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Direct MRI detection of the neuronal magnetic field: the effect of the dendrite branch

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Abstract
In recent years, neuronal current MRI (nc-MRI) was proposed as a new imaging method to directly map the magnetic field change caused by neuronal activity. Nc-MRI could offer improved spatial and temporal resolution compared to blood hemodynamics-based functional magnetic resonance imaging (fMRI). In this paper, with a finite current dipole as the model of dendrite or dendrite branch, we investigated the spatial distribution of the magnetic field generated by synchronously activated neurons to evaluate the possibility of nc-MRI. Our simulations imply that the existence of a dendrite branch may not only increase the strength of the neuronal magnetic field (NMF), but also raise the non-uniform and unsymmetry of the NMF; therefore, it can enhance the detectability of the neuronal current magnetic field by MRI directly. The results show that the signal phase shift is enlarged, but it is unstable and is still very small, \(\ll 1\) radian, while the magnitude signal may be strong enough for a typical MRI voxel to be detected. We suggest making further efforts to measure the magnitude signal which may induce a large effect in an nc-MRI experiment.

(Some figures in this article are in colour only in the electronic version)
1. Introduction

The present non-invasive brain imaging techniques suffer from either low spatial resolution or low temporal resolution. The electroencephalogram (EEG) and magnetoencephalogram (MEG) can record real-time brain activation in ms, but suffer from limited ability to localize the sources of neuronal activities since many different current distributions in the brain cortex may equivalently match the observed EEG/MEG signal. On the other hand, the hemodynamics-based functional magnetic resonance imaging (fMRI) technique is an indirect measurement of neuronal activation so its ability to accurately localize neuronal activities in space is also limited. Further, because of the slow hemodynamic response of brain tissue, fMRI has low temporal resolution.

Recently, neuronal current MRI (nc-MRI) was proposed as a new imaging method to directly map the magnetic field change caused by neuronal activity. In theory, nc-MRI can non-invasively localize brain activities with very high spatial and temporal resolution; thus, it may have a great effect on the study of human brain function.

The feasibility of nc-MRI is still a matter of debate though it has been pursued for over a decade. Previous works have shown that MRI can directly detect transient and weak magnetic field in phantoms (Scott et al. 1992, Bodurka et al. 1999, Hatada et al. 2004, Pell et al. 2006, Huang et al. 2006). Meanwhile, successful nc-MRI has also been demonstrated by experimental results in vivo, including the study of brain function in evoked potentials (Kamei et al. 1999, Bianciardi et al. 2004, Xiong et al. 2003a, Xue et al. 2009), spontaneous (Konn et al. 2004) as well as epileptic activities (Liston et al. 2004, Rodionov et al. 2010). Nevertheless, in contrast to the above findings, other groups reported that no NMF-related MRI signal was detected in their experiments (Chu et al. 2004, Parkes et al. 2007, Tang et al. 2008). In addition, different from the above studies which investigated the feasibility of nc-MRI by the dephasing mechanism at high magnetic fields. Kraus et al. (2008), based on the resonant interaction between magnetic fields and the spin population, proposed ultra-low field direct neural imaging (ULF-DNI) to execute nc-MRI.

In the past few years, by theoretical calculations and simulations based on the current-dipole model, the feasibility of detecting neuronal current has been argued in several papers (Xiong et al. 2003, Bandettini et al. 2005, Xue et al. 2006, Park and Lee 2007). However, the dipoles reconstructed from MEG cannot well approximate the NMF inside the brain (Blagoev et al. 2007), because the modeled dipole is the equivalent source of a small area which is usually much larger than a voxel. For nc-MRI, the detailed local field of each dendrite may have its independent contribution to the phase change because the nc-MRI signal is determined by the internal magnetic distribution in a voxel. On the other hand, Blagoev et al. (2007) and Cassarà et al. (2008) modeled the realistic magnetic signature of neuronal activity to evaluate the nc-MRI phase and magnitude signals, but this complex approach will have a limitation on the use of a particular type of neuron and cannot present the general brain activation. Heller et al. attempted to model the direct effects of the NMF on MRI as well. They first used a simpler mathematical model and approximate dendrites as spheres, but this spherical dipole model could not well reflect the real geometry of the dendrite and might overestimate the effect on the MRI signal (Heller et al. 2009). The reason for this overestimate is that the magnetic field near a point (or sphere) varies more rapidly than that near a line (or cylinder) of the same moment.

In this paper, to form a more realistic and simpler neuronal model, we took the dendrite branch into account. Each dendrite and each dendrite branch were modeled by a finite current dipole. We started with the calculation of the magnetic field generated by the unbranched dendrite. We then extended our simulation including the dendrite branch and estimated the
magnetic field produced by the main dendrite and its branch system. In the final section, we introduced the analytical relationship between the neuronal activity and the expected nc-MRI signal. We discussed the contribution of the dendrite branch to the nc-MRI signal.

