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## **Evaluating optimal strategies for electric field dosimetry from intracranial electrodes**

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**Presented by:** *Borja Mercadal*

Intracranial electrodes are used clinically for diagnostic (e.g. in drug-refractory epilepsy) or therapeutic (deep brain stimulation, e.g. epilepsy) purposes. Electrical stimulation delivered through such electrodes is key to understand how the resulting electric fields modulate neuronal (hyper)excitability. However, quantifying such fields in a patient-specific way is challenging, since etiology impacts brain anatomy (morphology) and biophysical properties (e.g., conductivity). Here, we evaluate how to approximate the electric fields from intracranial electrodes used clinically. Those results are the first step towards computationally tractable, patient-specific models of electric fields generated during neuromodulation protocols.

### **Introduction**

Stereoelectroencephalography (SEEG) is routinely used to identify epileptogenic zones (EZ) in drug-refractory epilepsy through the implantation of intracranial electrodes. Recording of spontaneous activity, and electrical stimulation via SEEG electrodes, are used to determine the 3-dimensional spatiotemporal organization of the epileptic network within the brain, and identify potential targets for surgical resection [1]. By electrically stimulating different brain regions, SEEG electrodes can provide a functional map where epileptogenic zones are distinguished from the functional cortex, possibly by triggering symptoms and seizures. Electrical stimulation using intracranial electrodes has also shown the potential to regulate pathological hyperexcitability, despite an incomplete understanding of the

underlying mechanisms and anatomical targets. Therefore, evaluating the electric field induced by SEEG electrodes is of considerable interest to develop further and optimize diagnostic and therapeutic applications in drug-refractory epilepsy.

Traditionally, numerical methods such as the finite element method (FEM) are used to calculate the electric field in volume conductor problems. The use of realistic head models based on magnetic resonance (MR) images including several tissue types significantly increases the complexity of modeling geometrically accurate electrodes, resulting in models that are computationally expensive and technically challenging to implement. Since a major problem consists in the generation of a proper mesh for the connection between two complex geometries [2], possible alternatives to overcome this problem consist in approximating the electrode's cylindrical shape (3d) by a point source (0d) or a line (1d). Here, using simplified head models, we aimed to evaluate if 0d and 1d current source approximations (point and line source, respectively) are satisfactory to quantify the electric field induced by SEEG electrodes, using a comparison with a realistic model of SEEG electrodes.

## Methods

A three-dimensional head model (100 × 100 × 100 mm) with a simplified representation of a sulcus, consisting of concentric cuboids, was built in Comsol Multiphysics v5.6 (Comsol AB, Stockholm, Sweden), and is presented in Figure 1. Each tissue type was represented with a cuboid where the outer one corresponds to the scalp with a conductivity of 0.3 S/m, followed by the skull set to 0.01 S/m, the cerebrospinal fluid (CSF) set to 1.79 S/m, and the grey and white matter with a conductivity of 0.4 and 0.15 S/m respectively. The thickness of the domain representing each tissue is shown in Figure 1.

The realistic geometry of the SEEG electrode and its position is shown in Figure 1. The lead consisted of seven cylindrical contacts, 2 mm long and 0.8 mm in diameter (shown in blue, conductivity of 1000 S/m), separated by 1.5 mm of insulating parts (conductivity of 0.001 S/m). In the point source approximation, points were located at the center of mass of the realistic electrodes. Finally, the line source approximation was built using lines with the same length as contacts and located along their central axis.

The three model geometries were meshed in COMSOL resulting in 6701125, 5921464, and 5903782 tetrahedral elements for the realistic, line source, and point source models, respectively.

The electric field magnitude was computed by solving the Laplace equation using a steady-state approach in COMSOL:

$$\vec{\nabla} \cdot (\sigma \vec{\nabla} V) \quad (Eq.1)$$

where  $V$  is the electric potential (V) and  $\sigma$  is the conductivity (S/m).

In the realistic model, a floating potential boundary condition was imposed at the surface of all contacts, with a zero current in the non-active contacts and 1 mA in the two active contacts. In the case of the line and point source approximations, a line or point source of 1 mA was defined at the active contacts.

