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A realistic spatiotemporal source model for EEG activity: Application to the reconstruction of epileptic depth-EEG signals

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Abstract— **The context of this work is the interpretation of depth-EEG signals recorded in epileptic patients. This study focuses on the relationship between spatial and temporal properties of neuronal sources and depth-EEG signals observed along intracerebral electrodes (source/sensor relationship). We developed an extended source model which connects two levels of representation: a model of coupled neuronal populations and a distributed current dipole model. This model was used to simulate epileptic spiking depth-EEG signals from the forward solution at each intracerebral sensor location. Results showed that realistic spikes were obtained in the model under two specific conditions: a sufficiently large spatial extension of the neocortical source and a high degree of coupling between activated neuronal populations composing this extended source.**

I. INTRODUCTION

STEREOELECTROENCEPHALOGRAPHY (SEEG) is a pre-surgical investigation technique of drug-resistant partial epilepsy, consisting in exploring the epileptogenic zone with multisensor intracerebral electrodes [1]. It provides depth-EEG signals that correspond to the electrical mean field potentials arising from the explored brain structures. Progress in the interpretation of such signals is crucial for the understanding of neuronal mechanisms that are at the origin of epileptic discharges.

Many questions remain open regarding the relationship between the properties of depth-EEG signals and the spatiotemporal organization of neuronal populations involved in the generation of these signals. In particular, these questions are related to the cortical area involved in the generation of transient epileptic spikes, and to the changes in excitation, inhibition and synchronization parameters that occur within activated populations of neurons during such epileptiform activities.

In the present work, these questions were addressed through a physiologically-relevant reconstruction of depth-EEG signals based on an extended source model which connects two levels of description: a biomathematical model of coupled neuronal populations and a biophysical distributed current dipole model.

II. EXTENDED SOURCE MODEL

At a microscopic level, the synaptic activation of a single neuron causes a variation of the postsynaptic membrane potential. This potential difference is compensated by a current flowing through the surrounding medium, so that the configuration of the electrical field around the neuron assumes that of a dipole [2]. At a macroscopic level, the electrical field generated by a population of neurons with appropriate spatial and temporal organization can be measured at a distance. This is typically the case for the pyramidal neurons of the cerebral cortex, which are lined up orthogonally to the cortical surface. When neurons are activated synchronously, the electrical contribution of a neuronal population can be represented by an equivalent current dipole, which time-varying moment depends on the time variations of average postsynaptic potentials generated by neurons [2].

Consequently, the extended source model we developed is based on the combination of both a model of coupled neuronal populations and a distributed current dipole model. The former allows for simulation of time-varying local field potentials generated by coupled neuronal populations from alterations of physiological parameters (excitation, inhibition, and coupling). The latter permits to represent the neuronal populations of a patch of neocortex as a dipole layer with anatomically-relevant spatial configuration.

A. *Temporal Dynamics of Neuronal Populations*

Local fields potentials generated by neuronal populations primarily reflect summated postsynaptic potentials in activated neurons. In order to realistically represent their time variations, we used a physiologically-relevant model consisting in a network of coupled neuronal populations [3].

Each neuronal population contains two subsets of cells that mutually interact via excitatory and inhibitory feedback: pyramidal neurons and local interneurons. The influence of neighborhood is modeled by an excitatory input that globally represents the average pulse density of afferent action potentials. The model accounts for interconnections between neuronal populations by using the average pulse density of action potentials of one population as an excitatory input to another population. A connection from a population i to a population j is characterized by a parameter K_{ij}, which represents the degree of coupling. Couplings can be unidirectional and/or bidirectional. For standard parameter values, the model produces normal background activity. When model parameters are altered according to hypotheses related to epileptogenesis (increase of excitation/inhibition ratio and coupling strength), it was shown to generate realistic epileptiform activities, such as

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spikes [3].

A model signal output $\alpha_i(t)$ represents the time variations of local field potentials generated by neuronal population i. The amplitude of these local field potentials is dealt with by the distributed current dipole model (see section II-B).