2. Theory and methods

2.1. Source for nc-MRI

A neuronal cell in the brain typically consists of a soma, a single axon and multiple dendrites. Since the dendrites and axons are spread out over a much wider region than the soma occupied, the NMF of a neuron would be determined by the action potentials (APs) which propagate along the axons and the postsynaptic potentials which occurred due to the chemical transmission in the dendritic tree of the neuronal cell. However, the NMF generated by APs which propagate along the axons can be ignored for the following three reasons. First, for a myelinated axon, the through-membrane current at nodes of Ranvier generates no NMF outside the neuronal membrane, and as the majority of axons in the brain are myelinated, the contributions of axons to NMF do not need to be considered (Xue et al. 2006). Second, since the axonal current accompanies depolarization and repolarization, the axon can be modeled as two oppositely oriented current dipoles, so-called current quadripole. These different polarities will lead to the cancellation of the axonal magnetic field and cause very little changes in the nc-MRI signal (Park and Lee 2007). Third, the APs along an axon are a result of a voltage-gated, all-or-none effect of short duration (in the millisecond range), while the postsynaptic potentials (dendrites) sum up in a graded manner, yielding a temporally modulated and longer-lasting (50–200 ms) magnetic field, so dendrites are the main source of the NMF (Cassarà et al. 2008, Hagverg et al. 2006). On the other hand, Chow et al. (2006) discussed the nc-MRI based on the axon activities of the adult human optic nerve. They found that axonal activities in the optic nerve might indeed be detectable using nc-MRI. However, in the cortex, many axons branch profusely and recurrently, whereas in the optic nerve, the magnetic field components would be aligned, and this may tend to increase the sum of the NMF (Blagoev et al. 2007).

In addition, the extracellular current will have a negligible effect on the measurement of the neuronal current by MRI since the magnetic field caused by this component is about a hundred times smaller than that of the intracellular current (Xue et al. 2006). In view of these facts, we calculate the NMF generated by neuronal current just by considering the dendrites and using the dendrite model as the whole single neuron. Since the dendrites are of thin cylindrical structure, we modeled each dendrite or each dendrite branch as a finite current dipole to build a realistic model of neuron. Because the radius of the dendrite is too small (0.25–0.5 μm (Weaver et al. 2004)), we did not consider the magnetic field inside the dendrite. We believe that this model is relatively simple and it can obtain a relatively realistic description of the neuron.

2.2. Parameter selections

Since the dendrites and their branches are different in their sizes and activity patterns, the choice of the dendrite parameters is very important. In our dendrite model, the following parameters are usually adopted: length of the dendrite: 1 mm (Weaver et al. 2004); length of the dendrite branch: 0.5 mm; intracellular current: 1 nA or 5 nA (Destexhe et al. 1998) and duration of each individual dendritic activities: 5 ms or 10 ms (Gulledge et al. 2005). In the MRI simulation, echo time (TE): 100 ms, the main dendrite density: 220 dendrites mm$^{-3}$ and the size of the voxel: 1 × 1 × 1 mm$^3$. 
2.3. The calculation of the NMF

Neuronal activity in the brain involves electric current, which produces the magnetic field. The magnetic vector field, $B$, caused by a neuronal current density, $J$, located at $r$ is (Hagverg et al 2006)

$$B(r, t) = \frac{\mu_0}{4\pi} \int \frac{J(r', t) \times (r - r')}{|r - r'|^3} \, d^3r' + \frac{1}{4\pi \sigma} \int \frac{\partial J(r', t)}{\partial t} \times (r - r') \, d^3r', \quad (1)$$

where $\mu_0$ is the permeability of the brain tissue, $\sigma$ is the electrical conductivity and $c$ is the speed of the electromagnetic wave. In brain electromagnetism, the quasi-static approximation of Maxwell’s equations is generally valid, and so the second term in equation (1) can be omitted. Meanwhile, since the extracellular current is two orders smaller than the intracellular current, it has a little effect on the nc-MRI signal and can be safely ignored. Consequently, the magnetic field induced by the intracellular current $I_i$ is

$$B_{nc}(r, t) = \frac{\mu_0}{4\pi} \int \frac{I_i(r, t) \times (r - r')}{|r - r'|^3} \, d^3r'. \quad (2)$$

