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Electromagnetohydrodynamic Modeling of Lorentz Effect Imaging

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Abstract

Lorentz Effect Imaging (LEI) is an MRI technique that has been proposed for direct imaging of neuronal activity. While promising results have been obtained in phantoms and in the human median nerve *in vivo*, its contrast mechanism is still not fully understood. In this paper, computational model simulations were used to investigate how electromagnetohydrodynamics (EMHD) may explain the LEI contrast.

Three computational models of an electrolyte-filled phantom subject to an applied current dipole, synchronized to oscillating magnetic field gradients of an LEI protocol, were developed to determine the velocity and displacement of water molecules as well as the resulting signal loss in an MR image. The simulated images were compared to images from previous LEI phantom experiments with identical properties for different stimulus current amplitudes and polarities.

The first model, which evaluated ion trajectories based on Stokes flow using different mobility values, did not generate an appreciable signal loss due to an insufficient number of water molecules associated with the ion hydration shells. The second model, which computed particle drift based on the Lorentz force of charged particles in free space, was able to approximate the magnitude, but not the distribution of signal loss observed in the experimental images. The third model, which computed EMHD based on the Lorentz force and Navier-Stokes equations for flow of a conducting fluid, provided results consistent with both the magnitude and distribution of signal loss seen in the LEI experiments. Our EMHD model further yields information on electrical potential, velocity, displacement, and pressure, which are not readily available in an experiment, thereby providing a robust means to study and optimize LEI for imaging neuronal activity in the human cortex.

Keywords

functional magnetic resonance imaging; neuronal current MRI; Lorentz effect imaging; electromagnetohydrodynamics; oscillating magnetic field gradients; computational modeling

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Introduction

Functional magnetic resonance imaging (fMRI) based on the blood oxygenation level-dependent (BOLD) contrast is widely used to study brain function, but indirectly detects neuronal activity, which limits its ability to accurately localize neuronal activity in space and time. To improve the accuracy of fMRI, contrast mechanisms more directly tied to the neuronal electrical activity itself have been proposed and are referred to as neuronal current MRI (ncMRI) [1]. Due to its potential for directly imaging neuronal activity with a much higher spatial and temporal specificity than BOLD fMRI, ncMRI has been described as the holy grail of functional neuroimaging, but its theory and feasibility are still a topic of debate [1].

One form of ncMRI called Lorentz Effect Imaging (LEI) [2-5] employs oscillating magnetic field gradients to amplify and detect the signal loss resulting from a spatially incoherent, yet temporally synchronized, water displacement caused by the neuronal activity. Ideally, the oscillating gradients are synchronized to the frequency of the neuronal currents of interest such that the electrical activity causing the incoherent water displacement occurs during the positive gradient lobes, but not during the negative gradient lobes (or inversely). Such oscillating gradients enhance the incoherent phase accumulation from the spatially incoherent water displacement occurring between the positive and negative gradient lobes, resulting in a maximal signal loss in the voxels of interest.

The LEI technique has successfully been used to detect electrical activity in various phantoms [4, 5] and in the human median nerve *in vivo* [3], which represents a promising step towards its application for detecting neuronal activity in the brain. Nevertheless, its underlying contrast mechanism is not yet fully understood. As a proof-of-concept, Truong et al. first demonstrated that the LEI technique can detect electrical currents in conductive wires embedded in a gel phantom with a temporal specificity on the order of milliseconds [4]. In this study, the Lorentz force acting on the wires caused an incoherent displacement of the water molecules in the surrounding gel, resulting in a signal loss. Truong and Song also demonstrated that the LEI technique can detect sensory nerve action potentials in the human median nerve *in vivo* [3]. Roth and Basser argued that the displacement of a nerve carrying an action current is too small and diffuse to be measured using MRI [6]. Furthermore, neural conduction in biological systems relies on ionic currents in solution, which do not have the same properties as electronic currents in conductive wires, therefore requiring a different model to investigate the LEI mechanism.

Truong et al. next demonstrated that the LEI technique can also detect ionic currents in an electrolyte-filled phantom [5]. In this case, the Lorentz force acting on the ions caused an incoherent displacement of the surrounding water molecules, resulting in a signal loss. The authors computed the trajectory of ions experiencing a Lorentz force to compare with the overall pattern of signal loss observed in the experiments, but did not explicitly model the displacement of the water molecules. Wijesinghe and Roth argued that this model used excessively high ion mobility values, which when corrected to standard values lead to undetectable displacements and a signal loss pattern not matching the experimental results [7]. They suggested that a different mechanism, magnetohydrodynamically induced flow, could significantly affect the MR signal in the electrolyte phantom and therefore warrants further theoretical investigation [7].

