Dipolar source localization from intracerebral SEEG recordings

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Abstract

This paper aims at exploring the feasibility of a brain source localization method from intracerebral stereo-electroencephalography (SEEG) measurements. The SEEG setup consists in multi-contact electrodes inserted in the brain volume, each containing about 10 collinear measuring contacts. In clinical context, these signals are usually observed using a bipolar montage (potential differences between neighbouring contacts of a SEEG electrode). The propagation of distant activity is thus suppressed, resulting in the observation of local activities around the contacts. We propose in this paper to take benefit of the propagation information by considering the original SEEG recordings (common reference montage), with the objective to localize sources possibly distant from the electrode contacts, and whose activities are propagating through the volume. Our method is based on an equivalent dipole model for the source and homogeneous infinite models for the propagation environment. This simple approach shows satisfactory localization performance under appropriate conditions, described in this paper. The proposed method is validated on real SEEG signals for the localisation of an intra-cortical electrical stimulation (ICS) generator.

Index Terms

EEG, Stereo-electroencephalography (SEEG), Equivalent Dipole Localization, Inverse problem, Intra-cortical electrical stimulations (ICS)

I. INTRODUCTION

During pre-surgical evaluation of epileptic patients, stereo-electroencephalography (SEEG) is considered as the golden standard for exploring targeted structures assumed to be involved in the epileptogenic process [1]. In such context, the SEEG signals are observed using a bipolar montage, thus suppressing the influence of far sources activity in the resulting signal. This modality is often used to confirm or infirm the results of a preliminary localization obtained either by clinical exploration or from scalp EEG recordings. Scalp-EEG based localization (issued from a forward/inverse problem modelling) have been extensively applied in order to localize brain sources. The inverse problem is severely ill-posed: the number of sources is unknown, the environment model is uncertain and the signals are noisy and sometimes redundant (highly correlated). For very complete reviews of the source localization/estimation approaches in EEG the reader is referred to [2], [3], [4]. As far as we know, this source localization problem has never been applied yet on real intracranial SEEG recordings, even if some papers addressed this problem on simulation [5], [6]. In fact, the main reason for the absence of studies on real signals is the validation problem.

Our aim is to extend the role of the SEEG from an exclusive clinical tool to a new modality for distant source localization on real signals. This paper describes a straightforward method, demonstrating the feasibility of the SEEG-based localization even when based on a simple forward/inverse models. The particularities of the SEEG inverse problem are discussed, both concerning the spatial distribution of the sensors and the influence of the signal to noise/perturbation ratio (SNR). The conclusions are evaluated and validated on simulation. Next, the proposed approach is applied on real SEEG signals recorded during electrical intra-cortical stimulation (ICS), and yields satisfactory results in retrieving this known dipole position and orientation.

The paper is structured as follows: in the second section, the general background is given for EEG source localization based on forward/inverse modelling. The third section presents the specificities of the localization problem in an SEEG context (environment model, sensor conditioning, noise issues). The fourth section details the results, both in simulation and on real ICS recordings. The paper ends with a conclusion and future research section.

II. SEEG FOR SOURCE LOCALIZATION

A. The propagation model

Electrical potentials recorded by the electrodes are generated by neural sources, generally modelled as equivalent current dipoles. For the frequency range of the brain activity and taking into account the distances between sources and sensors, it is assumed that no delay exists between them. Consequently, the mixing is said to be instantaneous or linear. Following [7], at a given time instant, the potentials $\mathbf{\Phi}_0$ recorded by the N_c electrodes can be written as:

$$\mathbf{\Phi}_0 = \mathbf{K} \cdot \mathbf{J} + r \cdot \mathbf{1} \tag{1}$$

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This work is supported by the CNRS-PEPS APSE and the french ANR SEPICOT

with $\mathbf{K} \in \mathbb{R}^{N_c \times (3N_s)}$ the so-called lead field matrix, coding the distances and the propagation coefficients between the N_s sources and the N_c captors, $\mathbf{J} \in \mathbb{R}^{(3N_s) \times 1}$ the current density vector (in three directions x, y and z) for the N_s sources, r the potential of the common reference electrode and $\mathbf{1}$ a vector $(N_c \times 1)$ of ones.