Therefore, regarding a dendrite or a dendrite branch with finite length and assuming a uniform current density along the dendrite (figure 1), the intracellular current $I_i$ is modeled as a finite current dipole and the magnetic field outside the dendrite is

$$B_p = \frac{\mu_0 I_i}{4\pi a} (\cos \theta + \cos \alpha). \quad (3)$$

2.4. The calculation of the nc-MRI signal

During the MRI experiment, the spins of the sample precess at the Larmour frequency $\omega_0 = \gamma B_0$ in a local static magnetic field $B_0$ (of the MRI scanner). The neuronal current can affect the MRI signal because the component of the NMF, $B_{n//}$, which parallels $B_0$ will cause the sample’s spins to rotate with different precession frequencies. These spins experience an additional phase and a loss of phase coherence, which in turn result in a decrease in the magnitude MRI signal within a voxel (figure 2). The following analyzes the phase and magnitude of the nc-MRI signal.
The additional phase shift accumulated by each spin at any point \((x, y, z)\) in the voxel during an echo time (TE) is according to

\[
\phi(\vec{r}, tE) = \int_0^{TE} \gamma B_{n/}(\vec{r}, t) \, dt,
\]

where \(\gamma\) is the proton gyromagnetic ratio. Only the component of the NMF, \(B_{n/}\), which parallels \(B_0\), will cause the phase shift. The average phase in radian is obtained by integrating the field over the image voxel. Since diffusion contributes relatively little to the MRI signal change (Blagoev et al 2007, Hagverg et al 2006), the total phase shift within a given voxel can be estimated by (Cassarà et al 2008)

\[
\phi_{\text{voxel}}(tE) = \langle \phi(tE) \rangle_{\text{voxel}} = \tan^{-1} \left[ \frac{\int_V \sin(\phi(\vec{r}, tE)) \, d\vec{r}}{\int_V \cos(\phi(\vec{r}, tE)) \, d\vec{r}} \right] \approx \frac{1}{2} \left[ \int \phi(\vec{r}, tE) \, d\vec{r} \right],
\]

where \(\langle \rangle\) is a notation of average value calculation and \(\langle \phi(tE) \rangle_{\text{voxel}}\) means that the average of the spins’ phase shift \(\phi(tE)\) is over an image voxel.

The inhomogeneities of the NMF result in the loss of phase coherence; thus, the magnitude signal observed is related to the accumulated phase by (Cassarà et al 2008)

\[
S_{\text{voxel}}(tE) = S_0 \sqrt{\left( \int_V \sin(\phi(\vec{r}, tE)) \, d\vec{r} \right)^2 + \left( \int_V \cos(\phi(\vec{r}, tE)) \, d\vec{r} \right)^2} \\
= S_0 \left( 1 - \frac{\langle \phi(tE) \rangle^2 - \langle \phi(tE)^2 \rangle^2}{2} \right),
\]

where \(S_0\) is the magnitude signal in the absence of neuronal current effects in an echo time (TE). The magnitude effect can then be obtained from the phase change according to

\[
\frac{\Delta S}{S} = \frac{S_0 - S_{\text{voxel}}}{S_0} = \frac{\langle \phi(tE) \rangle^2 - \langle \phi(tE)^2 \rangle}{2}.
\]
3. Results

3.1. Calculation of the magnetic field

3.1.1. Unbranched dendrite. Figure 3(a) shows the current-dipole model used for a dendrite. The current, along the z-axis, flows along the dendrite, and equation (3) is used to calculate the magnetic field outside the current dipole. Figure 3(b) shows the component of the induced magnetic field paralleled to the \( B_0 \) generated by neural activities of an unbranched dendrite. The magnitude of the intracellular current is 5 nA.

3.1.2. Dendrite and its branch. In the dendrite and its branch system, we took into account the effect of its spatial configuration which depends on the angle \( \theta \) between the main dendrite and its branch. To simplify our model, for each main dendrite, we just matched one branch. Figures 4(a) and (b) show the inphase (0 < \( \theta \) < \( \pi / 2 \)) and antiphase (\( \pi / 2 < \theta < \pi \)) configurations of this system. The magnetic field at any observation point is a vector summation of the magnetic field generated by the main dendrite and its branch. Figures 4(c) and (d) show the magnetic field distribution on the O plane generated by dendritic activities for inphase (figure 4(c)) and antiphase (figure 4(d)). For the inphase configuration, the magnetic field tends to cancel out each other in area between the dendrite and its branch and add up on the other sides. In contrast, for the antiphase configuration, the magnetic field is in the same direction in the area between the dendrite and its branch and opposite on the other sides.

3.1.3. The voxel system. An image voxel typically contains millions of dendrites and their branches, and here we reconstruct three kinds of voxels: a voxel formed of unbranched dendrites, a voxel with fixed intracellular current strength (5 nA) and angle (\( \theta = \pi / 4 \) or \( \theta = 3\pi / 4 \)) in the dendrite and its branch (figure 5), and a third one with fixed intracellular current strength (5 nA) in the main dendrite but random value in its branch. In addition, the angle of the third one is random too. We calculated the magnetic field in a single voxel by ‘replica’ of the dendrite (Cassarà et al 2008). Figure 5 shows a cubic voxel consisting of...
the second kind of voxel which is inphase and uniformly distributed. After calculation of the magnetic field of the dendrite and its branch, replicas were used to build up the field in an interesting voxel. We considered that the magnetic field distribution was the result of the integration of the fields produced by all the dendrites and branches. The other two kinds of voxels used the same replica method as well, and for all the three voxels, the dendrites were uniformly distributed in the voxel. For the unbranched dendrite case, they were uniformly distributed parallel (all of the dendrite currents are in the same direction) or anti-parallel (any two adjacent dendrite currents are in the opposite direction). For the other two cases, we considered the inphase (figure 4(a)) and antiphase (figure 4(b)) situations of the dendrites and their branches. In all our simulations, we assumed that the dendrite was parallel to the z-axis, the local static magnetic field $B_0$ (of the MRI scanner) was along the y-axis, and the spin density is homogeneous inside the image voxel.