B. Distributed Current Dipole Model

In the present work, the source of activity was assumed to be a patch of neocortex composed by N coupled neuronal populations. An anatomically realistic model of the cortical surface was built based on the segmentation of 3D magnetic resonance imaging data. The inner brain surface (grey-white matter boundary) was segmented and a high resolution triangular mesh was computed (approximately 1 mm^2 per triangle, Fig. 1a). Each triangle in the neocortical patch was assumed to correspond to a neuronal population, and its electrical contribution was represented by an elementary current dipole. Each current dipole was positioned at the barycentre of the corresponding triangle and was oriented normally to its surface (Fig. 1b-c).

The magnitude of the moment of each elementary current dipole depends on both the current density of the cerebral cortex and the surface of the corresponding mesh triangle. According to [4], an average value of the cortical volume current density is 175 nA/mm^2 for normal background activity. Assuming a cortical thickness of 3 mm and considering a neuronal population i of surface s_i, the value of the magnitude of the moment $m_i(t)$ of the corresponding current dipole is, at any time, $M = s_i \times 525$ nA.mm. As time variations of the moment $m_i(t)$ are imposed by those of LFPs of population i (see section II-A), we can finally write that $m_i(t) = M.\alpha_i(t)$, $i = 1 \ldots N$.

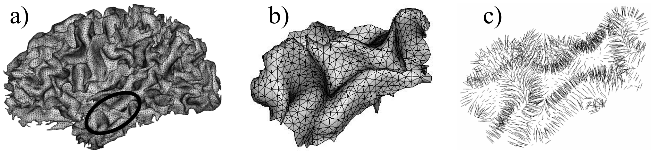

Fig. 1: The distributed current dipole model. (a) Triangular mesh of brain cortical surface. (b) Neocortical patch comprising N elementary triangles. (c) A current dipole is placed at the barycentre of each triangle and oriented normally to its surface.

III. RECONSTRUCTION OF DEPTH-EEG SIGNALS

Simulation of depth-EEG signals was performed from the extended source model by solving a *forward problem*, in which both the characteristics of the intracerebral electrode and the properties of the surrounding head tissues were taken into account. Depth-EEG recording is performed using intracerebral multisensor electrodes [1]. Along a given electrode, 10 to 15 cylindrical sensors (length: 2 mm, diameter: 0.8 mm, 1.5 mm apart) record signals from lateral (neocortical) and from mesial (deep) structures.

Geometrical and physical properties of the head tissues were described in two different volume conductor models: an infinite volume conductor model and a 3-shell spherical head model. In the former, only brain was considered and was assimilated to an infinite homogeneous volume conductor with constant isotropic conductivity. In the latter, the whole head was considered and was modeled by a set of three concentric spheres (brain, skull, and scalp). Each layer was also assumed to be homogeneous and to have constant isotropic conductivity. Brain and scalp were assumed to have the same conductivity, while conductivity of skull was 40 times lower than that of brain [5].

Quasi-static approximation is used to describe time-varying bioelectric currents and potentials in the head. Since the potential generated by a dipole layer is the linear superposition of potentials generated by elementary current dipoles, only one single current dipole is considered in the following theoretical expressions of the electrical potential at a given time instant.

A. Infinite Volume Conductor Model

Assuming that brain is an infinite volume conductor with a constant conductivity σ, and considering a current dipole $\mathbf{m}$ of arbitrary orientation and located at the origin of the coordinate system, the electrical potential generated by $\mathbf{m}$ at an observation point P placed at radius vector $r\mathbf{u}_r$ is [6]:

$$\mathrm{V(P)} = \frac{\langle \mathbf{m}, \mathbf{u}_r \rangle}{4\pi\sigma r^2} \tag{1}$$

where $\mathbf{u}_r$ is the unit vector from source to observation.

