Introduction to fMRI Course

Fa-Hsuan Lin fhlin@ntu.edu.tw

Highlights

- EPI favors high bandwidth acquisitions to reduce susceptibility artifacts.
- fMRI acquisition methods critically depend on the targeted spatiotemporal resolution.
- The spatiotemporal resolution of fMRI can be optimized by a combination of k-space trajectory design, receiver coil array, and reconstruction algorithm.
- Sequences using spin-echo or gradient-echo, the echo time, and the flip angle can tune the sensitivity of fMRI acquisitions.
- Physiological noise is a dominant noise source in high-field fMRI experiments.

Data acquisition considerations

Functional MRI (fMRI) in humans[1] using the blood-oxygen level dependent (BOLD) contrast[2,3] allows non-invasive detection of hemodynamic responses associated with neural activity. Neuronal activity results in a complex series of hemodynamic changes in blood flow, volume, and oxygenation, whose net effect results is BOLD signal increase or decrease[4]. Single-shot echo-planar imaging (EPI), which has been the principal technology for fMRI, has a sampling rate of 1–3 s and spatial resolution of 3–5 mm for 3D brain imaging. Note that spiral imaging (for review, see [5]) is also a widely used method in fMRI. Since EPI and spiral imaging share a lot of features, here we only discuss EPI.

The readout of EPI typically lasts for around 50–100 ms, which makes it susceptible to any disturbance during data acquisition. Notably, susceptibility can disturb the resonance frequency distribution and cause image distortion. Meanwhile, EPI can also suffer from signal loss due to intra-voxel dephasing. Taken together, acquisition methods with (effectively) high bandwidth and short readout without compromising the FOV and spatial resolution are desired.

High spatiotemporal resolution fMRI acquisition

The desired spatiotemporal resolution of EPI in an fMRI experiment depends on the hypothesis to be tested. The canonical hemodynamic response, the impulse response of the BOLD signal after a brief neuronal activity, has been commonly considered temporally smooth with most of the energy below 0.1 Hz. This spectral property supports the protocol of setting EPI repetition time (TR, the time between two consecutive volume acquisition) to about 2 s. While this TR is used in most fMRI experiments, faster EPI with a shorter TR may be favorable in experiments attempting to critically monitor physiological noise and interested in the fine temporal features of the BOLD signal.

Partial Fourier acquisition is a method of reducing the data acquisition time. It is based on the mathematical assumption that the *k*-space data points are partially redundant. In practice, one can take 6/8 of the *k*-space by leaving out the ¼ of high spatial harmonics *k*-space to save 25% of the data acquisition time at the cost of reduced signal-to-noise ratio.

Multi-shot sequences separate the *k*-space traversal into multiple acquisitions. Effectively this method can increase the bandwidth and reduce the echo spacing (thus reduce image distortion caused by susceptibility). However, multi-shot sequences can also be susceptible to shot-to-shot instabilities caused by subject motion and/or physiological noise[6]. Importantly, the sampling rate of a multi-shot sequence is much lower than that of a single-shot sequence.

Sharing part of the *k*-space data during dynamic scanning can also improve the sampling rate at the cost of losing some dynamic information. Key-hole imaging[7,8] is a method that only updates the central part of the k-space in a dynamic scan. Thus the sampling rate can be improved without

Proc. Intl. Soc. Mag. Reson. Med. 23 (2015)

reducing the spatial resolution. However, the contrast can be reduced since the high spatial harmonic information is repetitively used.

Parallel MRI is a method of reconstructing images using spatial information derived from multichannel RF receiver coil arrays. Parallel MRI can dramatically improve the sampling rate of dynamic MRI because the spatial encoding no longer completely depends on gradient, but rather the combination gradient and RF coil sensitivity[9-11]. Accelerated multi-slice EPI acquisitions based on simultaneous excitation, simultaneous echo refocusing, and signal separation using coil sensitivity profiles have been demonstrated at both 3T and 7T, offering maximal full-brain sampling resolutions of about 0.4 seconds [12-14]. There are also methods of single-shot highly accelerated fMRI affording a sampling rate up to 10 Hz (TR = 0.1 s) with whole-brain coverage [15-17]. Preliminary results suggest that the BOLD signal can carry physiologically meaningful information at the time scale of hundreds of milliseconds [18,19]. However, these methods have to lower the spatial resolution in order to achieve a high sampling rate.