This model is general and can be used for any recording modalities including EEG and SEEG[1].

B. (S)EEG Forward/Inverse problem

A critical issue to form a reliable **forward problem** is the accuracy of the models adopted for $\mathbf{K}$ and $\mathbf{J}$ in (1). In order to produce an electrical field able to be measured by EEG/SEEG electrodes, the neurons from a given brain region need to be synchronised. In this case, the brain region can be called a generator (source) and its activity is modelled as a current dipole. A dipole is a vector determined by 6 parameters (3 spatial coordinates for its origin and 3 for the orientation and the amplitude).

The potentials $\mathbf{\Phi}$ are obtained by (1) using a head model or lead field matrix $\mathbf{K}$. Different approaches exist, starting from simple analytical models (infinite homogeneous environment) to numeric anatomical models obtained for each patient using CT (Computed Tomography)/MRI (Magnetic Resonance Imaging) images. The main advantage of the infinite homogeneous model (IHM) is its fast calculation time and possibility to predict fairly well the measurements, provided that the hypothesis of homogeneity and isotropy are valid. While these assumptions are clearly false for surface EEG, it is reasonable to suppose that the SEEG measurements are (almost all) taken inside the brain, which is usually modelled as homogeneous and isotropic [11], [6]. For infinite homogeneous medium with conductivity σ, the 3D row vector $\mathbf{k}_{ij}$ (seen as an element of $\mathbf{K}$) writes:

$$\mathbf{k}_{ij} = \frac{1}{4\pi\sigma} \frac{(\mathbf{r}_{\Phi_i} - \mathbf{r}_{\mathbf{j}_j})}{||\mathbf{r}_{\Phi_i} - \mathbf{r}_{\mathbf{j}_j}||^3} \tag{2}$$

where $\mathbf{r}_{\Phi_i}, \mathbf{r}_{\mathbf{j}_j} \in \mathbb{R}^{1\times 3}$ are position vectors for the i-th electrode and for the j-th source respectively and $||\cdot||$ designates the classical 2-norm. Of course, these relations can be used to compute the potentials in every chosen point of the 3D space.

The general aim of the **inverse problem** is to estimate source parameters from the measurements and a given propagation model. Two classes of inverse problems appear in the literature, see [3] for a review: over-determined (or parametric) approaches where one or few dipoles are considered, and under-determined (or distributed) approaches, where the number of considered dipoles is much higher (in principle equal to the number of nodes in the cortex mesh).

In specific cases (ictal activities or interictal spikes for example), one of the brain regions (sources) generates a signal having a much higher amplitude than the other regions. In this case, the recorded electrical activity can be approximated with one dipole [1] and we are in the over-determined case, thus looking for an optimal solution. We focus in this research on this particular model. To better understand the influence of the different parameters on the results and assuming that the source of interest is the first one ($\mathbf{j}_1$), we rewrite the mixing model (1) as:

$$\mathbf{\Phi} = \mathbf{k}_1 \cdot \bar{\mathbf{j}}_1 \cdot s_1 + \mathbf{N} \tag{3}$$

where $\mathbf{k}_1$ $(N_c \times 3)$ is the vector corresponding to the projections on sensor i of the first source (seen as a dipole in 3D), $\bar{\mathbf{j}}_1$ (3×1) is a vector containing the projections of the *normalized* dipole $\mathbf{j}_1$ on the 3 axes, s_1 is its amplitude and $\mathbf{N}$ $(N_c \times 1)$ contains the projection of all the other sources on the electrodes, seen here as additive noise (from the main dipole point of view). As mentioned previously, the reference potential r is supposed to be null or suppressed and is no more considered.