In order to compare the different models, the results obtained were exported using a 3-D grid with a resolution of 0.25 mm. This data was used to calculate the relative error in the electric field magnitude between the realistic model and the approximations. In order to quantify the performance of the two approximations for different distances and estimate the regions in which they can be used safely, we computed the average relative error as a function of the distance from the lead. For each point of the grid, we computed its distance to the lead axis. These distances were then rounded to millimeters to group the grid points and calculate the mean error at each distance range.

We also computed the volumes enclosed by the field iso-surfaces for various field magnitudes. This was performed for all models using COMSOL built-in functions, with the goal of providing an additional tool to compare the different models.

## Results

We computed the electric field distribution generated by all consecutive electrode pairs in the lead using the realistic model and the two approximations. Figure 2 presents the results obtained with one of the pairs (see Figure 2a). The resulting electric field distributions for each model are shown in Figure 2b–d. Figure 2e shows the distribution of the relative error of the field magnitude between the realistic model and the two approximations. There is a region with a large error near the lead (1–2 mm from its center), which is seen not only at the active contacts but also near the non-active ones caused by the distortion of the field lines due to the presence of the conductor. The error near the active contacts was lower for the line source model. However, above a certain distance from the lead, the point source approximation provided a better estimation of the field magnitude. The field iso-lines indicate the same (Figure 2f). The iso-lines generated with the line source approximation more closely matched those from the realistic model for the more intense closest iso-line, while the furthest (less intense) iso-line was better approximated by the point source model.

Figure 2g presents the mean relative error between the realistic model and the approximations as a function of the orthogonal distance to the lead. The error was consistently lower for the point source approximation regardless of the distance. Using this approach, we quantified the minimum distance at which the relative error decreased below 0.1 and 0.05 for all consecutive pairs. The results are presented in Figure 3a–b. When using the point source model (Figure 3a), except for one pair, at distances of 2 and 4 mm, the mean error was below 0.1 and 0.05, respectively. These distances were larger when considering the line source approximation (Figure 3b). In this case, the minimum distances to obtain an error below 0.1 were generally larger, and in 3 out of the 6 contact pairs simulated, the model yielded an error above 0.05 throughout the entire range analyzed (15 mm).

Finally, we compared the volumes of the electric field iso-surfaces for different magnitudes. Figure 3c shows the volumes obtained with all contact pairs and the three models. The mean relative error between the volumes of the realistic model and the line and point source approximations are displayed in Figure 3d. For all the field magnitudes considered, the point source, on average, produced iso-surface volumes more similar to those obtained with the realistic model.

## Discussion

According to our results, the line source approximation better matches the morphology of the electric field distribution obtained with the realistic model near the active contacts. However, for distances of only 1–2 mm, the point source model consistently provides a better estimation of the field magnitude. The geometry of the line source model shapes the electric field more similarly to the realistic one. Therefore, at points nearby the active contacts, the error is lower compared to the point source model. However, the line source model considers a homogeneous current density along the entire line, while in the realistic model, this magnitude varies along the surface of the electrode (especially if the electrode intersects a tissue boundary). Thus, although the field distribution is shaped more similarly to the realistic model, the assumption of a homogeneous current density prevents this approximation from correctly estimating the field magnitude. As a consequence, the electric field magnitude is surprisingly more accurately estimated with the point source model despite being the most simplistic geometrically.

Although the values used in this study are not clinically relevant, the field iso-surfaces and their volumes are commonly used to assess the spatial coverage of brain stimulation [3]. Our results show that these volumes are more accurately estimated by the point source approximation. Similarly, the morphology of the iso-surfaces, except for the largest field values, seem to be better predicted by the point source approximation.

In an attempt to quantitatively assess the performance of the approximations as compared to the realistic model, we computed the average error as a function of the distance from the lead. Based on these results, it appears that the point source approximation can provide an accurate estimate of the field magnitude, in most cases, for distances larger than 4 mm from the lead axis. A relatively accurate estimate can also be expected for distances between 2 and 4 mm. While for shorter distances the error increases drastically. Therefore, unless an accurate estimation of the field near the contacts is needed (~2 mm scale), the point source approximation is a suitable model for estimating the electric fields generated during neuromodulation protocols in patient-specific models.