Aside from improving the temporal resolution of fMRI acquisition, there have also been efforts in pushing the limits of spatial resolution, which can be implemented by using specialized gradient coils and/or parallel MRI methods. Together with an advanced structural MRI reconstruction, EPI of 1 mm^3 isotropic resolution has been demonstrated to analyze the specificity of cortical laminar layers[20]. The methods of high spatial resolution fMRI have brought remarkable results. For example, in characterizing the human visual system, there have been reports on ocular dominance columns [21] and orientation dominance columns [22] mapping.

Optimizing the sensitivity of fMRI acquisitions

Draining veins can cause strong BOLD signal in typical gradient-echo-type sequences. This can strongly bias the estimation of true site of neuronal activity. Spin-echo-type sequences have been suggested to have higher specificity of the extra-vascular BOLD signal than gradient-echo-type sequences[23,24]. However, one of the challenges in spin-echo-type sequences is the reduced sensitivity[25,26]. At high fields, spin-echo magnetization preparation raises further concerns on specific-absorption rate and the sensitivity to inaccurate spin-echo due to a shorter wavelength.

The other imaging parameter to be optimized in fMRI experiment is the flip angle. It has been well-known that the flip angle can be set to the Ernst angle (arccos(exp(-TR/T1)) to maximize the signal strength. A recent study shows that, the flip angle can be set below this Ernst angle without detrimental effects when physiological noise is taken into consideration[27].

Similarly, the echo time (TE) should be also optimized in fMRI. Since BOLD is a T2*-weighted contrast, it can be derived that setting TE to T2* can obtain the maximal sensitivity. The T2* value depends on the magnetic field strength. However, TE = 30 ms and 20 ms has been quite commonly used in 3T and 7T studies, respectively. Note that T2* of the gray matter can also change among brain areas. Thus TE may be further tuned to improve the BOLD signal sensitivity if local T2* is known.

Physiological noise

The noise sources confounding the BOLD-contrast fMRI data processing can be categorized into two types: system noise and sample noise. System noise can arise from suboptimal instrumental performance. This includes, but is not limited to, thermal noise in the radio-frequency coils, preamplifiers, and other electronic components in the receiver processing chain. Sample noise is related to the properties of the object to be imaged. For example, resistive and dielectric losses due to the presence of the sample inside the RF coil contribute to sample noise. In fMRI experiments, motion during data acquisition is another significant source of noise [28]. Motion effects can be effectively reduced by either restricting head movement of the participant inside the RF coil or using image volume alignment to reduce image-to-image signal variation under the assumption of rigid body motion between acquisitions [29,30]. Other sources of sample noise can result from intrinsic physiological processes. In fMRI experiments, physiological noise can be further separated into

echo-time and non-echo-time dependent components [31], with the latter component closely related to periodic cardiac and respiratory activity. Comparing system and sample noise in terms of improving contrast-to-noise ratio (CNR) in high field fMRI experiments, the latter constitutes the major limitation. Physiological noise is generally proportional to the signal and going to higher field strength increases its contribution to overall variance [31]. In addition, at a given field strength (*e.g.* 3T), improvements to receiver hardware and signal reception [32] can result in physiological noise dominating the variance in fMRI time-course data.

Physiological noise in fMRI data can be reduced by a few approaches. First, it is common to use the pulse oximeter and respiration belt to monitor the cardiac and respiratory cycles synchronously with EPI acquisitions. Post-processing methods (DRIFTER[33] and RETROICOR[34], for example) can computationally remove these two major fluctuations from EPI time series. Alternatively, it has been suggested using high spatial resolution protocol to reduce physiological noise. This is because the physiological noise scales with the voxel size. Averaging imaging voxels of high spatial resolution can thus reduce the noise level without compromising the signal strength. Lastly, acquiring fMRI at the rate higher than the Nyquist frequency, *e.g.* 3 Hz, allows straightforward filtering of both cardiac and respiratory fluctuations.

Other concerns in fMRI data acquisitions

Since EPI uses a fast switching gradient to complete the *k*-space traversal in a fraction of a second, the Lorentz force generated by the gradient coil generates strong acoustic noise, which can even elicit complex neuronal responses [35]. One way to reduce the acoustic noise is tuning the echo-spacing to avoid acquiring data at peaks of acoustic resonance frequencies. However, cautions must be taken because echo-spacing also directly affects the image distortion in EPI.