Under these hypothesis (one dominant source), the (known) model inversion problem is non-linear and over-determined. In this paper we used the well known moving dipole approach, based on a simplex optimization as in [12]. In the following section are discussed the specificities of the intracranial SEEG recordings facing the EEG scalp recordings when considering the source localization issue.

C. SEEG specificities and sensor conditionement

SEEG uses sensors placed directly into the brain tissue. Ten to fifteen intra-cerebral multi-contact electrodes, each one having 10-15 equally spaced measuring contacts are placed within the desired brain areas in order to estimate the epileptogenic zone more accurately.

Main advantages of SEEG on EEG is to provide a high signal to noise ration (SNR), as the captors are in principle placed closer to the sources and are not impacted by the attenuating effect of the skull. Also, these intracerebral recordings are less affected by electromagnetic noise or by extra-cerebral artefacts (muscle, eyes, ...), constantly polluting the scalp measurements. These considerations make the SEEG a particularly interesting candidate for solving the source localization problem.

On the other hand, SEEG is a very spatially focused modality and it does not provide a global image of the brain. As said previously, in surface EEG the sensors are placed all around the brain volume, except of course for the inferior part. This

[1]Equation (1) highlights the presence of the unknown reference potential in the measurements. The problem is addressed by [7], [8] for scalp EEG and by [9], [10] in SEEG. In the present paper, we assume that r potential is 0 or close to 0, the non-null reference issue being left for future investigations.

is not the case in SEEG, and some regions of interest may be missed if they are far from the implantation site. Moreover, unlike in surface EGG, sensor geometry is highly sensitive, as it can be seen from some simple examples.

Indeed, in dipole localization, as 6 parameters are to be determined, at least 6 sensors are needed. The simplest recording setup uses one multi-contact depth electrode. The sensors are in this case collinear and the localization problem is undetermined, regardless of the number of available signals. The dipole component orthogonal to the plane determined by the needle and the origin of the dipole cannot be seen by any of the sensors. Consequently, at least two multi-contact electrodes are needed. Moreover, they have to be in different planes. Indeed, a symmetrically placed dipole (with respect to a plane) will produce the same potentials on coplanar sensors. Besides, dipoles having their origin in the plane are also undetermined (the orthogonal component is invisible to the sensors). Although this situation is hypothetical, as the electrodes are seldom inserted in the same plane, the noise (i.e. the background activity) can mask in part the dipole of interest on sensors situated in a sort of 'slice' of brain tissue, a kind of thicker version of a plane.

III. Application

According with the previous analysis, in simulations as well as in real situations, we considered at least 6 sensors on 3 or more non coplanar electrodes placed in an infinite homogeneous medium having the conductivity of the brain tissue ($\sigma = 0.33$ S/m).

A. Simulation

The method is evaluated on simulated setup in order to illustrate ill and well conditioned geometric configurations of the sensors with respect to its position and orientation. Influence of additive (independent white) noise on the localization performance has also been evaluated.

As indicated, at least 6 sensors are needed. We defined a prism with dimension $5cm \times 5cm \times 10cm$, with one sensor positioned on each of its 6 sides (configuration C0), providing well controlled geometrical configurations for our tests. Each sensor belongs to a different virtual electrode and corresponds to its deepest contact. The configuration C1 is then defined as these 6 contacts, along with a supplementary sensor on each electrode, 3.5mm far from the first one (12 nearest sensors configuration). In configuration C2, the supplementary sensors of C1 are replaced by 6 external sensors on each nail, 6cm distant from the deepest ones. Finally, configuration C3 consists in the whole set of the 18 sensors obtained in such way. The 6 nail electrodes are not parallel one to the other and are not perpendicular to any side of the prism, avoiding possible unwanted ill-conditioned configurations as those described in section II-C.

