Upper Bound Estimation of Neuronal Current-Induced Magnetic Field Changes in Humans

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Introduction: Direct MRI detection of neuronal activity is theoretically possible since the resulting ionic currents produce transient magnetic field changes that affect the measured signal. Since MRI/fMRI measurements have many noise components the question of whether these field changes are large enough to be detected reliably is an ongoing topic of debate. In this study, we employed EEG time series statistics to aid in the detection of these small effects and determine the lower limits of detectability in phantoms and humans [1,2]. Tang and Norcia detected visual steady-state evoked responses in EEG by employing adaptive filters to give multiple estimates of the magnitude and phase of the stimulation frequency f_0 for use in a T_{circ}^2 statistic [2]. By splitting the data into numerous temporal bins, this statistic can determine whether f_0 is significantly present in the noisy time series. Due to the slow convergence of adaptive filters attributable to the low sampling rate of fMRI, simple DFTs were used in this study to provide the magnitude and phase estimates. The sensitivity of this technique was investigated using a current phantom, simulations and human activation data. From the data, we have obtained an upper bound estimate of the size of the neuronal current effect using fMRI in humans on the order of 1nT.

Methods *Imaging Setup:* 3T General Electric HDx whole body MRI scanner equipped with an 8-element receive-only brain array. Single shot, full k-space gradient recalled EPI was used for all functional scans. Single slice fMRI with TR=70ms, TE=27ms, matrix=64x64, FOV/slice=24cm/4mm, flip angle=20°, reps=4200 was performed. Both magnitude and phase images were reconstructed. *Current Phantom*: A phantom with an electrically insulated thin copper wire (60 mm diameter) supported by a plastic frame immersed in a copper sulfate water based solution with a T_2*=36±16ms was used (see [3]). To provide an electric current, a pulse generator connected with a 10kΩ resistor in series was employed. Six single axial slice (orientation along the length of the wire) runs were collected whilst supplying a sine wave with amplitude of 50, 10, 8, 6, 4 and 2μA respectively. The frequency of the sine wave was 3.57Hz giving an oversampling factor of 4. A further eleven runs were collected with a coronal slice (orientation perpendicular to the wire) whilst supplying a sine wave of 10μA throughout. *Simulations*: Eleven resting state datasets were collected from a volunteer with a single axial slice through the visual cortex. Artificial 3.57Hz sine wave activations were inserted into these noise datasets with effect sizes of 0, 0.02%, 0.04%, 0.08% and 0.1%. *Activation data:* A contrast reversing checkerboard supplied 5 subjects with a constant visual stimulus at a frequency of 3.57Hz, phase-locked to the beginning of each run. Eleven runs were collected for each subject with a single slice through the visual cortex (the most active BOLD slice determined by a visual localizer). *Analysis:* Two types of analysis were performed on all datasets, a standard DFT and the T_{circ}^2 technique. Before the standard DFT was performed, datasets with 11 identical runs were concatenated together. To perform the T_{circ}^2 method datasets were split into small temporal bins (100 timepoints long for short current phantom runs, 1000 time points long for all others) and individual DFTs were performed on each. The magnitude and phase at the stimulation frequency (3.57Hz) were calculated for each of the bins. The T_{circ}^2 formula was used and the result converted into a $SNR_{T_{circ}^2}$ value as described in Tang and Norcia [1]. If $SNR_{T_{circ}^2} > 1$, there is a significant signal present at the stimulation frequency.

Results and Discussion: A current as small as 2μA is detectable in the current phantom. Figure 1 displays the results from the magnitude data with the left most column depicting the normalized power at the stimulation frequency using the standard DFT technique. In the 8μA run (corresponding to a B_0 change of 0.4nT in the voxel adjacent to the wire), the wires are still clearly visible and remain so until the current is reduced to 2μA (ΔB_0 =0.1nT in the voxel adjacent to the wire). Although the $SNR_{T_{circ}^2}$ method (displayed in the center column) is only slightly more sensitive to the effects of the 2μA current, the main advantage is that it is a statistical measure with a specific cutoff threshold. The right column in Figure 1 shows the average DFT spectrum across the 50 most active voxels along with the corresponding $SNR_{T_{circ}^2}$ average (±std). It is evident that at a current smaller than 2μA the effect will become undetectable. The phase images give almost identical results but are slightly less sensitive to the effect: the average $SNR_{T_{circ}^2}$ in the 2μA condition for the magnitude image is 0.78±0.36 compared with 0.71±0.4 in the phase image.

However, there are voxels further away that also exhibit the effect. The smallest field change detectable was derived from the axial current phantom images; the furthest activated voxel from the wires determined by the $SNR_{T_{circ}^2}$ method was 32mm away translating into a ΔB_0 of ~62pT.

Detection power is highly dependent on the noise characteristics and a B_0 change of 62pT would not be detectable in human visual cortex where the TSNR is lower: 82±22 compared with 357±80 in the current phantom. Figure 2 shows the simulation results using noise drawn from the visual cortex and demonstrates that an effect size of ~0.04% is the minimum detectable above the noise. Since 100μA block localizer yielded an effect size of 0.9%±0.07%, this translates into a current of 4.6μA or ΔB_0=0.26nT. This is four times the size of the minimum field change detectable in the phantom, corresponding to a TSNR four times lower. Assuming a linear correspondence, the relationship between TSNR and detectable field change size (DFCS) in a voxel beside the wire is given by: DFCS = 3.17×10^{-12} * TSNR.

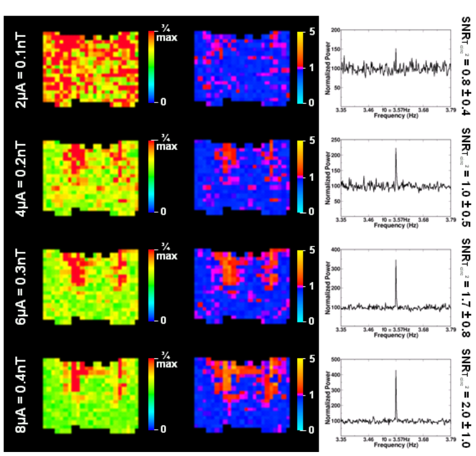

Figure 1

The average $SNR_{T_{circ}^2}$ in the visual cortex of the 5 subjects in the activation data condition was 0.42±0.19 in the magnitude data and 0.53±0.22 in the phase data, neither of which where greater than noise. This negative result suggests that the neuronal current effect must be smaller than 0.26nT, assuming a perfectly sinusoidal response to the visual stimulus. This may not be the case; however, this technique has been employed successfully in detecting steady-state evoked potentials in EEG whilst making this assumption [2]. Although the field changes due to neuronal currents may be higher, it is unlikely that they are more than 1nT, otherwise detection with this technique would be possible.

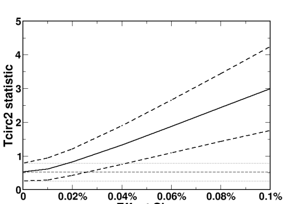

Figure 2

References:

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