

Realistic Simulations of Neuronal Activity: Contribution to the Debate on Direct Detection of Neuronal-Currents by MRI

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Introduction

Simulations of neurons with realistic morphology and biophysical features are of importance to evaluate the feasibility of direct detection of neuronal activity by neuronal current MRI (nc-MRI).

Methods

Two morphologically and biophysically reconstructed pyramidal neurons, N1 and N2 of the hippocampal CA1 were used, and selected based on the known biophysical details [1]. The reconstructed neurons include: 1) sodium (Na⁺) and A-type potassium channels uniformly distributed over the entire (basal and apical) dendritic arborisation, with peak conductances that increase linearly with the distance from the soma; 2) excitatory AMPA-like conductances placed randomly on oblique dendrites that mimic synaptic inputs from CA3 Schaffer collaterals with synchronous activation. Simulations reproduced the spreading of neuronal currents over the neuronal tree. The NEURON simulator environment (v5.9) [2] was used with a fixed time step feature of 0.005 ms. Multi-compartmental modelizations of the 3D morphometric reconstructions were performed. The magnetic field and the ensuing MRI signals were evaluated inside a cubic voxel (MRI voxel with side lengths = 1.2 mm), on the 27000 vertices of a 3D grid (side lengths=42 μm, n=30 points/side). Neurons were placed uniformly within the voxel, creating a layer of parallel neurons with y as main axis. Branches were represented as collections of finite cylinders and the magnetic field generated by currents in each cylinder was calculated from:

$$B_y^k = -\frac{\mu_0}{4\pi} \frac{x-x_k}{R_k^2} \left[\frac{z-z_{i+1}^k}{\sqrt{R_k^2+(z-z_{i+1}^k)^2}} - \frac{z-z_i^k}{\sqrt{R_k^2+(z-z_i^k)^2}} \right]$$

Here Z is the cylinder orientation; (x_k,y_k) its position with endpoints; (z_i^k, z_{i+1}^k); (x,y,z) the coordinates of a point in space; I_i the current flowing through the ith cylinder at time t; R_k = √((x-x_k)² + (y-y_k)²) the radial distance from the kth cylinder.

Changes in MR signals (phase and magnitude) within the entire voxel were calculated from [4] while the phase at a point (x,y,z) at each time step t was calculated by integrating the phase effects caused by the component of the magnetic field parallel to the static magnetic field B₀. A total of (2n-1)² synchronously active neurons contributed to the total signal, with n² neurons placed inside the voxel and the remainder externally within a distance of 600 μm from the voxel walls. 30 different layers of pyramidal neurons were simulated (runs), each one with the same number of neurons and electrical activity, but with different sets of random rotations of the neurons about the y axis. No T₂* relaxation nor instrumental noise were taken into account; nuclear spins were uniformly distributed over the voxel.

Results and discussion

Figures 1a and 1b show the temporal evolution of the phase distributions (averaged and RMS values for the ensemble of runs at each time step) for neurons N1, and N2, respectively, for different orientations of B₀ (y=parallel; x,z: perpendicular) relative to the neuronal axis. In general, for symmetry reasons no significant signal changes are expected for the perpendicular configurations while phase changes on the order of a few μrad may build up during tens of ms for the parallel configuration. The corresponding changes in magnitude were on the order of parts per billion (10⁻⁹). The phase signal has two contributions: the onset of a mean field due to the integrative activity of post-synaptic potentials at the oblique dendrites and the soma; and time-varying B-field changes caused by action potentials (APs) at firing frequencies lower than the synaptic activity. The first effect is responsible for a linear increase of the phase signal over time, while single APs produce non-linear, low intensity variations of the linear behaviour. We remark that the use of MEG-EEG results to predict nc-MRI signal changes can be erroneous since different complex distributions of electrical/current sources may have similar electromagnetic activity in the far field region (i.e. the multipolar expansion), while the near-field will be directly influenced by the exact spatio-temporal characteristics of the current sources. nc-MRI potentially represents a powerful tool to measure these characteristics.

To conclude, we believe that 1) if detectable, MR signals from pyramidal neurons are detectable in phase and not in magnitude images; 2) the MR sequences used for neuronal current detection should be carefully designed, taking into account realistic properties of neuronal current spreading ; 3) the highest nc-MRI sensitivity is obtained for neurons placed parallel to the external field.

References

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