3.2. Computation of the induced nc-MRI signal

3.2.1. Results for the unbranched dendritic system. Based on equations (6) and (7), we estimated the nc-MRI signal over an image voxel which was constructed by unbranched dendrites. No matter whether the configuration is parallel or anti-parallel, the nc-MRI phase signal for the activated voxel is always zero and undetectable since the phase shift depends on the global average magnetic field and the magnetic field induced by the activated dendrites is symmetrical (half positive and half negative in figure 3(b)). On the other hand, the nc-MRI magnitude signal depends on the voxel size, the evaluated dendritic density, the strength of the intracellular current and the duration of each individual dendritic activity. Figure 6.
Figure 5. Illustration of a voxel with dendrites and their branches. In this case, all the dendrites are uniformly distributed. The calculation of the magnetic field generated by all the neurons in the voxel was conducted by the superposition principle. The magnetic field at any observation point is a vector summation of the magnetic field generated by all the dendrites and their branches.

Table 1. The nc-MRI magnitude signal change $\Delta \tilde{S} / S_0 (%)$ generated by the parallel configuration corresponding to the intracellular current strength and the duration of dendritic activities.

<table>
<thead>
<tr>
<th>Neuronal current</th>
<th>5 ms</th>
<th>10 ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 nA</td>
<td>-0.0044%</td>
<td>-0.0174%</td>
</tr>
<tr>
<td>5 nA</td>
<td>-0.11%</td>
<td>-0.44%</td>
</tr>
</tbody>
</table>

The parameters for this computation are as follows: the voxel size is $1 \times 1 \times 1 \text{mm}^3$ and the unbranched dendritic density is 40 000 dendrites mm$^{-3}$.

shows the trend of the magnitude signal change for the length of the cubic voxel (figure 6(a)) and the evaluated neuronal density (figure 6(b)). When the configuration is anti-parallel, the magnitude signal tends to be zero, and the magnitude signal variations (negative) of the parallel configuration increase approximately with the square of the voxel size, and the dendritic densities have the same trends since both the situations mean that the total number of dendritic activities during TE increases. The effects of the intracellular current strength and the duration of dendritic activities on the magnitude signal change induced by parallel configuration are listed in table 1. The nc-MRI signal could be up to $-0.44\%$, assuming that the intracellular current is 5 nA, the duration of each dendritic activities is 10 ms and 40 000 dendrites fired in a cubic voxel with length 1 mm. The trend shown in figure 6 is consistent with the previous report (Xue et al 2006). For realistic neuronal activity, there will be a greater number of dendritic activities (excitatory postsynaptic potentials) and the nc-MRI magnitude signal should be strong enough to be detected by MRI techniques.

3.2.2. Results for the dendrite with a branch system. In a realistic neuron, most of the dendrites have branches; therefore, we take the dendrite branch into account. In this section, we consider the two kinds of voxels formed of the dendrites and branches which have been described previously. As the unbranched dendrite system, we investigate the relationship between the nc-MRI signal and the voxel size.

Figure 7 shows the relationship between the nc-MRI signal and the length of the cubic voxel. Different from the unbranched dendrite situation, the magnitude signal induced by
Figure 6. Relationship between the magnitude signal change and the voxel size (a) and the dendritic density (b). The duration of each individual dendritic activities is 10 ms and the intracellular current is 5 nA. Uniform spin density across the voxel is considered.

Figure 7. The relationship between the nc-MRI signal and the voxel size. (a) The magnitude signal change of the voxel with the same current for the dendrites and branches. (b) The magnitude signal change of the voxel consisted of fixed current in dendrite but random current values in branches. (c) The phase signal induced by fixed current in dendrite but random current values in branches.

3.2.3. Contribution of neighboring voxels. The above calculations are based on a single activated voxel. However, usually there are multiple voxels synchronously activated in a realistic neuronal activity area and the intervoxel effect must be considered. For the voxel
reconstructed by fixed current in dendrites and random current values for the branches is more similar to the realistic neuronal activity; we use this model for our simulated computation. Furthermore, because we just investigate the mutual effect between voxels, for saving computation, we just consider a case of dendritic density (220 dendrites mm$^{-3}$).