B. 3-shell Spherical Head Model

Assuming that head is a set of three concentric spheres, and considering a current dipole $\mathbf{m}$ and an observation point P both located inside the innermost sphere (brain), the electrical potential V(P) is related to the primary current density $\mathbf{j}_\mathrm{P}(\mathrm{P})$ through the Poisson's equation:

$$\Delta \mathrm{V}(\mathrm{P}) = \frac{\mathrm{div}\left(\mathbf{j}_\mathrm{P}(\mathrm{P})\right)}{\sigma} \tag{2}$$

where σ is the conductivity of brain.

Computation of electrical potential requires solving this linear non-homogeneous second order differential equation. The solution is of the form $V = V_1 + V_2$, where i) V_1 is a particular solution to the non-homogeneous equation (2), and ii) V_2 is the general solution to the associated homogeneous equation ($\Delta V = 0$).

i) A single current dipole embedded in an infinite region with constant conductivity σ is considered. Particularly, assuming the dipole $\mathbf{m}$ is parallel to the z-axis and located at $(r_0,\theta_0,0)$, the electrical potential generated at an observation point P placed at (r,θ,φ) can be written as in equations (3)-(4), where $\mathrm{P}_k^l(.)$ are the associated Legendre functions [7].

ii) Assuming a solution of the form $V_2 = F(r)G(\theta)H(\varphi)$, the general solution of homogeneous equation ($\Delta V = 0$) is given by equation (5), where coefficients A_k, B_k, C_l and D_l are determined by the problem's boundary conditions [7].

$$\mathrm{V}_1^{r<r_0}(r,\theta,\varphi) = \frac{\|\mathbf{m}\|}{4\pi\sigma r_0^2}\sum_{k=0}^{\infty}\sum_{l=0}^{k}\left(2-\delta_l^0\right)\left(l-k-1\right)\frac{(k-l)!}{(k+l)!}\left(\frac{r}{r_0}\right)^k \mathrm{P}_{k+1}^l\left(\cos\theta_0\right)\mathrm{P}_k^l\left(\cos\theta\right)\cos\left(l\varphi\right) \quad \text{when } r<r_0 \tag{3}$$

$$\mathrm{V}_1^{r>r_0}(r,\theta,\varphi) = \frac{\|\mathbf{m}\|}{4\pi\sigma r_0^2}\sum_{k=0}^{\infty}\sum_{l=0}^{k}\left(2-\delta_l^0\right)\left(l+k\right)\frac{(k-l)!}{(k+l)!}\left(\frac{r_0}{r}\right)^{k+1} \mathrm{P}_{k-1}^l\left(\cos\theta_0\right)\mathrm{P}_k^l\left(\cos\theta\right)\cos\left(l\varphi\right) \quad \text{when } r>r_0 \tag{4}$$

$$\mathrm{V}_2(r,\theta,\varphi) = \sum_{k=0}^{\infty}\sum_{l=0}^{k}\left(A_k r^k + B_k r^{-(k+1)}\right)\left(C_l\cos(l\varphi)+D_l\sin(l\varphi)\right)\mathrm{P}_k^l\left(\cos\theta\right) \tag{5}$$

C. *Simulation of Depth-EEG Signals*

In order to take into account geometrical properties of multisensor intracerebral electrodes (2 mm long sensors, 1.5 mm apart), *L* equidistant observation points were considered along each sensor axis. Electrical potentials from the *N* elementary current dipoles of the extended source were summated at each observation point. Finally, an estimate of the total potential at each sensor (analogous to that actually reflected in depth-EEG signals) was obtained by averaging values computed at the *L* points.

Simulated depth-EEG signals were compared to real depth-EEG signals using a root mean square error (RMSE) between simulated and real maximal electrical potentials averaged over all sensor locations, and computed as follows:

$$\mathrm{RMSE} = \sqrt{\frac{1}{n_s}\sum_{k=1}^{n_s}\left(\tilde{\mathrm{V}}_k^{\mathrm{real}} - \tilde{\mathrm{V}}_k^{\mathrm{sim}}\right)^2} \tag{6}$$

where n_s is the number of sensors along the intracerebral electrode, and $\tilde{\mathrm{V}}_k^{\mathrm{real}}$ and $\tilde{\mathrm{V}}_k^{\mathrm{sim}}$ denote the maximal spike potential measured at sensor number *k*, in real and simulated data, respectively.