Electromagnetohydrodynamics (EMHD) describes the flow of a conductive fluid under electric and magnetic fields, based on a Lorentz body force on the conductive fluid [8-11]. Although most EMHD models have been developed to explain plasma and liquid metal flows [9], a few have been created for studying conducting or charged fluid flows [10-12].

While Wijesinghe and Roth made some estimates regarding the significance of EHMD in LEI [7], a full computational EMHD model relevant to the problem of an electrolyte fluid subject to an applied current under an LEI protocol has yet to be developed.

To better understand the LEI contrast mechanism and further optimize this technique for detecting neuronal activity in the brain, we develop three computational models based on various theoretical Lorentz force mechanisms. The first two models are based on the previously proposed ionic flow principle [5] and particle drift estimates [7]. A third, more comprehensive model is presented that incorporates the effects of EMHD on the LEI signal loss. The simulated data are compared to those obtained in the phantom experiments of Truong et al. [5]. The results show that EMHD is the primary contrast mechanism explaining both the scale and patterns of signal loss. The latter model will be useful in understanding what can be measured using LEI in future studies, such as for mapping neuronal activity in the human cortex.

Methods

The computational models described here were developed to simulate the electrolyte-filled phantom experiments of Truong et al. [5]. Each model differs with regard to the nature of the primary Lorentz force mechanism underlying the water motion. The mechanisms explored are: ion flow based on the study by Truong et al. [5], particle drift based on the estimates by Wijesinghe and Roth [7], and EMHD of a conducting fluid. Our modeling assumptions and analysis reflect our primary interest in the overall scale of the LEI signal loss in comparing the model results to those of the experiments. Therefore, an in-depth analysis of the implications of the spatial distribution of signal loss or other output parameter values was not performed.

Implementation of the computational models and data analysis were performed in MATLAB v7.11. A computational phantom model was implemented based on the central MRI slice of the experiments [5]: a 12×12 cm square viewing domain with an imbedded 10×10 cm square phantom domain and a slice thickness of 5 mm. The matrix size was 128×128 , resulting in an in-plane resolution of 0.94×0.94 mm. Representing the phantom as a square instead of a circle simplified the use of a finite difference method for computing the fluid dynamics. Compared to a circular domain, the square domain changed the velocity profiles mostly near the corners, which were clipped and resulted in less than 1% mean difference in velocity and displacement magnitudes in the phantom domain. Phantom voxels outside of the central 10×10 cm circle were ignored in the result analysis and display to allow for a better comparison with the experimental results.

The phantom domain (Fig. 1A) had two electrodes at the left and right poles with opposite polarities, which were modeled as point sources using Dirichlet boundary conditions. We imposed a no-flux boundary condition at all other points along the phantom domain boundary. The phantom filled with a 2.8 g/l CuSO_4 solution had a homogeneous conductivity of $\sigma = 140$ S/m, an inter-electrode resistance of $R = 10^3$ Ω , and a magnetic permeability of $\mu_m = -9 \times 10^{-6}$ H/m. Based on the applied stimulus current (I), the inter-electrode resistance was used to compute the electric potentials ($\phi_{1,2} = \pm I \cdot R/2$) of the point sources, and a ground ($\phi = 0$) was placed as a reference potential at the center point of the phantom domain (see Fig 1B for a distribution of electrical potentials for a 5 mA stimulus current). The viewing domain outside of the phantom was considered to be air, insulated from the electrical field within the phantom, with no magnetic properties, and given a reference signal strength of $S = 0$.

An LEI protocol from the phantom experiments (Fig. 1C) was used for our model simulations, and consisted of fifteen cycles of oscillating gradients with a lobe duration of 2 ms and an amplitude of ± 36 mT/m, applied with the positive gradient lobes synchronized to the current-on periods. Model gradient lobes were made rectangular rather than trapezoidal for simplification.

When computing fluid displacement in the phantom, we ignored the magnetic field changes from the gradients. We also assumed that the temperature, fluid, and charge density are uniformly distributed throughout the phantom over the entire simulation time window, which allowed us to compute the electric field generated by the electrical activity independently of the magnetic field effects and fluid motion. Thus, we implemented a two-part method to: 1) compute the electric and magnetic field effects on fluid velocity and displacement, then 2) compute the induced signal loss based on fluid displacement along the applied magnetic field gradients.