Tables 2 and 3 show the nc-MRI signal changes of an activated voxel and its neighboring voxels (un-activated) along the $x$- and $y$-directions separately. No matter the neighboring voxels are along the $x$- or $y$-direction, for the magnitude signal, the contributions from the activated voxel to the neighboring voxel decay quickly. However, since the activated voxel induced the unsymmetrical magnetic distribution field, the phase signal induced by the neighboring voxel is still a few microradian and cannot be distinguished from the activated voxel. In view of this fact, we suggest to detect the magnitude signal in MRI experiment since this signal is strong enough to be measured and the activated voxels have a little effect on the inactivated voxels.

If there are multiple voxels activated, the NMF of any voxel is the vector sum of the contributions from all activated voxels. Table 4 shows both the magnitude and phase changes of each voxel of two, three and four contiguous activated voxels along the $x$- and $y$-directions. For the two contiguous activated voxels, all the nc-MRI signals induced from each voxel are relatively equal. But for the contiguous with three or four voxels, if the activated voxels are in a row along the $x$-direction, the most sensitive voxels are on the edge of the activated area, while if the activated voxels are in a row along the $y$-direction, the most sensitive voxels will be the voxels in the center.

In an MRI experiment, the voxel size may be 1–27 mm$^3$ or larger, and the magnetic field changes in it will be averaged, and partial volume effects will thus take place. Likewise, if the voxel is not completely occupied by activated dendrites, we should consider the partial volume effect. Table 5 shows the link between the nc-MRI signal and the partial volume effect. The nc-MRI magnitude signals generated by the voxel with half dendrites and branch activities are one order smaller than the activated voxel without partial volume effect, no matter along the $x$- or $y$-direction. As the previous result, the phase signal change is still a few $\mu$microradian and cannot be distinguished from the completely activated voxel.

4. Discussions

4.1. Effects of orientation of the dendrites

All our simulations are based on the assumption that all the dendrites are parallel to the $z$-axis. Since only the component of the magnetic field parallel to the $B_0$ can cause the phase shift, the nc-MRI signal strongly depends on the orientation of the NMF. Any rotation of the dendritic orientation will cause the reduction of $B_{n//}$ and then affect the nc-MRI signal. Concerning the orientation of neurons, which are anisotropically oriented locally, we can yield that the nc-MRI signal will vary with the anisotropy distributed in neuronal orientation. This situation is similar to the case of fMRI contrast, which is due to small capillaries.

4.2. Effects of the number of dendrites

In view of the above calculations in section 3.2, the number of dendritic activities during the TE will strongly impact the nc-MRI signal. Different from the MEG which is induced by all individual dendritic activities simultaneously, since the nc-MRI technique measures the accumulated effect of the NMF, the nc-MRI signal depends on the total number of neurons fired during TE. All neuronal activities during TE will contribute to the dephasing of the proton spins and cause MRI signal change, no matter these neurons fire simultaneously or not.
Table 2. The nc-MRI magnitude signal change $\Delta S/S_0$ and phase shift (rad) of an activated voxel and its neighboring voxels along the s-direction.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Activated voxel</th>
<th>First neighbor</th>
<th>Second neighbor</th>
<th>Third neighbor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnitude</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inphase</td>
<td>$-1.8 \times 10^{-7} \pm 8.6 \times 10^{-9}$</td>
<td>$-2.0 \times 10^{-8} \pm 1.6 \times 10^{-9}$</td>
<td>$-1.4 \times 10^{-9} \pm 4.4 \times 10^{-11}$</td>
<td>$-2.8 \times 10^{-10} \pm 8.2 \times 10^{-12}$</td>
</tr>
<tr>
<td>Antiphase</td>
<td>$-1.4 \times 10^{-8} \pm 2.0 \times 10^{-9}$</td>
<td>$-9.6 \times 10^{-10} \pm 1.6 \times 10^{-10}$</td>
<td>$-6.1 \times 10^{-11} \pm 1.2 \times 10^{-11}$</td>
<td>$-1.2 \times 10^{-11} \pm 2.4 \times 10^{-12}$</td>
</tr>
<tr>
<td>Phase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inphase</td>
<td>$-3.8 \times 10^{-6} \pm 1.1 \times 10^{-5}$</td>
<td>$7.2 \times 10^{-4} \pm 1.0 \times 10^{-5}$</td>
<td>$3.7 \times 10^{-4} \pm 5.3 \times 10^{-6}$</td>
<td>$2.3 \times 10^{-4} \pm 6.8 \times 10^{-5}$</td>
</tr>
<tr>
<td>Antiphase</td>
<td>$-4.8 \times 10^{-7} \pm 1.2 \times 10^{-5}$</td>
<td>$1.5 \times 10^{-4} \pm 1.5 \times 10^{-5}$</td>
<td>$7.6 \times 10^{-5} \pm 7.4 \times 10^{-6}$</td>
<td>$5.1 \times 10^{-5} \pm 5.0 \times 10^{-6}$</td>
</tr>
</tbody>
</table>

