MRI of neural currents: numerical study

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Functional MRI (fMRI) contrast generation is based on the slow (relative to the neural activity) changes in blood oxygenation in the vicinity of the activated brain region. In recent years synthesis of fMRI and magneto-encephalography (MEG) has allowed a significant increase in the spatio-temporal resolution in noninvasive brain imaging. However the reconstruction of the current sources generating the MEG signal is intrinsically an ill-posed problem. It is therefore important to develop a fast, non-invasive imaging technique free of ambiguities in source localization. MRI gives the opportunity to develop such a technique with the added benefit of much higher spatial resolution compared to MEG. The current sources in the brain produce local magnetic fields and these fields in principle can be measured as changes in the transverse magnetization relaxation rates similar to susceptibility contrast MRI used in fMRI. MRI is tomographic and neural current reconstruction is a well-defined problem. In the past decade several groups have imaged currents using MRI both in vivo[1] (using external electric stimulation) and in phantoms[2]. Recently[3] it has been suggested that fast changes in the T_2 relaxation rate seen in an echoplanar imaging experiment with visual stimuli in humans is due to a dephasing of the average magnetization caused by local neural currents induced by the stimulus. In this talk we will address the feasibility of using MRI for fast, functional imaging based on the local neural currents (FMRI) using two models of 1 mm^3 of neural tissue. Such development would greatly benefit clinical epileptologists in seizure focus localization .

The first model is based on the local field potentials measured with intracranial electrode array with 22 electrodes (distance between electrodes 150 μm) distributed in the radial direction, perpendicular to the cortical surface[4]. A cylinder of approximately 200 μm in diameter spanning the cortical layers is believed to contribute to the measured signal. In this model we distribute randomly these parallel cylinders of neural tissue in the 1 mm^3 voxel. In addition we assume that the activity in all cylinders is synchronized. The magnitude of the signal is scaled so that the magnetic field observed at 3 cm from the cortex is 3 fT. In designing our model we looked for a brain area and neural stimulus, which maximizes the observed MEG signal. Our preliminary search suggests that medial nerve stimulation generates MEG signals of the order of 300 fT and is one of the strongest signals observed in human subjects. In current MEG experiments approximately 1cm^2 of cortex contributes to the observed signal. Because our voxel encloses 1 mm^2 of cortical surface we scale down the field strength 100 times. The field strength as a function of time is shown in Fig. 1. The upper panel shows the field at 3 cm from the center of the voxel, while the second panel shows the field in the center of the voxel. Half a million particles were generated uniformly in the region of interest, and propagated with 100 moves per each time step (Δt = 0.5 ms), which gives a total of 200,000 moves per particle. For each move, the angles were sampled uniformly, but the displacement was kept fixed, $d = (6\, D_{CSF}\, dt)^{1/2}$, with dt = 5 μs. The time evolution of the dephasing angle and its cosine are shown in Fig. 2. The predicted strength of the signal is compatible with the experimental sensitivity achieved presently, one part in a million routinely observed in fMRI. The second model under development is based on a cortical column consisting of reconstructed neurons embedded in cerebrospinal fluid (CSF). There are two major effects controlling the dephasing of the magnetization in the voxel. The first is related to the spatially and temporally varying magnetic fields produced by neural stimulation. The MEG magnetic field is measured outside the scalp and various calculations show that the neuronal dendritic processes are mainly responsible for the observed signal. In FMRI the dephasing to a large degree measures the local magnetic field and it is not clear *a priori* that axonal currents would not contribute to the signal. The second source of dephasing comes from water diffusion. The diffusion coefficient of the CSF is approximately D_{CSF} = 2 μm^2/msec. In a typical experiment the time necessary to observe the signal is of the order of 200 msec and therefore the variation in the position of a water molecule will be $d = (6D_{CSF}\, t)^{1/2}$ = 49 μm, i.e. 5% of the voxel. Signal propagation from neuron to neuron is fast along the axons (the local magnetic field variation is of the order of 1 msec [5]), and slower along the dendrites (of the order of 10 msec). In addition, there are the much slower leakage currents in the extra-cellular space. The magnetic field of an axon has been measured and its integral over time is close to zero. This means that in the frame of reference rotating with the Larmor frequency of the external magnetic field the total phase accumulated due to the axonal magnetic field will be close to zero and therefore the axonal current contribution to the dephasing of the hydrogen spins can be a consequence of the water diffusion during the axon excitation. Since the typical time duration of this field is 1 msec the variation of the position of the water molecule is approximately 3.5 μm. On this scale the local magnetic field is constant and we conclude that the axonal currents will contribute relatively little to the MRI signal. We will present data from a detailed neuronal model (with anatomically reconstructed neurons) of a cortical column based on a high-performance neuro-simulator developed at the Los Alamos National Laboratory. In our simulations the currents in the extra-cellular space are included and to our knowledge this is the first simulation of its kind.

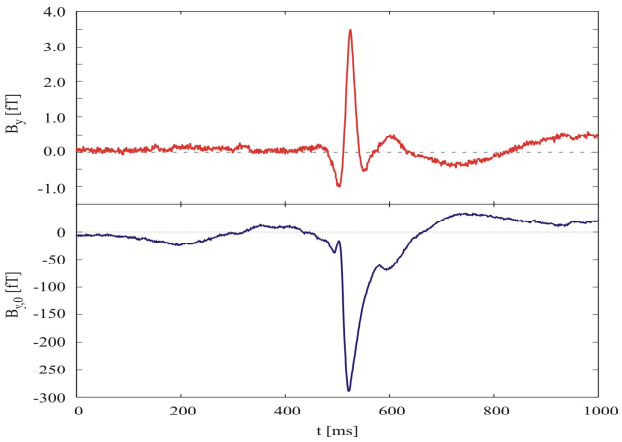

Fig.1

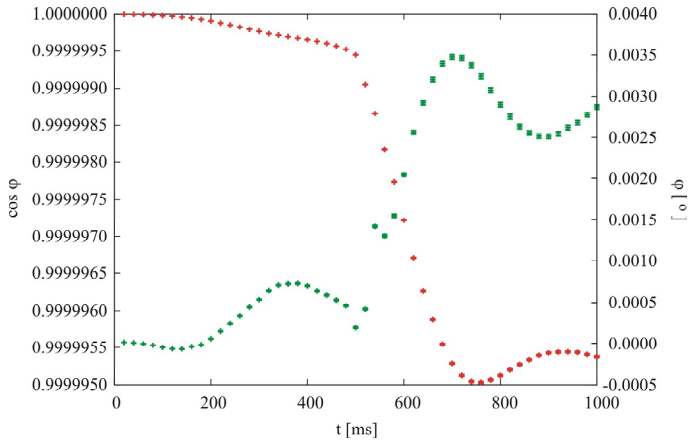

Fig.2.

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