1) Lorentz Force and Fluid Displacement Models

Fluid displacement is computed based on the fluid velocity generated by the Lorentz force mechanism studied in each model: ion flow, particle drift, or EMHD.

a) Ion Flow: Lorentz Force on Ions—As proposed by Truong et al. [5], the ion flow model assumes that fluid motion is primarily caused by the Lorentz force generated on the charged ions in the conducting fluid. Their model shows ion trajectories based on the Lorentz force, but does not describe a relationship between the ions and water molecules. Solute-solvent interactions may be described by the solvation shell and coordination numbers for the ions [13]. To determine the maximal signal loss generated by ion flow, we overestimated the ion-water interactions by assuming that the ion-associated water molecule displacement is equal to that of the ion, without adding mass or reducing the Lorentz force-induced acceleration on the ion. Based on the solvation numbers of the simulated Cu and SO₄ ions [14], we modeled a range of 4-24 water molecules per simulated ion. The Lorentz force ($\mathbf{F}^{\text{EM}}$) on each ion is computed as follows:

$$\mathbf{F}^{\text{EM}} = \mathbf{F}_E + \mathbf{F}_B = q\mathbf{E} + q(\mathbf{v} \times \mathbf{B}) \quad (1)$$

where $\mathbf{F}_E$ is the electric force (N), $\mathbf{F}_B$ is the magnetic force (N), q is the electric charge (C) of the ion, $\mathbf{E}$ is the electric field (V/m), $\mathbf{v}$ is the particle velocity (m/s), and $\mathbf{B}$ is the magnetic field (T).

b) Particle Drift: EMHD Estimate—Based on the particle drift theory principles used by Wijesinghe and Roth [7], we computed displacements from a force balance inherent in the equation for drift velocity ($\mathbf{v}_D$) of charged particles in free space [8]:

$$\mathbf{v}_D = \mathbf{E} \times \mathbf{B} / |\mathbf{E}|^2 \quad (2)$$

where E is the electric field strength. Their approximation also assumed that the full drift velocity is achieved by the end of the magnetic damping time T_M [7]:

$$T_M = \rho / \sigma B^2 \quad (3)$$

where ρ is the fluid density (kg/m^3), σ is the conductivity (S/m), and B is the magnetic field strength. Hence, the particle velocity $\mathbf{v}$ achieved by the end of a current pulse is based on the ratio between the current pulse period T_G and T_M :

$$\mathbf{v} = \mathbf{v}_D T_G / T_M \quad (4)$$

Using this method, we compute particle displacement from drift velocity and assume a conditional boundary condition where particles that reach the phantom bounds remain there. Comparing the full EMHD results with this approximation will allow us to determine the relative effect of the fluid dynamics on the overall scale of signal loss achieved within the phantom.

c) EMHD: Lorentz Force on a Conducting Fluid—Modeling EMHD as the primary mechanism for fluid flow assumes that all particles within a conducting fluid are acted on by a Lorentz body force ($\mathbf{f}^{\text{EM}}$, N/m^3). This force is the result of an electric field crossed with a magnetic field and is in the direction of $\mathbf{E} \times \mathbf{B}$ with magnitude $\mathbf{J} \times \mathbf{B}$, based on the Lorentz force equation [8]:

$$\mathbf{f}^{\text{EM}} = \mathbf{J} \times \mathbf{B} \quad (5)$$

where $\mathbf{J} = (\mathbf{E} + \mathbf{v} \times \mathbf{B})$ is the current density (A/m^2). The gold standard for EMHD was modeled using the incompressible Navier-Stokes equations to solve for the velocity field of a conductive fluid under the influence of $\mathbf{f}^{\text{EM}}$ (Eq. 5). Unlike the particle drift model, this method accounts for a pressure gradient ($-\nabla p$), a convective acceleration ($\mathbf{v} \cdot \nabla \mathbf{v}$), and a viscous force ($\mu \nabla^2 \mathbf{v}$), and assumes that the fluid is incompressible ($\nabla \cdot \mathbf{v} = 0$):

$$\begin{cases} \rho \left(\frac{d\mathbf{v}}{dt} + \mathbf{v} \cdot \nabla \mathbf{v} \right) = -\nabla p + \mu \nabla^2 \mathbf{v} + \mathbf{f}^{\text{EM}} \\ \nabla \cdot \mathbf{v} = 0 \end{cases} \quad (6)$$