The parameters for this computation are as follows: the voxel size is $1 \times 1 \times 1$ mm$^3$, the main dendritic density is 220 dendrites mm$^{-3}$, the duration of each individual dendritic activities is 10 ms and the magnitude of intracellular current is 5 nA.
Table 3. The nc-MRI magnitude signal change $\Delta S/S_0$ and phase shift (rad) of an activated voxel and its neighboring voxels along the y-direction.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Activated voxel</th>
<th>First neighbor</th>
<th>Second neighbor</th>
<th>Third neighbor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnitude</td>
<td>$-1.8 \times 10^{-7} \pm 8.6 \times 10^{-9}$</td>
<td>$-2.7 \times 10^{-8} \pm 1.5 \times 10^{-9}$</td>
<td>$-1.6 \times 10^{-9} \pm 6.3 \times 10^{-11}$</td>
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</tr>
<tr>
<td>Antiphase</td>
<td>$-1.4 \times 10^{-8} \pm 2.0 \times 10^{-9}$</td>
<td>$-1.4 \times 10^{-9} \pm 2.5 \times 10^{-10}$</td>
<td>$-7.3 \times 10^{-11} \pm 1.1 \times 10^{-11}$</td>
<td>$-1.4 \times 10^{-11} \pm 2.0 \times 10^{-12}$</td>
</tr>
<tr>
<td>Phase</td>
<td>$-3.8 \times 10^{-6} \pm 1.1 \times 10^{-5}$</td>
<td>$4.5 \times 10^{-7} \pm 3.9 \times 10^{-6}$</td>
<td>$1.1 \times 10^{-7} \pm 5.3 \times 10^{-6}$</td>
<td>$7.8 \times 10^{-8} \pm 4.8 \times 10^{-7}$</td>
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<tr>
<td>Antiphase</td>
<td>$-4.8 \times 10^{-7} \pm 1.2 \times 10^{-5}$</td>
<td>$1.8 \times 10^{-6} \pm 3.2 \times 10^{-6}$</td>
<td>$7.9 \times 10^{-7} \pm 7.4 \times 10^{-6}$</td>
<td>$1.5 \times 10^{-7} \pm 3.6 \times 10^{-7}$</td>
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</table>

The parameters for this computation are as follows: the voxel size is $1 \times 1 \times 1 \text{mm}^3$, the main dendritic density is 220 dendrites $\text{mm}^{-3}$, the duration of each individual dendritic activity is 10 ms and the magnitude of intracellular current is 5 nA.
Table 4. The nc-MRI magnitude signal change $\Delta S/S_0$ and phase shift (rad) of multiple activated voxels along the x- and y-directions.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>x-direction (two voxels)</th>
<th>y-direction (two voxels)</th>
<th>x-direction (three voxels)</th>
<th>y-direction (three voxels)</th>
<th>x-direction (four voxels)</th>
<th>y-direction (four voxels)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Magnitude</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inphase</td>
<td>Voxel 1: $-9.1 \times 10^{-8}$</td>
<td>$-3.0 \times 10^{-7}$</td>
<td>$-8.7 \times 10^{-7}$</td>
<td>$-3.7 \times 10^{-7}$</td>
<td>$-6.7 \times 10^{-7}$</td>
<td>$-4.0 \times 10^{-7}$</td>
</tr>
<tr>
<td></td>
<td>Voxel 2: $-8.9 \times 10^{-8}$</td>
<td>$-3.0 \times 10^{-7}$</td>
<td>$-8.3 \times 10^{-7}$</td>
<td>$-4.8 \times 10^{-7}$</td>
<td>$-2.6 \times 10^{-7}$</td>
<td>$-5.5 \times 10^{-7}$</td>
</tr>
<tr>
<td></td>
<td>Voxel 3:</td>
<td>$-8.0 \times 10^{-8}$</td>
<td>$-3.7 \times 10^{-7}$</td>
<td>$-2.6 \times 10^{-7}$</td>
<td>$-5.3 \times 10^{-7}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Voxel 4:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antiphase</strong></td>
<td>Voxel 1: $-8.5 \times 10^{-8}$</td>
<td>$-1.6 \times 10^{-8}$</td>
<td>$-7.9 \times 10^{-9}$</td>
<td>$-2.1 \times 10^{-7}$</td>
<td>$-7.9 \times 10^{-9}$</td>
<td>$-1.4 \times 10^{-7}$</td>
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<tr>
<td></td>
<td>Voxel 2: $-9.8 \times 10^{-9}$</td>
<td>$-1.2 \times 10^{-8}$</td>
<td>$-7.4 \times 10^{-9}$</td>
<td>$-3.0 \times 10^{-8}$</td>
<td>$-6.9 \times 10^{-9}$</td>
<td>$-1.9 \times 10^{-8}$</td>
</tr>
<tr>
<td></td>
<td>Voxel 3:</td>
<td>$-7.2 \times 10^{-9}$</td>
<td>$-2.1 \times 10^{-8}$</td>
<td></td>
<td>$-5.5 \times 10^{-9}$</td>
<td>$-2.2 \times 10^{-8}$</td>
</tr>
<tr>
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<td>Voxel 4:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Phase</strong></td>
<td>Inphase</td>
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<td></td>
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<tr>
<td></td>
<td>Voxel 1: $-6.6 \times 10^{-4}$</td>
<td>$6.0 \times 10^{-6}$</td>
<td>$-0.001$</td>
<td>$-3.0 \times 10^{-6}$</td>
<td>$-0.0012$</td>
<td>$3.3 \times 10^{-6}$</td>
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<td>Voxel 2: $-6.7 \times 10^{-4}$</td>
<td>$4.6 \times 10^{-6}$</td>
<td>$-1.5 \times 10^{-6}$</td>
<td>$-3.0 \times 10^{-6}$</td>
<td>$-3.3 \times 10^{-4}$</td>
<td>$-6.3 \times 10^{-6}$</td>
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<td>Voxel 3:</td>
<td>$0.001$</td>
<td>$-3.8 \times 10^{-6}$</td>
<td>$-3.3 \times 10^{-4}$</td>
<td>$-7.8 \times 10^{-6}$</td>
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<td></td>
<td>Voxel 4:</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Voxel 1: $-1.5 \times 10^{-4}$</td>
<td>$1.5 \times 10^{-6}$</td>
<td>$-2.0 \times 10^{-4}$</td>
<td>$1.4 \times 10^{-6}$</td>
<td>$-2.4 \times 10^{-4}$</td>
<td>$-1.4 \times 10^{-6}$</td>
</tr>
<tr>
<td></td>
<td>Voxel 2: $-1.3 \times 10^{-4}$</td>
<td>$2.6 \times 10^{-6}$</td>
<td>$-1.2 \times 10^{-6}$</td>
<td>$-9.3 \times 10^{-6}$</td>
<td>$-8.6 \times 10^{-6}$</td>
<td>$-1.9 \times 10^{-6}$</td>
</tr>
<tr>
<td></td>
<td>Voxel 3:</td>
<td>$2.1 \times 10^{-4}$</td>
<td>$1.7 \times 10^{-6}$</td>
<td>$6.7 \times 10^{-6}$</td>
<td>$-2.2 \times 10^{-6}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Voxel 4:</td>
<td></td>
<td></td>
<td></td>
<td>$2.4 \times 10^{-4}$</td>
<td>$-1.4 \times 10^{-6}$</td>
</tr>
</tbody>
</table>

