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Non-Invasive Estimates of Local Field Potentials for Brain-Computer Interfaces: Theoretical derivation and comparison with direct intracranial recordings

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1. Introduction

Recent experiments have shown the possibility to use the brain electrical activity to directly control the movement of robots or prosthetic devices in real time. As such, it is particularly relevant as an aid for paralyzed humans, although it also opens up new possibilities in human-robot interaction for able-bodied people. Such neuroprostheses can be invasive or non-invasive, depending on how the brain signals are recorded.

Initial demonstrations of the feasibility of controlling complex neuroprostheses have relied on the invasive approach using intracranial electrodes implanted in the brain of monkeys (Wessberg *et al.*, 2000; Meeker *et al.*, 2002; Serruya *et al.*, 2002; Taylor *et al.*, 2002; Carmena *et al.*, 2003; Mehring *et al.*, 2003). In these experiments, one or more array of microelectrodes records the extracellular activity of single neurons (their spiking rate) in different areas of the cortex related to planning and execution of movements—motor, premotor and posterior parietal cortex. From the real-time analysis of the activity of the neuronal population, it has been possible to predict either the animal's movement intention (Meeker *et al.*, 2002; Mehring *et al.*, 2003) or the monkey's hand trajectory (Wessberg *et al.*, 2000; Taylor *et al.*, 2002; Carmena *et al.*, 2003), and to drive a computer cursor to desired targets (Serruya *et al.*, 2002; Taylor *et al.*, 2002). Thus, in principle, invasive approaches could provide a more natural and flexible control of neuroprostheses, However, for humans, non-invasive methods are preferable because of ethical concerns and medical risks.

Non-invasive approaches mainly use scalp electroencephalogram (EEG) signals and their main disadvantage is that these signals represent the noisy spatiotemporal overlapping of activity arising from very diverse brain regions. As a consequence, current EEG-based brain-actuated devices are limited by a low channel capacity and are considered too slow for controlling rapid and complex sequences of movements. This is probably why so far control tasks based on human EEG have been limited to simple exercises such as moving a computer cursor to the corners of the screen (Wolpaw and McFarland, 1994) or opening a hand orthosis (Pfurtscheller and Neuper, 2001) or need to resort to intelligent robotics (Millan et al 2004) to attain an acceptable control performance. It is not surprising that some

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people still believe that only invasive approaches will provide natural and flexible control of robots (Nicolelis, 2001; Donoghue, 2002). The rationale is that surgically implanted arrays of electrodes will be required to properly record the brain signals because the non-invasive scalp-recordings with the EEG lack spatial resolution.

However, recent advances in EEG analysis techniques have shown that the sources of the electric activity in the brain can be estimated from the surface signals with relatively high spatial accuracy (6-9mm). This resolution compares with the resolution provided by the methods used to detect activation in functional magnetic resonance imaging (fMRI) using 1.5/3 Tesla machines. Note that this is very different to the resolution of the anatomical images provided by the MRI. Aiming at combining the benefits of both approaches, we propose to rely on the non-invasive estimation of local field potentials (eLFP) in the whole human brain from the scalp measured EEG data using a recently developed distributed linear inverse solution termed ELECTRA (Grave de Peralta Menendez *et al.*, 2000). The use of linear inversion procedures yields an on-line implementation of the method, a key aspect for real-time applications.

The development of a brain interface based on ELECTRA—i.e., non-invasive estimates of LFP— would allow for methods identical to those used for EEG-based brain interfaces but with the advantage of targeting the activity at specific brain areas. In this respect our approach aims to parallel the invasive approaches described before that directly feeds intracranial signals into the classification stage of the brain interface, except that we calculate these intracranial signals from the surface EEG data. An additional advantage of our approach over scalp EEG is that the latter represents the noisy spatio-temporal overlapping of activity arising from very diverse brain regions; i.e., a single scalp electrode picks up and mixes the temporal activity of myriads of neurons at very different brain areas. Consequently, temporal and spectral features, which are probably specific to different parallel processes arising at different brain areas, are intermixed on the same recording. For example, an electrode placed on the frontal midline picks up and mix activity related to different motor areas known to have different functional roles such as the primary motor cortex, supplementary motor areas, anterior cingulate cortex, and motor cingulate areas.