where ρ is the fluid density (10^3 kg/m^3 for water), p is the pressure (Pa), and μ is the dynamic viscosity ($10^{-3} \text{ Pa} \cdot \text{s}$ for water at 20°C). Implementation of the Navier-Stokes solver method was adapted from a MATLAB code developed by Seibold and published by Strang [15]. This method uses finite differencing on a staggered grid with implicit diffusion and a Chorin projection method for updating pressure. The solver method was modified from use of the non-dimensional Navier-Stokes equations to the dimensional form shown in Eq. 6 using SI units with density ρ and viscosity μ instead of a non-dimensional Reynolds number. In addition, the Lorentz force, $\mathbf{f}^{\text{EM}}$ from Eq. 5, was added as an electromotive body force in the velocity update at each time step prior to pressure gradient computation, thereby completing the EMHD force balance. The final EMHD model assumes no charge carrier redistribution (uniform charge density throughout the phantom), no magnetization of the fluid, insignificant polarization forces compared to the main component of the Lorentz force, and no background flow.

2) Phase Accumulation and Signal Loss

In our LEI protocol, the oscillating magnetic field gradients are synchronized to the frequency of the applied current such that the current, and hence the Lorentz force, is turned on during the positive gradient lobes, resulting in a maximal incoherent water displacement and phase accumulation caused by the electrical activity, whereas it is turned off during the negative gradient lobes, resulting in a minimal water displacement and phase accumulation. The motion-induced phase accumulation of each particle spin, p , is therefore enhanced by

the application of oscillating gradients over the total oscillating gradient period. The phase accumulation of each p, ϕ_{Rp} is computed as follows [16]:

$$\phi_{Rp}(t) = \int_0^t \omega_R(\tau) d\tau = \gamma \int_0^t \mathbf{G}(\tau) \cdot (\mathbf{v}(\tau)\tau + \mathbf{x}_0) d\tau \quad (7)$$

where ϕ_R is the relative spin frequency, γ is the gyromagnetic ratio ($2\pi \cdot 42.58 \cdot 10^6$ rad/s/T), $\mathbf{G}$ is the magnetic field gradient (T/m), and $\mathbf{x}_0$ is the location of p at the start of the protocol.

a) Computation of Phase Accumulation from Particle Displacements—We compute ϕ_{Rp} and the resulting signal loss based on fluid particle displacements along the oscillating gradients of strength $\mathbf{G} = (G_x, G_y)$. Specifically, we use the Reynolds transport theorem, the Eulerian form of the time integral of particles moving through a defined set of fixed coordinates, thereby enforcing a uniform charge distribution. For a spin p detected at position $\mathbf{x}$, its relative frequency and phase are defined in Eq. 7. For all spins p passing through a region $A(t)$ bounded by a set of grid points g with fixed positions $\mathbf{x} = (x, y)$, the following is true:

$$\frac{d}{dt} \iint_{A(t)} \phi_{Rp} dx dy = \iint_{A(t)} \left(\frac{d\phi_{Rp}}{dt} + \nabla \phi_{Rp} \cdot \mathbf{v} + \phi_{Rp} \nabla \cdot \mathbf{v} \right) dx dy \quad (8)$$

After substituting the first term on the right-hand side of Eq. 8 with $d\phi_{Rp}/dt = \omega_R(t)$ and ignoring the third term due to incompressible flow ($\nabla \cdot \mathbf{v} = 0$), the following expression is used to evaluate the Eulerian form of ϕ_R for each g:

$$\frac{d\phi_R}{dt} = \omega_R(t) + \nabla \phi_R(t) \cdot \mathbf{v}(t) \quad (9)$$

Note that ϕ_{Rp} in Eq. 8 represents the relative phase of an individual spin p, whereas ϕ_R in Eq. 9 represents the relative phase computed at a fixed coordinate in the phantom space, accounting for spins entering and exiting the finite region $A(t)$. The same coordinates were used for g and the finite difference grid. Using a small Δt , we update ϕ_R at each time step in two dimensions as follows:

$$\phi_R(t_{k+1}) = \phi_R(t_k) + \Delta t \gamma (G_x x + G_y y) + \Delta t \left(\frac{\partial \phi_R(t_k)}{\partial x} v_x(t_{k+1}) + \frac{\partial \phi_R(t_k)}{\partial y} v_y(t_{k+1}) \right) \quad (10)$$

This new form of ϕ_R accounts for the accumulation of phase in a finite region of the phantom space based on the position of particle spins along the oscillating gradients, as well as the spatial distribution and movement of spins in and out of the region where ϕ_R is being computed. We used a time step Δt of 2 μ s, which is 1000 $\times$ smaller than one current pulse or one oscillating gradient lobe. Using a time step of 0.2 μ s resulted in less than 1% mean relative changes in velocity and displacement. Since we only simulated the central slice containing both electrodes, the simulated spins only move within that slice, because the Lorentz force only has non-zero components in the x-y plane.