The dipole to estimate is placed in the center of the prism, either oriented towards the centre of one side of the prism (case d1), or towards a corner of the prism (d2). The purpose is here to illustrate that 6 measurements might not be sufficient for a reliable localization. Indeed, for d1, the origin of the dipole is in a plane defined by 4 of the 6 sensors. The dipole is perpendicular to this plane, which is thus the zero potential plane. Any position in this plane is then eligible and an ambiguity remains between the position and the amplitude of the dipole regarding its projection on the two non-zero sensors. In the d2 case, no such ambiguity exists.

Table I illustrates these simulations. The localization results seem to improve with the number of available well distributed sensors (C3 gives better results than C2 and C1, and it compares well with C0 for d2). Overall, the results are satisfactory, with position errors consistently below 1 mm. Localization (position) errors in the ideal case (SNR=∞) are provided in table I. When the number of sensors is limited, (i.e comparing C1 to C2) we might conclude that the addition of close sensors is more advantageous that adding far ones.

TABLE I

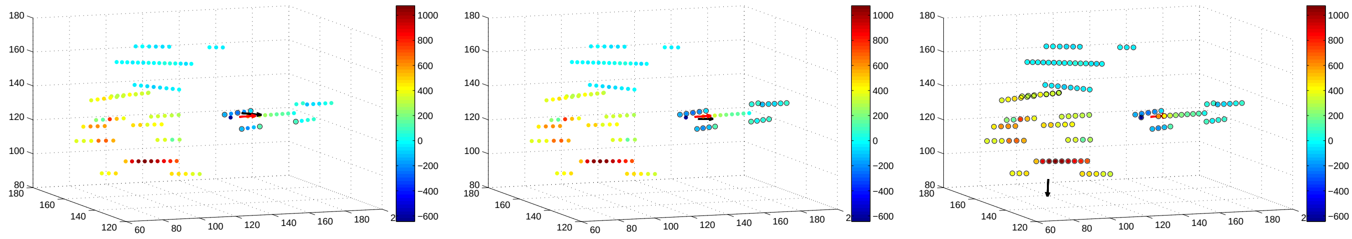
Position errors for different configurations and dipoles for noisy signals (SNR given in dB)

	d1					d2				
SNR	∞	60	40	20	3	∞	60	40	20	3
C0	61.66	61.65	54.94	12.88	25.08	0.00	0.26	0.10	0.90	15.46
C1	0.29	0.30	3.84	12.52	34.45	0.23	0.23	0.26	1.93	21.05
C2	0.81	6.03	7.04	23.74	45.43	0.28	0.28	0.30	2.04	30.45
C3	0.11	0.13	1.06	16.53	44.08	0.19	0.19	0.24	2.48	23.00

Given the same conditions, the influence of the additive noise $\mathbf{N}$ (3) (modelled as independent white Gaussian noise, often used to model the residual background noise) was also evaluated. Although not very accurate, this noise model can be used for background brain activity, in the absence of significant perturbing patterns. Several powers of noise were used, normalized with respect to the highest absolute potential value obtained on the sensors due to the propagation of the simulated dipole. The results for different configurations, dipoles and signal to noise ratios are presented in table I. As it can be seen, for high SNR (60 dB), the results are very close to the ideal case. It is worth noticing that the noise has a regularisation effect on the ill-conditioned case C0-d1. Indeed, the performances improve from a 60 mm error for a 60 dB SNR to a 12 mm error when the SNR decrease to 20 dB. In low noise situations though, this type of configuration having 4 coplanar captors should be avoided. It can also be observed that it is better to consider the whole set of sensors when the SNR is high, thus when the background noise has low impact even on far contacts. On the other hand, using recordings from far sensors when the SNR decreases acts as an introduction of additional uncertainties and leads to a decrease of the localization performances (C3 and especially C2 are less performant than C1 and C0).

B. Real ICS signals

Based on the observations from the previous simulations, we applied the method on real SEEG signals recorded during intracerebral stimulation (ICS). The considered signals were obtained from one patient during a clinical diagnostic procedure at the University Hospital (CHU) from Nancy, France. The patient gave his informed consent and the study was approved by the ethics committee of the hospital.