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## Figures

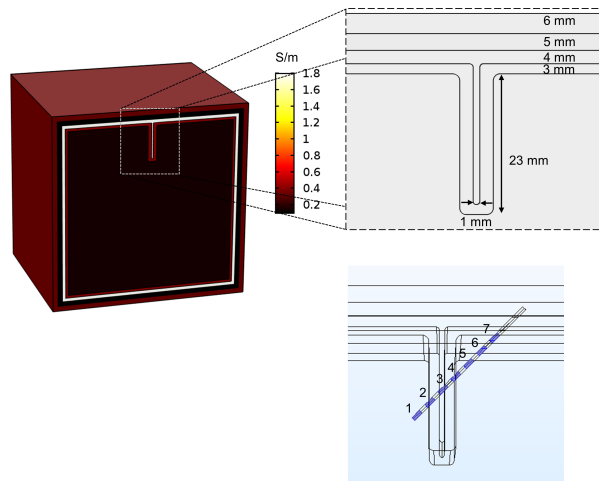


Figure 1. The three-dimensional head model used in the present study, including five layers of different conductivity matching those measured or estimated in vivo.

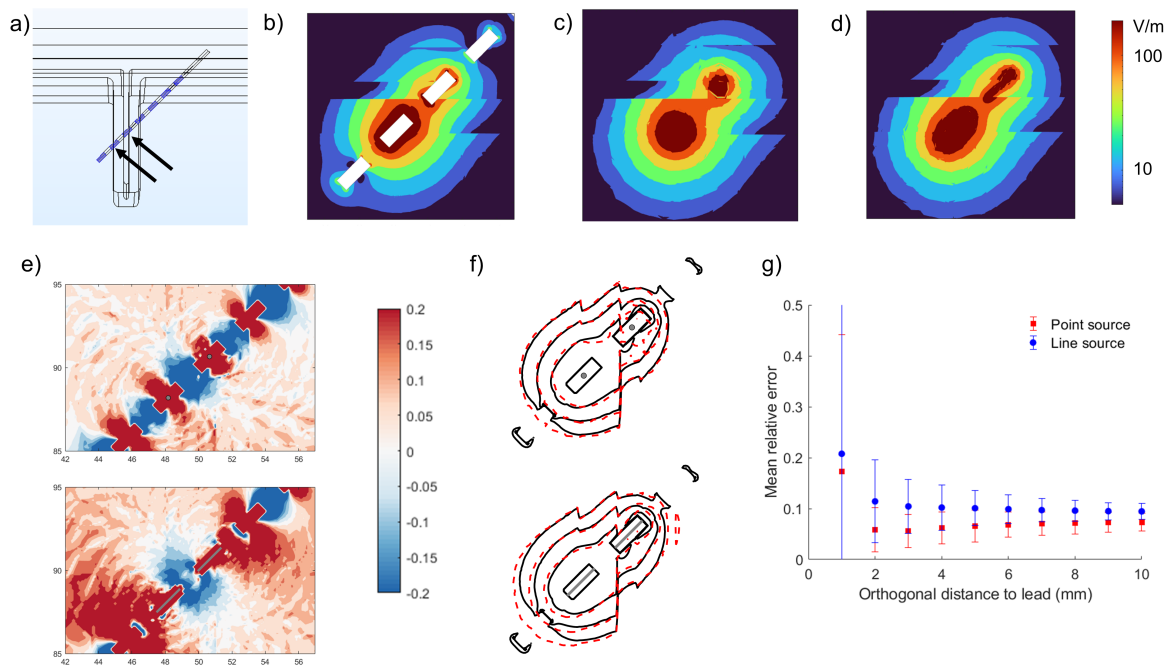


Figure 2. a) Pair of active contacts used in the simulation. b) c) and d): Electric field distribution in a plane containing the lead when injecting a 1 mA current with the contact pair using (b) the realistic model, (c) the point source approximation, and (d) the line source approximation. e) Relative error in a plane containing the lead between the realistic model and the point source approximation (top), and between the realistic model and the line source approximation (bottom). f) Field isolines (for 20, 40, and 100 V/m) in the same plane for the realistic model (black lines), the point source approximation (red dashed lines, top), and the line source approximation (red dashed lines, bottom). g) Mean relative error and standard deviation between the approximations and the realistic model as a function of the orthogonal distance from the lead.