b) Computation of the Signal Loss from Phase Accumulation—The signal contribution s of each spin p detected at $t = n \Delta t$ is defined as follows [16]:

$$s(t) = m(t)e^{-i\phi(t)} = m(t)e^{-i\phi_0(t)}e^{-i\phi_R(t)} \quad (11)$$

where $m(t)$ is the relative signal magnitude for p , including T_1 and T_2 relaxation effects. We compute the total voxel signal strength S at detection time t as the integral of the signal contribution from all spins p within the x - y bounds of the voxel [16, 17]. In evaluating S , we assume that $m(t)$ remains the same with or without the application of oscillating gradients. We also discretize the time integral to evaluate ϕ_R (using Eq. 10) for each p and compute the spatial integral along x and y over the voxel by summing all s detected in the voxel:

$$S(t) = m(t)e^{-i\gamma B_0 t} \sum_{p=1}^N \exp \left[-i \sum_{k=0}^n \phi_R(t_k) \right] \quad (12)$$

where N is the total number of simulated spins per voxel. Note that N simply reflects the number of points per voxel that were used in the finite difference grid for solving the system of equations and that the results do not critically depend on N , as long as it is sufficiently large. In this work, we used $N = 16$. Using larger values required very long computation times, but did not significantly change the results.

In the absence of oscillating gradients, we assume a homogeneous static magnetic field B_0 , making ϕ_0 constant for the reference voxel signal S_0 , which is computed as follows:

$$S_0(t) = \int_x \int_y m(t) e^{-i\phi_0(t)} dx dy = m(t) e^{-i\gamma B_0 t} N \quad (13)$$

We display the intensity of each MRI voxel as S_R , the percent change in the magnitude of S relative to S_0 :

$$S_R = \left\| \frac{S(t) - S_0}{S_0} \right\| = \frac{1}{N} \left\| \sum_{p=1}^N \exp \left[-i \sum_{k=0}^n \phi_R(t_k) \right] \right\| - 1 \quad (14)$$

Note that in the absence of gradients ($G_x = G_y = 0$) and moving spins ($v_x = v_y = 0$), Eq. 10 shows that there is no phase accumulation ($\phi_R = 0$), whereas Eqs. 12 and 14 show that there is no signal loss ($S(t) = S_0(t)$ and $S_R = 0$).

The primary numerical results computed for all models were velocity and displacement. Maps of the velocity were displayed using a grayscale contour plot of the velocity magnitudes overlaid with streamlines of the velocity trajectories and arrows indicating flow direction. Mean and maximal velocity and displacement within the phantom were computed at the end of the last current pulse and at detection, respectively. In addition, maps of the electrical potential and pressure within the phantom were displayed using grayscale contour plots at all Navier-Stokes finite difference grid points. Lastly, maps of the relative signal difference (Eq. 14) were displayed for each voxel simulated using a grayscale map with bounds set at -40% and 40% to match the experimental results [5]. Mean and maximal relative signal differences in the phantom were also reported.

Results

Using a 5 mA current stimulus, the standard mobility value for copper $\mu = 5.4 \times 10^{-8}$ (m/s)/(V/m) [7], and 24 water molecules moving with each ion, the first model (ion flow) resulted

in a maximal displacement and signal loss of only 5×10^{-5} cm and $2.2 \times 10^{-5}\%$, respectively. Using the higher mobility value of $\mu = 0.128$ (m/s)/(V/m) from [5], the maximal displacement was unrealistically higher at 13 cm, beyond the bounds of the 10-cm phantom due to the lack of a boundary condition, and the maximal signal loss was only 0.027%. With either mobility value, there were no appreciable areas of signal loss in the simulated image despite overestimating the ion-water interactions in this approach.

For the same 5 mA current stimulus, the second model (particle drift) resulted in a mean - maximal velocity, displacement, and signal loss of 0.12 - 20 m/s, 0.024 - 7.4 cm, and 18% -96%, respectively, showing good agreement with previous analytical approximations of the magnetohydrodynamic effect [7]. However, the simulated image (Supplementary Figure 1) did not show a high correlation with the experimental image.

