Disentangling physiological and task related information in fast multiband data using temporal ICA

Klaudius Kalcher[1,2], Roland Boubela[1,2], Christian Nasel[3], and Ewald Moser[1,2]

[1]MR Center of Excellence, Medical University of Vienna, Vienna, Austria, [2]Department for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria, [3]Department of Radiology, State Clinical Center Danube District, Tulln, Lower Austria, Austria

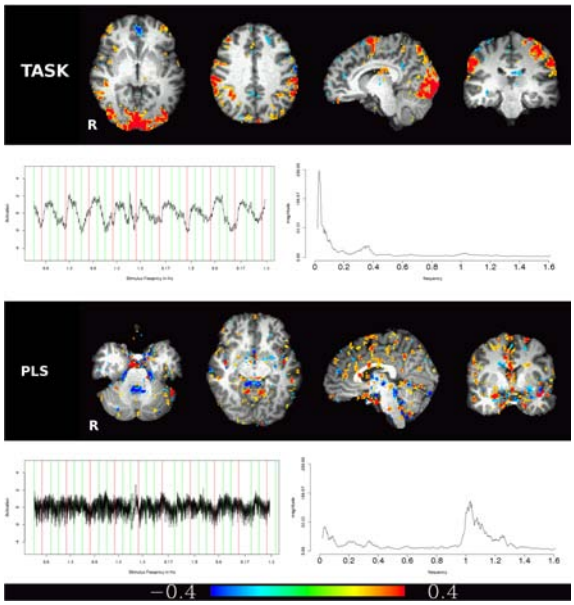
Target Audience: Researchers and users interested in functional MRI, BOLD response function extraction, artifact reduction and protocol optimization.

Purpose: In this work we explore improvements in data acquisition and analysis to measure fMRI data at 3 Tesla with increased spatial and temporal resolution, leading to increased functional contrast and, ultimately, novel possibilities to identify specific signals in the brain with increased specificity.

Background: Functional MRI at 3 T has become a workhorse for the neurosciences, e.g., neurology, psychology, and psychiatry, enabling non-invasive investigation of brain function and connectivity. However, BOLD-based fMRI is a rather indirect measure of brain function, confounded by fluctuation related signals, e.g. head or brain motion, brain pulsation, blood flow, intermixed with susceptibility differences close or distant to the region of neuronal activity. Even though a plethora of preprocessing strategies have been published to address these confounds, their efficiency is still under discussion. In particular, high-frequency physiological signal fluctuations closely related to brain supply may mask BOLD signal changes related to "true" neuronal activation. Here we explore recent technical and methodological advancements aimed at disentangling these various components, employing fast multiband sequences to critically sample them and temporal ICA to separate these different signal sources from the measured data.

Methods: Ten healthy subjects (5 females / 5 males, mean age 31.9 y, SD 8.9 y) were recruited at Medical University of Vienna, written informed consent was provided and the study was approved by the local IRB. MRI scans were performed on a TIM Trio using the standard 32-channel head coil and whole-body gradients (Siemens Medical Solutions, Erlangen, Germany). To induce a reliable BOLD response in the visual and motor cortex the subjects performed a task consisting of a visual stimulus of a checkerboard flickering at 8 Hz alternating with a block of rest (looking at a fixation point), each block being active for 15 seconds. During the flickering of the checkerboard subjects were instructed to perform conscious tapping with their right hand index finger and middle finger against their thumb. The BOLD fluctuations were measured with an advanced, low TR multi-band EPI sequence (Feinberg, 2010) using 1.7x1.7x2.0 mm^3 resolution, 2mm gap, 128 x 128, 32 axial slices, TE/TR = 31/333 ms, flip angle 30°, multiband factor 8, BW=1776 Hz/Pixel, collecting 660 volumes. In addition, high-resolution anatomical images (MPRAGE, 1x1x1.1mm^3, 160 axial slices, TE/TR = 4.21/2300ms, flip angle 9^0, inversion time 900ms) were acquired. All data were preprocessed with a combination of AFNI and FSL, using an analysis framework in R (Boubela et al., 2012; R Development Core Team, 2013). Anatomical images were skull stripped and normalized to MNI152 standard space. Functional images were corrected for intensity inhomogeneity using a bias field estimation by FSL FAST, skull stripped and realigned to the 600th volume. Subsequently, functional images were aligned to the anatomical images in MNI152 standard space and resampled to 2 x 2 x 2 mm^3 isotropic resolution, and motion parameters (3 translations and 3 rotations) were regressed out using a generalized linear model (GLM). After preprocessing, voxel time-series were scaled to mean 0 and standard deviation 1. Temporal ICA was performed using R, where the step of prewhitening and dimensionality reduction prior to ICA via PCA was computed by an iterative algorithm for singular value decomposition. ICA itself was performed via the fastICA algorithm (Hyvärinen, 1999; Boubela et al. 2013). Time series, their power spectra as well as the corresponding spatial maps were computed for all tICA components.

Results: Temporal ICA could identify a unique task components with mostly low frequency fluctuations correlated with the stimulus timings and with activation located in the occipital as well as the motor cortex. In addition, high-frequency pulsations could be differentiated from the other signals as separate components, most easily distinguished by their peak in the power spectrum at about 1 Hz. (See Fig. 1)



Discussion: Initial results indicate that fast (TR<0.5s) scanning may help to identify physiologic components and distinguish them from other signal sources, thus increasing tSNR and functional contrast. In addition, biological variability can be studied and task performance can be correlated more readily to other measures. This should increase specificity and reliability in fMRI studies. Furthermore, the identification of these high-frequency components could lead up to the possibility of investigating physiological signals and their variability during scanning, which could eventually be recognized as a source of novel information rather than a nuisance. As we are currently still undersampling the complexity of the brain, even at a rather coarse macroscopic level, we should be very cautious in the interpretation of neuroscientific findings, in particular when comparing different groups (e.g., age, sex, medication, pathology, etc.). From a technical point of view our goal should be to sample brain activity at layer specific resolution with low TR, covering as much of the brain as possible without violating SAR limits (Moser & Ranjeva, 2010). We hope to stimulate discussion towards a better understanding and a more quantitative use of fMRI.

Conclusion: The combination of low TR (<500ms) and ICA leads to a better identification of the task-related HRF, including both its spatial extent and its time course – indeed well enough to examine variations in amplitude, time-to-peak and shape across the brain and between subjects. Given the complex physiological mechanisms which drive the brain, not only when performing tasks but also during rest, only low TR data may be adequate to analyze these data and differentiate between signal changes related to neuronal processes and processes of other origin.

References: [1] Boubela, R.N. (2012), *Mag. Reson. Mater. Phy.*, 25, 313–20. [2] Baglama, J., and Reichel, L. (2005), SIAM J. Sci. Comput. 27, 19-42. [3] Hyvärinen, A. (1999), IEEE Trans. Neural Netw., 10, 626–34 [4] Boubela, R.N., Front. Hum. Neurosci., (2013) 7, 168 [5] Moser, E., Ranjeva, J.-P. Mag. Reson. Mater. Phy., (2010) 23, 276-78

Acknowledgements: This work was funded by the Austrian Science Fund, FWF Projects Nr. 22813-B09 and 23533-B13.