IV. RESULTS

The model was used to interpret real depth-EEG signals recorded in a patient suffering from lateral temporal lobe epilepsy and candidate for epilepsy surgery. Simulated signals were generated from an extended source of activity corresponding to a neocortical patch located in the left middle temporal gyrus, recorded by an orthogonally implanted intracerebral electrode. Although the model of coupled neuronal populations allows for simulation of different epileptiform activities (ictal alpha-like activity, ictal theta-like activity, fast onset activity), the present work focuses on simulating interictal single spikes.

A. *Influence of the Coupling Strength*

Couplings between neuronal populations were assumed to be bidirectional and all parameters K_{ij} were set to a same value *K*. The influence of the coupling strength was analyzed by varying *K* in simulations.

Fig. 2 illustrates the effect of increasing parameter *K*, in a network of five interconnected populations. Parameters of the five populations (excitation/inhibition ratio and local connectivity constants) were adjusted so that they all generated background activity, and remained unchanged. Hence, for null coupling (*K*=0), the five resulting signals reflected normal background activity (Fig. 2a). When parameter *K* was increased, sporadic spikes appeared randomly and independently in the populations (Fig. 2b). For high values of parameter *K*, synchronization between activities from populations was enhanced and single spikes involving jointly all populations were produced (Fig. 2c).

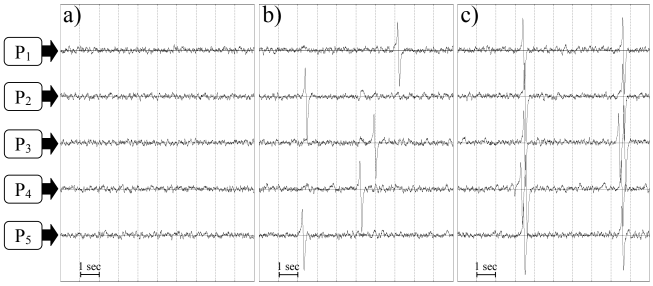

Fig. 2. Influence of the coupling strength in a network of 5 interconnected neuronal populations.

High amplitude spikes were obtained in the model only for high values of coupling parameter *K*. This condition in the model may be interpreted as an increase of the global excitability of the modeled neocortical tissue during epileptic activity, and corroborates some common physiopathological hypotheses in epileptogenesis.

B. *Spatial Extent of the Source during Epileptic Activity*

Simulations were performed by progressively increasing the surface *S* of the extended source from 1 to 40 cm². Since electrical potential values are highly dependent on brain conductivity value (see equations (1)-(5)), for each *S* value, brain conductivity *σ* was varied from 20 to 40x10^{-5} S/mm.

For high *K* value, the RMSE was computed between real and simulated maximal spike potential for variations of parameters *S* and *σ*, for both the infinite brain model and the 3-shell spherical head model. A global minimal RMSE was found among all performed simulations, in both volume conductor models. Optimal simulation was obtained for *S* = 20 cm² and *σ* = 25x10^{-5} S/mm in the infinite case, and for *S* = 22 cm² and *σ* = 32.5x10^{-5} S/mm in the spherical case.

Fig. 3 illustrates the reconstruction of depth-EEG signals obtained for minimal RMSE, in both volume conductor models. Two main remarks can be made from the analysis of these results. First, the morphology of both simulated spikes (Fig. 3b-c) was strikingly similar to that of real ones (Fig. 3a). Second, plots of the maximal spike potential with respect to sensor locations (Fig. 3d) showed that the model generated realistic potential values (in the order of 1 mV for the more lateral sensor). In addition, one can notice that amplitude gradients along the intracerebral electrode obtained from simulated signals (square and triangle) were also close to that obtained from real data (circle).