For the same 5 mA current stimulus, the third model (EMHD) resulted in a mean -maximal velocity, displacement, and signal loss of 0.34 - 36 m/s, 1.9 - 9.2 cm, and 17% - 100%, respectively (Table 1), which were similar in magnitude to the particle drift results. Looking only at signal loss in the experiment ($S_R < 0$), the EMHD simulated image (Fig. 2A) had three large areas of signal loss in the lower half of the phantom similar in location to those of the experiment (Fig. 2B), but with no overlap between the signal loss regions. Note in Fig. 2A that the signal loss ranges from 0 to 100%, but that with the chosen grayscale map, any voxel with a signal loss larger than 40% is shown as black. Signal gains ($S_R > 0$) were not seen in the EMHD simulations but the grayscale ranges were kept to match those of the experiment.

The electric potential contours in the EMHD model with the 5 mA current stimulus on show a range of potentials from +2.5 V to -2.5 V extending from the point sources at the left and right ends of the phantom, respectively (Fig. 1B). When the current stimulus was turned off, the potential distribution was uniformly zero throughout. At the end of the current pulse, the flow velocities computed on the Navier-Stokes finite differences grid were maximal and trended downward (Fig. 2C). Areas of highest flow velocity were around the electrodes. Note that the streamlines appear to be quite smooth because they only reflect the mean trajectory in each voxel. However, different water molecules within a voxel actually have different trajectories. Such an incoherent displacement results in an intravoxel dephasing, which in turn leads to a signal loss, as observed in the simulated image (Fig. 2A). Furthermore, the EMHD model was able to report pressure values in the phantom with a pressure gradient (Fig. 2D) that opposes the general direction of velocity; pressure was minimal at the top and maximal at the bottom of the phantom.

For a current stimulus with an equal magnitude but opposite polarity (-5 mA), contours of the electric potential (left-right mirror image of Fig. 1B), velocity (Fig. 3C), and pressure (Fig. 3D) were identical but opposite in direction as compared to the case with a positive current polarity (Figs. 1B, 2C, 2D). In addition, the magnitude of the mean and maximal velocity, displacement, and relative signal loss values were equal. Lastly, the areas of signal loss were similar but occurred in the top half of the phantom (Fig. 3A) rather than in the bottom half (Fig. 2A). These results show that the LEI contrast is reversible when changing the current polarity, which was also observed in the experiments (Figs. 2B vs. 3B).

We next used a smaller current to understand how the LEI contrast scales with current strength. For 0.5 mA current pulses, the mean - maximal velocity, displacement, and signal loss were 0.034 - 3.6 m/s, 0.23 - 6.1 cm, and 2.54% - 100%, respectively (Table 2). The simulated image shows regions of greatest signal loss around the electrodes and a thin region of signal loss at the bottom (Fig. 4A). However, the signal loss seen in the

experimental image (Fig. 4B) was focused mainly around the electrodes, extending more inward with no obvious signal loss at the bottom.

Discussion

To gain a better understanding of the LEI contrast mechanisms proposed in previous studies [5, 7], three different models of the Lorentz effect were developed and the simulated images were compared with those obtained in the phantom experiments of Truong et al. [5]. In the first model, the Lorentz effect on ion flow was explored and found to be incapable of explaining appreciable signal losses, as it resulted in 1% maximal signal loss regardless of the mobility value selected. This was likely due to the limited amount of water molecules associated with each travelling ion. These results show that the Lorentz effect on ions is not a principal mechanism explaining the signal losses observed in the LEI experiments [5], regardless of the mobility value selected.

The particle drift and EMHD models, on the other hand, were able to demonstrate detectable LEI signal losses. In addition, the directionality, reversibility, and scalability of the velocity, pressure, and signal loss patterns based on the current polarity and amplitude were demonstrated with EMHD. The downward trend in the EMHD velocity is supported by the particle drift theory: with the magnetic field pointing in the +z direction and the electric field pointing in the -x direction (for a positive current pulse), the drift velocity trends in the $\mathbf{E} \times \mathbf{B}$ direction, i.e., the -y direction. The simulated pressure gradient also opposed the downward direction of the Lorentz force and velocity, with higher pressure near the lower boundary, supported by accepted EMHD theory [8].

Comparing the quantitative results of the particle drift model vs. the EMHD model for a 5 mA current stimulus, there was a similar mean (18% vs. 17%) and maximal (96% vs. 100%) signal loss, but a lower mean (0.12 vs. 0.34 m/s) and maximal (20 vs. 36 m/s) velocity and a lower mean (0.024 vs. 1.9 cm) and maximal (7.4 vs. 9.2 cm) displacement. In addition, patterns of signal loss in the particle drift model did not match those of the experiments. Although the particle drift and EMHD models provided similar overall flow velocity direction and signal loss magnitudes, the EMHD model was able to more accurately predict the spatial distribution of signal loss seen in the experiments by accounting for the full fluid dynamics, including the viscosity forces, convective acceleration, and pressure gradients in the fluid space, especially near the boundaries.