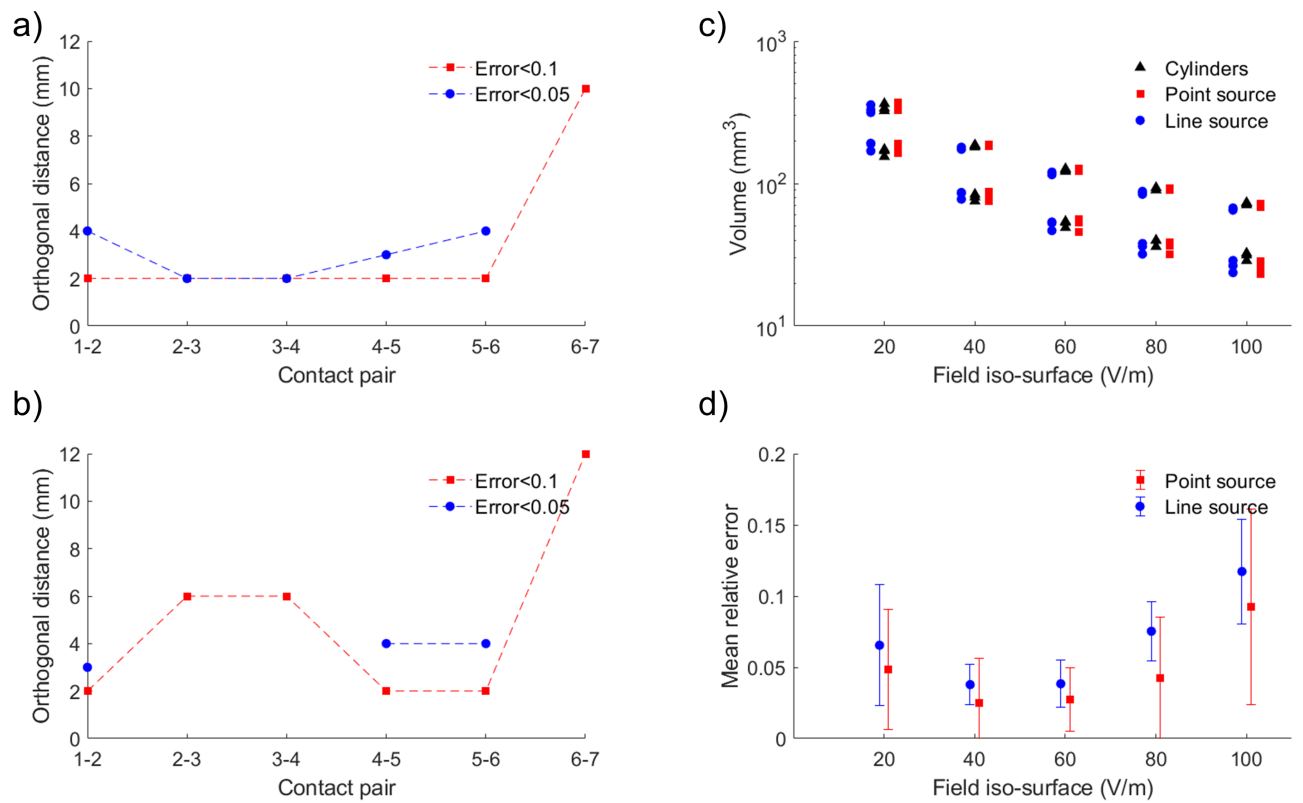


Figure 3. a) Distance at which the mean relative error between the point source approximation and the realistic model is below 0.1 and 0.05 for all consecutive contact pairs. If no value is shown for a contact pair, it means that the error was larger throughout the entire range of distances (15 mm). b) Same as a) when comparing the line source approximation and the realistic model. c) Volume of the field iso-surfaces at different field values for all consecutive contact pairs and for the three-electrode models. d) Mean relative error and standard deviation when comparing the volumes shown in c) between the realistic model and the approximations.