# Modelling optic nerve axonal fields for direct neuronal detection MR studies

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**INTRODUCTION** A number of studies have now shown that direct detection of neuronal firing may be possible by MRI. The optic nerve carries all visual information from the eye to the brain through 1 million axonal fibres and is a particularly promising target for these measurements. A simulation of the Bo field modulation which could feasibly be produced by the optic nerve has been developed to help understand the factors affecting the ability of MR to measure weak axonal fields in-vivo and hence optimise experimental technique. Visual information is encoded in the eye as a set of action potentials from retinal ganglion cells following pre-processing of the photo-receptor voltages by retinal horizontal, amacrine and bipolar cells. The Hodgkin-Huxley equations were calculated for each element in an array of model ganglion cell axons which were assumed to act as voltage to pulse frequency converters. The dependence of the modulating waveform on relative action potential firing start time was investigated.

**METHODS** Axon firing was simulated using the Hodgkin-Huxley (HH) equations (1) programmed in MATLAB (Mathworks Inc., USA). A 1000x1000 array of contrast values was assumed to produce a voltage at each of the model ganglion cells for a duration of 250 milliseconds which generated an action potential response train. To speed up the calculation without loss of generality, each contrast value along a line of the array was set to the same value producing a 2D grayscale ramp. Voltage and current waveforms were calculated for each location every 25 μs and then the current values were summed over the entire array for a total of 300 milliseconds to produce the overall temporal response from the model optic nerve. The locations with highest contrast values were programmed to fire first and the locations with lower contrast values were set to fire at later times in a number of different simulations. The start delay between array lines was adjusted from 0 ms in 17.5ms increments up to a total delay of 70 ms to investigate the effect on the summed current waveforms. The simulated modulating waveforms were applied to a D-A converter and used to modulate a 6 coil phantom with between 1 and 6 loops per coil producing calculated fields in the range 0.27 – 94nT, which produced ghost images using the GRACE gradient echo technique with TR=13ms, TE=4 ms, FOV = 400mm, SLT = 5mm on a 3T Intera MR system (Philips, Best,NL). The positions of the ghost images can be calculated from the formula S = f x TR x FOV x NEX x m [1] where s is the distance of the ghost from the object, f is the stimulus frequency and m is the order of the ghost harmonic (2). GRACE images were also acquired at 3T from three dark adapted adult volunteers with TR=200ms,TE=20 and 39ms, FOV=300mm, NEX=1, Frames = 4 which produced high signal from the optic nerves, in an attempt to observe similar harmonic ghosts in response to a 1.6Hz strobe stimulus. Video images acquired in training sessions prior to MR imaging confirmed there was no stimulus correlated motion of the eyes.

**RESULTS**

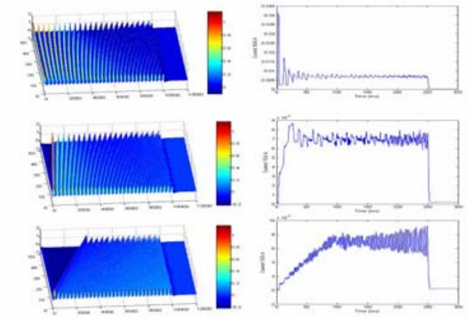

Figure 1

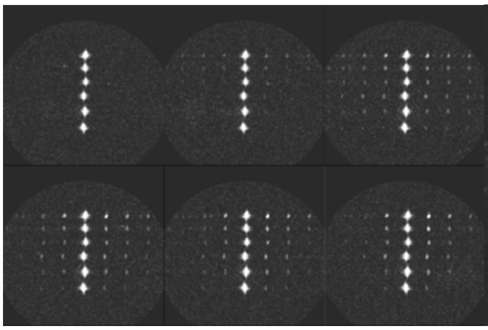

Figure 2

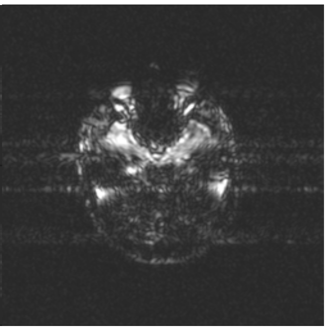

Figure 3

Figure 1 shows action potential surfaces for a linear grayscale contrast (voltage) array at the ganglion cells with 0, 17.5 and 75 ms delays (top to bottom). The integrated current waveforms are shown on the right hand side of Figure 1. It can be seen that an increasing start delay modifies the predicted waveform considerably. Figure 2 shows GRACE images of the phantom using the simulated waveforms corresponding to zero current (top left), 0, 17.5 ms delays top left-right and 35, 52.5, 70ms delays (bottom left-right) for fields in the range 14-84nT. Figure 3 illustrates a TE=39ms GRACE image through the optic nerves. Line profiles integrated over the entire optic nerve showed weak ghosts at the positions calculated from equation (1) and these were significantly different from those acquired without stimulus at $p<0.05$ in two out of three volunteers.

**DISCUSSION AND CONCLUSION** The phantom images presented in this study indicate the ghosting patterns caused by phase modulation of the Bo field by the magnetic fields of the synthesized optic nerve currents. Such patterns might also be expected from the optic nerve in vivo, making the assumption that the simulations are a valid representation of optic nerve output. Applying the simulated waveforms repetitively at a fixed frequency through a digital-analogue converter to a modulating coil in the scanner, in combination with the GRACE analysis technique, now allows us to observe MR images associated with arbitrary time and space dependent contrast functions applied to a HH model optic nerve. The model can be extended to take into account more sophisticated retinal processing such as oscillating potentials linked to spatial correlations as the voltage at each array location can easily be made time dependent. Preliminary experiments in volunteers showed evidence for first harmonic GRACE ghosts in two out of three volunteers. This work may eventually lead to better understanding of primary visual encoding and hence provide input for design of electronic visual prostheses.

**REFERENCES** 1. Hodgkin and Huxley. 1952. JPhysiol;117:500. 2. Yang et al., MRM, 2003;50:633.