The parameters for this computation are as follows: the voxel size is $1 \times 1 \times 1 \text{mm}^3$, the main dendritic density is 220 dendrites $\text{mm}^{-3}$, the duration of each individual dendritic activity is 10 ms and the magnitude of the intracellular current is 5 nA.
Table 5. The nc-MRI magnitude signal change $\Delta S/S_0$ and phase shift (rad) for each activated voxel due to the partial volume effect.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Activated voxel</th>
<th>x-direction</th>
<th>y-direction</th>
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</thead>
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<tr>
<td><strong>Magnitude</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Inphase</td>
<td>$-1.8 \times 10^{-7} \pm 8.6 \times 10^{-9}$</td>
<td>$-8.3 \times 10^{-8} \pm 5.3 \times 10^{-9}$</td>
<td>$-5.5 \times 10^{-8} \pm 3.8 \times 10^{-9}$</td>
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<tr>
<td>Antiphase</td>
<td>$-1.4 \times 10^{-8} \pm 2.0 \times 10^{-9}$</td>
<td>$-6.4 \times 10^{-9} \pm 7.3 \times 10^{-10}$</td>
<td>$-5.1 \times 10^{-9} \pm 1.0 \times 10^{-9}$</td>
</tr>
<tr>
<td><strong>Phase</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inphase</td>
<td>$-3.8 \times 10^{-6} \pm 1.1 \times 10^{-5}$</td>
<td>$2.9 \times 10^{-4} \pm 9.6 \times 10^{-6}$</td>
<td>$-2.5 \times 10^{-6} \pm 7.8 \times 10^{-6}$</td>
</tr>
<tr>
<td>Antiphase</td>
<td>$-4.8 \times 10^{-7} \pm 1.2 \times 10^{-5}$</td>
<td>$6.0 \times 10^{-5} \pm 7.2 \times 10^{-6}$</td>
<td>$-2.6 \times 10^{-7} \pm 5.2 \times 10^{-6}$</td>
</tr>
</tbody>
</table>

The parameters for this computation are as follows: the voxel size is $1 \times 1 \times 1$ mm$^3$, the main dendritic density is 220 dendrites mm$^{-3}$, the duration of each individual dendritic activity is 10 ms and the magnitude of the intracellular current is 5 nA. Only half the volume of each voxel contains dendrites and branches.
Based on the literature, a reasonable estimation for the number of dendritic activities during a typical TE (100 ms) should be up to several millions for a typical fMRI voxel of $3 \times 3 \times 3$ mm$^3$; thus, the dendritic density is close to several 100 000 dendrites mm$^{-3}$ (Xue et al 2006). The nc-MRI signal generated by such a number of activated dendrites should be strong enough to be detected using MRI techniques.