Note that the EMHD model does not account for all of the effects seen in the phantom (e.g. the signal gains). The model was developed to explain the mechanisms of signal loss expected to dominate in any practical implementation of the LEI method. The signal gains that were observed in the experimental phantom may be due to some additional effects (perhaps nonlinear) related to flow [5] that were not considered in the current version of the model.

Comparing the quantitative results of the EMHD model vs. the experiments, the mean signal loss in the phantom was consistently larger in the model (17% vs. 9.06% for 5 mA and 2.54% vs. 1.68% for 0.5 mA). This was expected since the experiment images showed both areas of signal loss and signal gain (from effects not accounted for in the model), thereby increasing the mean relative signal change (lowering the mean signal loss) computed in the experimental phantom.

Nevertheless, comparing the results qualitatively, the main regions of signal loss were in similar locations. As a general trend, for low current amplitudes (from 0 to 0.5 mA), the main areas of signal loss were near the electrodes and began to include a thin region of

signal loss near the lower boundary of the phantom as the current was increased. For high positive current amplitudes (+1 to +5 mA), signal loss expanded from near the electrodes to a region along the lower boundary of the phantom. For high negative current amplitudes (-1 to -5 mA), signal loss areas flipped to the upper half of the phantom. In general, regions of signal loss in the experiments differed from those of the EMHD model in that at lower currents, signal loss around the electrodes extended more inward (Figs. 4A vs. 4B), and at higher currents, there was some overlap between the signal loss areas (Figs. 2A vs. 2B). This distribution of signal loss was likely affected by the physical dimensions of the experimental electrodes extending inward (2 mm diameter, 4 mm length) [5], whereas the electrodes were point sources in the EMHD model.

From our results, we can make some predictions regarding the optimization of LEI in other settings. For example, our simulations generated larger signal losses with narrower current pulses and gradient oscillations (results not shown), hence allowing improved detection of more rapidly alternating electrical activity. In addition, with a 10× smaller current strength, the mean and maximal velocity also scaled 10× less, but the mean and maximal displacement only scaled 8.3× and 1.5× less, and the mean signal loss only scaled 6.7× less, while the maximal signal loss remained at 100%. Because the signal loss does not decrease as quickly as the current strength, it may be possible to detect even smaller current strengths, but the exact limit of dipole strengths detectable using LEI has yet to be explored with our model.

Since the main objective of this study was to investigate whether EMHD can explain the LEI contrast observed in the experiments of Truong et al. [5], the simulations were performed with the same setup and parameters as those used in the experiments to compare the results. However, further studies performed with different setups and parameters more relevant to *in vivo* applications are needed to optimize the LEI technique and to investigate its feasibility for imaging neuronal activity in the human cortex. First, simulations need to be performed with a large number of smaller dipoles oriented in multiple directions within a voxel to simulate an active portion of cortex (with 10^5 pyramidal cells/mm² and 1000 synapses per neuron [18]) rather than the single dipole used in this study to simulate the phantom. Second, even though the current densities detected in our study (64 - 640 nA/mm²) have the same order of magnitude as current densities in activated cortex (100 - 250 nA/mm² [18]) and despite the fact that the signal loss does not decrease as quickly as the current strength, simulations also need to be performed with 10^3 × smaller currents similar to those generated by cortical axons and dendrites (1 - 10 nA vs. 0.5 - 5 mA simulated in this study) to better estimate the sensitivity of LEI for imaging neuronal currents in the human cortex. Finally, further studies are needed to explore other aspects of the LEI protocol (e.g., the frequency of the oscillating gradients, which must be synchronized to the neuronal currents of interest) to optimize its use for different patterns of neuronal activity.

Note that the water displacement induced by neural activity *in vivo* is expected to be much more incoherent than in the phantom, not only because of the presence of complex microstructure, but also because of the presence of a substantially larger number of dipoles oriented in multiple directions within a voxel, as opposed to the single dipole used in the phantom. Such an incoherent displacement would still predominantly result in an intravoxel dephasing and signal loss in magnitude images rather than a coherent phase shift in phase images. Although the EMHD model may need to be modified to account for the presence of complex microstructure *in vivo*, we expect that the current model applied to a large number of dipoles oriented in multiple directions within a voxel can already provide very useful and more realistic results.

