Detection of MR signal modulation due to magnetic fields from axonal currents in the human visual system using LED stimulation

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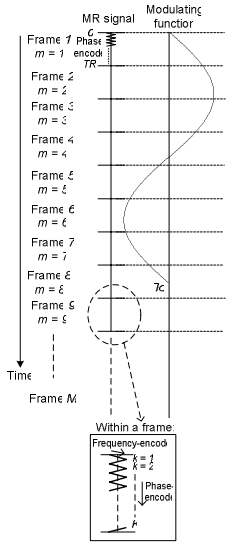
Introduction: Axonal currents produce weak, transient magnetic fields, and the hypothesis being investigated here is that the components of these parallel to the B_o field can potentially modulate the MR signal, thus providing a means of direct detection of nerve impulses. A theory for the phase and amplitude changes of the MR signal over time due to such external magnetic fields has been developed to predict this modulation. This study aims to directly detect the in-vivo axonal currents in the human optic nerve, visual cortex and corpus callosum, with LED stimulation using a short *TR* gradient echo EPI sequence with intermediate *TE* at *1.5T* and *3.0T*.

Theory: Figure 1 illustrates the time series for data acquisition assuming a sinusoidal modulating magnetic field. During each frame the sinusoid completes only a fraction of its cycle, and the phase change between individual phase-encode views will be a further sub-fraction of this. The sinusoidal modulating function at the k^{th} phase-encode view in the m^{th} frame is $F(k,m) = I_o \sin(\omega_o((m-1)TR + k\Delta t))$ where I_o is the peak current and $\Delta t = TR/K$, where K is the number of phase-encode views per frame. If the MR signal from a particular proton spin isochromat with no modulation is S, then the signal due to a modulating field from an axonal 'wire' at distance r is $S_1(k,m) = S \times e^{j\phi(k,m)}$ where $\phi(k,m) = \gamma TE\mu_o F(k,m)/(2\pi r)$ assuming the field is co-polar with B_o at the spins. The 2D image of each frame is obtained by Fourier transformation of the signal along the frequency and phase axes, and thus for the m^{th} frame the Fourier transform in the phase direction yields $\tilde{S}_1(\omega_k, m) = \tilde{S} * \Im|_k \left\{e^{j\phi(k,m)}\right\}$. The original image is therefore convolved with the modulation spectrum along the phase axis. The phase function in continuous time is $\phi = \Delta\phi \sin(\omega_o t)$ so that $e^{j\Delta\phi \sin(\omega_o t)} = \sum_{n=-\infty}^{\infty} J_n(\Delta\phi) e^{jn\omega_o t}$ where $\Delta\phi = \gamma TE\mu_o I_o/(2\pi r)$.

Figure 1: Illustration of MR signal modulation



For discrete time intervals within a frame m, this continuous function is essentially sampled at intervals of Δt, and is then further multiplied by a *rect* windowing function of width TR to account for the finite number of samples to yield $\sum_{n=-\infty}^{\infty} J_n(\Delta\phi) e^{jn\omega_o t} \times \sum_{k=-\infty}^{\infty} \delta(t - k\Delta t) \times rect\left(\frac{t-(m-1/2)TR}{TR}\right) * \delta(t - t_m)$ whose spectrum is then

$\Im|_k \left\{e^{j\phi(k,m)}\right\} = 2\pi \sum_{n=-\infty}^{\infty} J_n(\Delta\phi)\delta(\omega_k - n\omega_o) * \frac{2\pi}{\Delta t} \sum_{i=-\infty}^{\infty} \delta\left(\omega_k - i\frac{2\pi}{\Delta t}\right) * (TR)Sa\left(\omega_k \frac{TR}{2}\right) \times e^{-j\omega_k t_m}$. This represents the image convolving function in the phase-encode direction for a particular frame m due to the phase modulation of a proton spin isochromat by an external magnetic field from a 'wire' axon. The term involving t_m accounts for the position of the *rect* function within the modulation cycle since $TR < T_o$, and transforms to a phase shift in the frequency domain where $t_m = (m-1)TR$. Over successive frames the voxels containing such proton spin isochromats will be modulated by this image convolving function, so that a 1D Fourier transform down the time series m at such an affected voxel will yield spectral components of the axonal modulating field. Repeating this over a selected area in the frame thus produces a 2D frequency map showing the spatial distribution of the spectral response. A symmetrical intra-voxel field distribution, which can be plausibly hypothesized for a nerve containing millions of axons, would result in phase cancellation within a voxel and hence only amplitude changes would be expected, whereas an asymmetrical intra-voxel field distribution would produce both phase and amplitude modulation.