### 4.3. The nc-MRI phase and magnitude signals

Considering the contrast mechanisms between the NMF and the nc-MRI signal, the nc-MRI phase signal depends on the average phase shift of the spin ensemble over a voxel, and the nc-MRI magnitude signal induced by the loss of phase coherence is a consequence of the spatial magnetic field inhomogeneities. In a word, the phase signal relies on the symmetry and the magnitude signal relies on the inhomogeneity of the neuronal magnetic distribution field. The magnetic field distribution of an unbranched dendrite or the fixed main dendrite and its branch is symmetrical, and thus the phase shift will be cancelled out and always be zero. In contrast, for fixed current in dendrite and random situations in the branch system, since these random branches may not only increase the NMF but also raise the non-uniform and unsymmetry of the NMF, the phase signal should no longer be zero, and the average of the NMF for the branches dendrite system over a voxel will be different for different voxel sizes (figure 7(c)), which causes the phase shift to be unstable.

For the amplitude signal, dendrites in the parallel configuration cause the inhomogeneity of the magnetic distribution, and this geometry will give rise to changes in the magnitude signal effect, whereas the anti-parallel configuration will make the magnitude signal to be zero (figure 6). In the real neuronal activities, for the existence of the excitatory postsynaptic potentials (EPSPs) and the inhibitory postsynaptic potentials (IPSPs), the antiparallel configuration of the dendrites is possible. However, our results show that the existence of the anti-parallel configuration may add to the difficulty of the nc-MRI detection. In fact, the feasibility of the nc-MRI depends on how many activated dendrites there are in parallel configuration rather than anti-parallel configuration. In the case of the voxel containing the
branch, because all of the main dendrites are parallel, the magnitude signal change caused by the antiphase or inphase geometry will not be zero (figures 7(a) and (b)).

In the case of multiple voxels, for the magnitude signal, the activated voxel has little effect on its adjacent inactivated voxel (tables 2 and 3), however, there is anisotropic for multiple activated voxels (table 4); the most sensitive voxels are on the edge of the activated area if the activated voxels are in a row along the x-direction, and the most sensitive voxel will be the voxels in the center if the activated voxels are in a row along the y-direction.

4.4. The effect of the random timing and position

In a real situation, dendrite currents will not be perfectly synchronized and uniformly distributed. However, the random timing has no effect on the nc-MRI as long as the dendritic activities are in the TE period (figure 8). Figure 8(b) shows that each dendrite may last approximately 10 ms and its neighboring dendrite may have a time delay of about 5 ms (Xue et al 2006, Blagoev et al 2007); we can see that the final phase shift is the same for the two cases: the two currents corresponding to B1 and B2 work simultaneously (figure 8(a)) of non-simultaneously (figure 8(b)) (figure 8(a)) and the delay case (figure 8(b)). In fact, since all the dendritic activities during TE will contribute to the nc-MRI signals, in our work, although the currents are random timing in real situation, neuronal currents were modeled as synchronized dipole currents which have the same duration as of the dendritic activities (10 ms).

Figure 9 shows the effect of the random position on a voxel. When the main dendrites are uniformly distributed in a voxel, the magnitude signal change is $-4.45 \times 10^{-7}$ and its phase shift is zero. Different from the uniform situation, the random position is similar to the partial volume effect. The magnitude signal change is two orders smaller (average (AVG): $-8.45 \times 10^{-9}$; root mean square (RMS): $1.21 \times 10^{-9}$) and the phase shift will be a few microradians (figure 9). In fact, the partial volume is just a more ideal condition of the random situation. If only half the volume of a voxel contains dendrites, the nc-MRI magnitude signals are one order smaller than the activated voxel without partial volume effect and the phase signal change will not be zero (table 5).
5. Conclusion

Here, the feasibility of nc-MRI has been demonstrated by theoretical calculation using the finite current-dipole model. Our results show that the existence of the dendrite branch may not only increase the strength of the NMF, but also raise the non-uniform and unsymmetry of the NMF; therefore, it can enhance the detectability of the NMF by MRI directly. The expected phase shift is enhanced, and its magnitude signal remains strong enough for a typical MRI voxel to be detected. Whereas the phase change is unstable and very small, ≪1 radian, we suggest to measure the magnitude signal which causes the greatest effect in nc-MRI experiment. Indeed, the nc-MRI signal will depend highly on the local distribution of the magnetic field, the strength of the intracellular current, the voxel size and other dendrite parameters. Meanwhile, in order to increase the sensitivity of nc-MRI signal, ways of increasing specificity in nc-MRI by minimizing secondary hemodynamic and metabolic effects as well as optimizing the nc-MRI method should be considered in future studies.

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