank J. Echo-planar time course MRI of cat brain oxygenation changes. Magn Reson Med 22: 159-66; 1991.

Weiskopf N, Hutton C, Josephs O, Deichmann R. Optimal EPI parameters for reduction of susceptibility-induced BOLD sensitivity losses: a whole-brain analysis at 3 T and 1.5 T. Neuroimage 33: 493-504; 2006.

Xiang QS, Ye FQ. Correction for geometric distortion and N/2 ghosting in EPI by phase labeling for additional coordinate encoding (PLACE). Magn Reson Med 57: 731-41; 2007.

Zaitsev M, Hennig J, Speck O. Point spread function mapping with parallel imaging techniques and high acceleration factors: fast, robust, and flexible method for echo-planar imaging distortion correction. Magn Reson Med 52: 1156-66; 2004.