(a) (b) (c)

Fig. 1. Results on ICS. For all figures, the colour scale used for the electrodes indicates the recorded potential. The electrodes used for localization are circled in black: (a) 6 manually chosen contacts on two electrodes, same brain hemisphere as the ICS; (b) all electrodes from the ICS hemisphere without the contacts of the needle electrode used for stimulation; (c) all implanted electrodes, inluding those situated far from the stimulation site, in the oposite hemisphere. The red dipole indicates the (known) ICS position, while the black dipole indicates the estimated position and orientation. The position errors (in mm) and the angle errors (in degrees) are as follows: (a) $\varepsilon_p = 2.5, \quad \varepsilon_a = 14.3°$; (b) $\varepsilon_p = 2.1, \quad \varepsilon_a = 5.3°$; (c) $\varepsilon_p = 78.6, \quad \varepsilon_a = 98.95°$.

The role of the ICS in epileptic patients is (i) to identify the epileptogenic cortical structures whose stimulation usually elicit the usual seizures and (ii) to evaluate the residual cognitive function of these epileptogenic structures and predict the functional post-surgical outcome [13]. The ICS is generated differentially between two neighbouring contacts of a SEEG electrode as a succession of bipolar pulses. Consequently, at a given time instant, it can be modelled as a dipole with known position and orientation. The ICS source amplitude is well above other brain activities, making the single source hypothesis valid for reasonably close sensors. This stimulation will be used as a ground truth to evaluate the accuracy of the localization approach.

Different subsets of sensors were considered (see details below). Their positions were determined using the method presented in [14]. The initial dipole position given to the localization algorithm was the barycentre of all considered sensors positions weighted function of their absolute amplitudes, while the dipole direction was estimated as a vector pointing from lowest recorded potential to the highest.

Results are presented in figure 1. The localization using 6 manually chosen sensors shows good performance (fig 1(a)) considering these rough data. When extending the set of considered measurements to the whole set of sensors placed in the stimulated (right) brain lobe (at the exception of the stimulation needle due to saturation effects), the result slightly improved (fig 1(b)). This confirm the observation made in section III-A that when the SNR is good (which is the case in this context of highly energetic ICS source), a large number of sensors even far from the sources can be trustfully introduced in the localization process. The example of the figure 1(c) points out the importance of sensor selection. When using electrodes of the opposite brain hemisphere, the performance is poor. As secondary sources (considered here as noise) exist in this part of the brain, the SNR with regards to the source of interest is low these sensors, thus affecting severely the localization performance.

IV. Conclusion and Future Research

In this paper, a straightforward localization approach based on an infinite homogeneous propagation model is evaluated on simulated and real SEEG recordings. First, a feasibility study for dominant source localization is carried out on simulated data for different sensor configuration and noise levels. The simulation confirms that 6 well positioned sensors yield satisfactory localization performances. Nevertheless, when the noise is weak or absent, increasing the number of well conditioned sensors increases the accuracy of the localization. On the other hand, the addition of white Gaussian noise (roughly simulating the presence of background noise) is found to affect the localization performances.

Our tests on real ICS-SEEG data confirmed these observations. A manual selection of 6 well chosen measurements bring satisfactory localization performance. This setup is outperformed when the whole set of captors placed in the stimulated brain lobe (except those of the stimulation nail electrode, amplitude saturated) is considered.

Further improvements of the method need to be developed, such as a selection strategy of the most relevant measurements regarding the source of interest, the introduction of a more realistic head propagation model, the reference cancelling and the extension of the method to the case of several sources of interest. Validations on a large amount of real SEEG measurements need to be performed, with the objective to localize unknown spike generators in epileptic patients. These validations will be carried out with the help of neurologists, and they are expected to provide a reliable alternative to the clinical localization by visual inspection of the SEEG signals on bipolar montage.

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