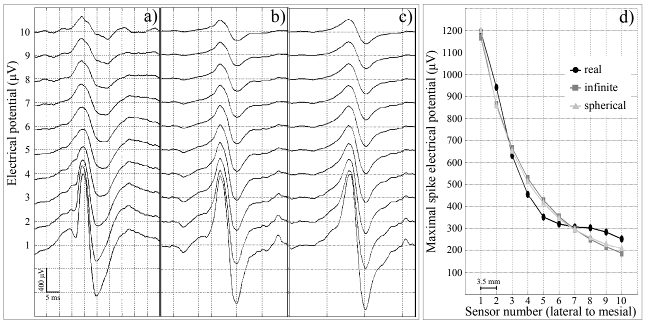

Fig. 3: A simulation example of an epileptic spike. (a) Real depth-EEG signals recorded in the left middle temporal gyrus, from mesial (*top*) to lateral (*bottom*) part. Corresponding simulated signals, obtained for minimal RMSE, for infinite brain model (b) and for 3-shell spherical head model (c). (d) Comparison of real (circle) and both simulated (square and triangle) maximal spike potentials along the intracerebral electrode.

Our results showed that spatial extent of the neocortical source involved in the generation of epileptic spiking activities, such as those observed in temporal lobe epilepsy, is rather large. Indeed, estimated source areas ranged from 20 to 26 cm^2 in infinite volume conductor model, and from 18 to 25 cm^2 in the spherical one. These results corroborate those in two recently published studies [8] [9] about the spatial extent of cortical sources in temporal lobe epilepsy. In [8], simultaneous scalp and cortical recordings showed that most scalp-recordable interictal spikes were generated by cortical sources with areas ranging from 10 to 30 cm^2. In [9], a source of epileptic activity was simulated by using a distributed current dipole model close to that in the present study, and results showed that cortical sources with areas ranging from 6 to 24 cm^2 were involved in the generation of scalp interictal spikes.

Finally, although estimated source areas are of the same order in both volume conductor models, results were found to significantly differ in terms of brain conductivity. Indeed, minimal RMSE was obtained for conductivity in the order of 25x10^{-5} S/mm in the infinite case, against 32.5x10^{-5} S/mm in the spherical case. This latter value seems to be more realistic if one refers to the average brain conductivity value given in literature, which is in the order of 33x10^{-5} S/mm [5]. Indeed, electrical potentials were found to be underestimated in the infinite brain model, which was compensated in the model either by underestimating brain conductivity or by overestimating the neocortical source area.

V. CONCLUSION

We developed an extended source model which connects two levels of description: a model of coupled neuronal populations and a distributed current dipole model. Combining these two representations ensures a realistic description of both spatial and temporal properties of the neuronal sources of brain electrical activity. From this extended source model, depth-EEG signals were simulated by solving a forward problem in which the geometrical characteristics of multisensor intracerebral electrodes were taken into account. In order to analyze the effect of the properties of surrounding media, the forward solution was computed both in an infinite volume conductor model and in a 3-shell spherical head model.

Results showed that morphological features of simulated spikes are very similar to those in real depth-EEG signals during transient epileptic activity under two particular conditions in the model: the degree of coupling between neuronal populations must be significantly high and the spatial extent of the neocortical source must be relatively large. The former condition corroborates the physio-pathological hypothesis of hyperexcitability in neuronal tissue involved in the generation of epileptic activities. The cortical area involved in the generation of transient epileptic spikes, such as those observed in temporal lobe epilepsy, was estimated to vary from 18 to 25 cm^2, for brain conductivity values ranging from 30 to 35x10^{-5} S/mm. Finally, the comparison between the results obtained in the infinite brain model and those obtained in the 3-shell spherical head model confirmed that volume conductor models accounting for the different tissues of the head are needed to accurately estimate electrical potentials at each sensor location, even if sensors are strictly located inside the brain.

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