In conclusion, our study has shown that EMHD is a principal mechanism explaining the patterns of signal loss in the LEI phantom experiments of Truong et al. [5]. This model has the added benefit of providing information regarding velocity, displacement, pressure, and other parameters not readily available in an actual experiment. Thus, the EMHD model developed here is a robust platform for studying the LEI contrast mechanism and for optimizing LEI protocols in future experiments.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Electromagnetohydrodynamics (EMHD) in Lorentz Effect Imaging (LEI) was explored
- Computational models and experimental results were compared to study LEI contrast
- Particle drift approximated magnitude but not distribution of LEI signal loss
- EMHD approximated magnitude and distribution of signal loss, velocity, and pressure
- EMHD is a robust model to study/optimize LEI in other settings like cortical mapping

Fig. 1. Computational model and experimental LEI protocol

A. Computational model showing the 10-cm diameter circular phantom domain within a 12×12 cm viewing domain. Electrolyte properties and parameters simulated are based on the experiment [5]. A stimulus current, I , was applied across two point electrodes with the anode at the left-most point and the cathode at the right-most point.

B. Contour plot of the electric potential with the 5 mA current stimulus on, showing a range of potentials from +2.5 V to -2.5 V. Electric potential with the current stimulus off was uniformly zero.

C. Pulse sequence in the LEI experiment. Fifteen gradient oscillations with positive lobes synchronized to the applied current pulses were used. Computational model gradient lobes were rectangular rather than trapezoidal.

Fig. 2. EMHD and experimental images of the relative signal change and EMHD maps of the velocity and pressure for 5 mA current pulses

A. Image of the relative signal change from the EMHD model, showing three main regions of signal loss in the lower half of the phantom. The mean and maximal relative signal loss values are reported in Table 1.

B. Corresponding image of the relative signal change from the experiment, showing three main areas of signal loss overlapping in the lower half of the phantom. Areas of signal gain were due to flow effects, which were ignored in the EMHD model.

C. Contour plot of the velocity magnitude (m/s) with streamlines and arrows indicating flow directions at the end of the final current pulse. Mean and maximal velocity magnitudes are reported in Table 1. Of note, flow direction trends downward.

D. Contour plot of pressure values (Pa) at the end of the final current pulse. Pressure values are minimal at the top and maximal at the bottom of the phantom, resulting in a pressure gradient that opposes the direction of flow velocity.

Fig. 3. EMHD and experimental images of the relative signal change and EMHD maps of the velocity and pressure for -5 mA current pulses

A. Image of the relative signal change from the EMHD model, showing three main areas of signal loss in the upper half of the phantom. The mean and maximal relative signal loss values are reported in Table 1.

B. Corresponding image of the relative signal change from the experiment, showing three main areas of signal loss overlapping in the upper half of the phantom. Areas of signal gain were due to flow effects, which were ignored in the computational model.

C. Contour plot of the velocity magnitude (m/s) with streamlines and arrows indicating flow directions at the end of the final current pulse. Mean and maximal velocity magnitudes are reported in Table 1. Of note, flow direction trends upward.

D. Contour plot of pressure values (Pa) at the end of the final current pulse. Pressure values are maximal at the top and minimal at the bottom of the phantom, resulting in a pressure gradient that opposes the direction of flow velocity.

Fig. 4. EMHD and experimental images of the relative signal change and EMHD maps of the velocity and pressure for 0.5 mA current pulses

A. Image of the relative signal change from the EMHD model, showing regions of greatest signal loss focused around the electrodes. Mean and maximal relative signal loss values are reported in Table 2.

B. Corresponding image of the relative signal change from the experiment, showing regions of greatest signal loss focused around the electrodes.

C. Contour plot of the velocity magnitude (m/s) with streamlines and arrows indicating flow directions at the end of the final current pulse. Mean and maximal velocity magnitudes are reported in Table 2. Of note, flow direction trends are similar to those of Fig. 2.

D. Contour plot of pressure values (Pa) at the end of the final current pulse. Pressure values are minimal at the top and maximal at the bottom of the phantom, resulting in a pressure gradient that opposes the direction of flow velocity.

Table 1
EMHD model mean and maximal velocity, displacement and signal loss for ± 5 mA
current pulses

	Mean	Max
Velocity at the end of the final current pulse	0.34 m/s	36 m/s
Displacement at the end of the final negative gradient lobe	1.9 cm	9.2 cm
Relative signal loss at detection	17%	100%

Table 2
EMHD model mean and maximal velocity, displacement and signal loss for 0.5 mA
current pulses

	Mean	Max
Velocity at the end of the final current pulse	0.034 m/s	3.6 m/s
Displacement at the end of the final negative gradient lobe	0.23 cm	6.1 cm
Relative signal loss at detection	2.54%	100%