Finally, scanning experiment participants with care and necessary interactions (via microphone, for example) can always be valuable to ensure the quality of fMRI data. It is also helpful to monitor and check fMRI images on the scanner console during acquisition to ensure both the participants are following your instructions and the MRI scanner is stable. Your immediate attention may bring both safety to your participants and high quality images to you.

References

1 Belliveau J., Kennedy D., McKinstry R. *et al.*Science.1991; 254:716-719.
2 Kwong K. K., Belliveau J. W., Chesler D. A. *et al.*Proc Natl Acad Sci U S A.1992; 89:5675-5679.
3 Ogawa S., Lee T. M., Kay A. R. *et al.*Proc Natl Acad Sci U S A.1990; 87:9868-9872.
4 Logothetis N. K., Pauls J., Augath M. *et al.*Nature.2001; 412:150-157.
5 Glover G. H.Neuroimage.2012; 62:706-712.
6 Glover G. H. & Lee A. T.Magn Reson Med.1995; 33:624-635.
7 van Vaals J. J., Brummer M. E., Dixon W. T. *et al.*J Magn Reson Imaging.1993; 3:671-675.
8 Jones R. A., Haraldseth O., Muller T. B. *et al.*Magn Reson Med.1993; 29:830-834.
9 Griswold M. A., Jakob P. M., Heidemann R. M. *et al.*Magn Reson Med.2002; 47:1202-1210.
10 Pruessmann K. P., Weiger M., Scheidegger M. B. *et al.*Magn Reson Med.1999; 42:952-962.
11 Sodickson D. K. & Manning W. J.Magn Reson Med.1997; 38:591-603.
12 Feinberg D. A., Moeller S., Smith S. M. *et al.*PLoS ONE.2010; 5:e15710.
13 Larkman D. J., Hajnal J. V., Herlihy A. H. *et al.*J Magn Reson Imaging.2001; 13:313-317.
14 Setsompop K., Gagoski B. A., Polimeni J. R. *et al.*Magn Reson Med.2011;

15 Hennig J., Zhong K. & Speck O.Neuroimage.2007; 34:212-219.
16 Lin F.-H., Wald L. L., Ahlfors S. P. *et al.*Magn Reson Med.2006; 56:787-802.
17 Lin F. H., Witzel T., Mandeville J. B. *et al.*Neuroimage.2008; 42:230-247.
18 Lin F. H., Ahveninen J., Raij T. *et al.*PLoS One.2014; 9:e100319.
19 Lin F. H., Witzel T., Raij T. *et al.*Neuroimage.2013; 78:372-384.
20 Polimeni J. R., Fischl B., Greve D. N. *et al.*Neuroimage.2010; 52:1334-1346.
21 Cheng K., Waggoner R. A. & Tanaka K.Neuron.2001; 32:359-374.
22 Yacoub E., Harel N. & Ugurbil K.Proc Natl Acad Sci U S A.2008; 105:10607-10612.
23 Duong T. Q., Yacoub E., Adriany G. *et al.*Magn Reson Med.2003; 49:1019-1027.
24 Yacoub E., Shmuel A., Logothetis N. *et al.*Neuroimage.2007; 37:1161-1177.
25 Boxerman J. L., Hamberg L. M., Rosen B. R. *et al.*Magn Reson Med.1995; 34:555-566.
26 Ogawa S., Menon R. S., Tank D. W. *et al.*Biophys J.1993; 64:803-812.
27 Gonzalez-Castillo J., Roopchansingh V., Bandettini P. A. *et al.*Neuroimage.2011; 54:2764-2778.
28 Hajnal J. V., Myers R., Oatridge A. *et al.*Magn Reson Med.1994; 31:283-291.
29 Cox R. W. & Jesmanowicz A.Magn Reson Med.1999; 42:1014-1018.
30 Woods R. P., Grafton S. T., Holmes C. J. *et al.*J Comput Assist Tomogr.1998; 22:139-152.
31 Kruger G. & Glover G. H.Magn Reson Med.2001; 46:631-637.
32 Bodurka J., Ye F., Petridou N. *et al.*Neuroimage.2007; 34:542-549.
33 Sarkka S., Solin A., Nummenmaa A. *et al.*Neuroimage.2012; 60:1517-1527.
34 Glover G. H., Li T. Q. & Ress D.Magn Reson Med.2000; 44:162-167.
35 Zhang N., Zhu X. H. & Chen W.Magn Reson Med.2005; 54:258-263.