Method: A LED light source was used for visual stimulation on the *1.5T* MR system with a *280mm* quadrature head coil, and on the *3.0T* MR system with a 6 channel SENSE head coil. The GE-EPI sequence parameters were: *TR = 158ms* (*1.5T*) or *77ms* (*3T*), *TE = 30ms*, matrix *K = 80, M=500* time frames, *FOV = 240mm*, slice thickness = *5mm*, *FA = 90°*. Both magnitude and complex data were acquired for comparison. Swimming goggles were modified to hold a set of optical fibres for transmitting light from the LED's (located outside the screened room) to one or both eyes. The LED frequencies (*0.7-6.0Hz*) were chosen to be easily differentiated from the heartbeat and respiration rates. Subsequently two signal generators were used to apply two different asynchronous stimulus frequencies to the same eye concurrently. The experiments were performed in a darkened room to ensure no other stimuli produced visual interference, with dark adapted volunteers. A total of *61* in-vivo experiments were performed on two adult human subjects. Motion was analysed using 2D auto-correlation; any data sets with motion components were counted as 'not detected'. A mean magnitude or phase signal from an ROI in the optic nerve, visual cortex or corpus callosum was used to create a 1D time series from successive time frames, which was then Fourier transformed. The spectra were scaled to represent the percentage modulation of the fully relaxed equilibrium signal by correcting for relaxation time effects using the standard equation for signal dependence of a GE sequence and using *T1 = 718ms* at *1.5T* and *T1 = 832ms* at *3.0T*.

Results: Figure 2 shows a *2x1*-voxel ROI in the optic nerve, which was used to produce the frequency spectra in Figure 3 from magnitude data. Two LED responses were detected with simultaneous *0.7Hz* and *2.5Hz* stimuli at *0.3%* (*SNR=6:1*) and *0.17%* (*SNR=3:1*) respectively in Figure 3(b) after subtracting the background noise, but were not found in control data in Figure 3(a). The frequency maps in Figure 4 also differentiate the LED responses at the respective stimulus frequency. The frequency maps acquired with and without stimulation in the optic nerve ROI were assessed using a Student's t-test ($p < 0.05$) with Bonferroni correction to verify significant difference. There were no significant spectral components in the phase data. Tables 1 and 2 summarize all the in-vivo experiments for magnitude data, showing a significant detection rate of 51%. The mean magnitude signal change relative to the fully relaxed equilibrium signal was ~0.15% for the optic nerve, ~0.06% for the visual cortex, and ~0.02% for the corpus callosum. These responses correspond to a mean predicted RMS axonal field range of *0.1-1.2nT* using the Lorentzian field model, with the absence of phase modulation implying a symmetrical intra-voxel field distribution.

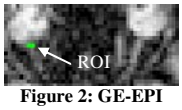


Figure 2: GE-EPI magnitude image

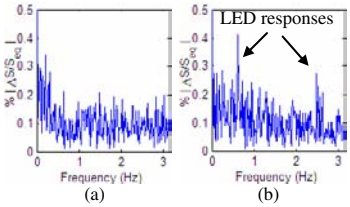


Figure 3: Frequency spectra: (a) without stimulation, (b) with simultaneous 0.7Hz and 2.5Hz LEDs stimulus.

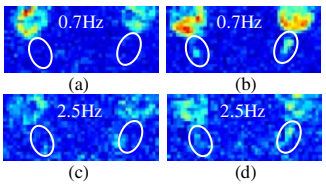


Figure 4: Frequency map at LED stimulus frequency: (a) and (c) from non-stimulated data, (b) and (d) from stimulated data.

Table 1: In-vivo experiments with 2 simultaneous LEDs stimuli

Freq (Hz)	Lower freq		Higher freq	
	detected	not	detected	not
0.7 & 2.5	1	1	1	1
0.8 & 1.6	-	4	3	1
0.8 & 1.7	2	2	3	1
1.5 & 2.5	-	4	-	4
2.0 & 3.0	1	1	-	2
Total	**4**	**12**	**7**	**9**

Table 2: In-vivo experiments with 1 LED stimulus

Freq (Hz)	detected	not
1.3	2	4
1.5	3	1
1.6	6	2
1.9	-	1
2.0	13	1
2.5	2	2
2.7	2	-
3.0	11	7
3.5	3	3
4.0	5	3
4.5	2	5
5.0	-	3
5.5	-	3
6.0	1	3
Total	**50**	**38**

Conclusion: This study provides preliminary evidence for the detection of axonal currents in the human visual system, assuming modulation of the MR signal by their magnetic fields. In-vivo MR signal fluctuations have been shown to be consistent with an existing Lorentzian model for symmetrical axonal field distributions within a voxel, from which estimates of axonal field strengths have been made.