In addition, the proposed approach bears two main advantages over invasive approaches. Firstly, it avoids any ethical concern and the medical risks associated to intracranial electrocorticographic recordings in humans. Secondly, the quality of the signals directly recorded on the brain deteriorates over time requiring new surgical interventions and implants in order to keep the functionality of the device.

In this chapter we describe in detail the theoretical framework needed for the non invasive estimation of Local field potentials, the rationale for its application and compare these estimates with the raw EEG (used to estimate the eLFP). To shed some light on the question of the feasibility of non-invasive brain interfaces to reproduce the prediction properties of the invasive systems, we compare the classification results of eLFP non invasively estimated from the EEG with intracranial recordings (IR) during a visuo-motor task.

2. Theoretical and practical aspects of LFP estimation

2.1 From the sources to the scalp fields

Brain function is investigated at two different scales: 1) A microscopic level encompassing the activity of a single or few neurons studied by means of single or multiunit recordings and 2) A macroscopic level reflecting the activity of larger neuronal ensembles recorded by

either intracranial local field potentials in patients or animals or by scalp-recorded electric and magnetic fields.

At the origin of all these measurements are identical neural phenomena. During cell activation, large quantities of positive and negative ions cross the cell membrane, moving from the intracellular to the extracellular fluid, and vice versa. For all practical purposes, this ion movement is equivalent to a current flow, and it is responsible for all the recorded neurophysiological signals. The name used to refer to these microscopic currents varies somewhat. Within the modeling community, they are referred to as impressed currents while most neurophysiological researchers term them active currents. Active or impressed are terms used to differentiate these currents from the passive (also termed return or volume) currents that manifest as the electrical response of the media to compensate for charge accumulation at specific sites driven by the active currents.

At the microscopic level the redistributions in extracellular ionic charge due to neuronal transmembrane current flows generate extracellular volume currents throughout the head. These microscopic volume currents, in turn set up field potential gradients that follow Ohm's law and are proportional both to the magnitude of the local currents and to the tissue conductivity. As such, they are termed ohmic currents.

For axonal and cardiac tissue several comparisons of the relative field strength from both impressed and volume currents at the microscopic level show only the latter to be significant (see Plonsey, 1982 and references therein). Consequently, at the macroscopic level observable by Local Field Potentials, electroencephalography (EEG), and magnetoencephalography (MEG), the primary currents are dominated by the microscopic volume currents and can therefore be modeled as ohmic currents. Macroscopic passive volume currents, result from the gross conductivity changes associated to the existence of different compartments in the head, that is, brain, cerebrospinal fluid, skull and scalp.

Importantly, since macroscopic primary sources are dominated by the microscopic volume currents, then the primary currents perceived by EEG and MEG are ohmic. The mathematical implication is that they can be modeled as irrotational currents (Grave de Peralta Menendez et al. 2000).

2.2 Theoretical aspects of LFP computation

The formal relationship between intra-cerebral currents and scalp-measured fields can be derived from Maxwell equations that describe the propagation of electromagnetic fields within arbitrary volume conductor models, i.e.:

$$\nabla \circ \mathbf{E} = \rho / \varepsilon \tag{1'}$$

$$\nabla \times \mathbf{E} = -\partial\ \mathbf{B} / \partial\ t \tag{2'}$$

$$\nabla \circ \mathbf{B} = 0 \tag{3'}$$

$$\nabla \times \mathbf{B} = \mu(\mathbf{J} + \varepsilon \partial\ \mathbf{E} / \partial\ t) \tag{4'}$$

where **E** and **B** are the electric and magnetic fields, **J** is the total current density vector, ε and μ stand for physical properties of the media, and ρ is a (charge or current) density.

Equations (2') and (4') indicate that time varying electric and magnetic fields are interrelated. However, since the range of frequencies (Plonsey and Heppner 1967) associated with

electromagnetic fields in vivo-media is usually less than 1000 Hz, it is possible to suppress the contribution of the temporal terms. This is referred to as the quasi-static approach and implies that the capacitive and inductive effects produced by the temporal variations of the electric field **E** and the magnetic field **B** (see 2′ and 4') are irrelevant. The practical consequence of the quasi-static approach is that electric and magnetic fields recorded at the scalp are instantaneously reflecting the underlying neural processes and thus, electromagnetic processes taking place in the past are irrelevant for the present measurements. No evidence against this approximation has been reported so far.
This quasi-stationary assumption, allows for the separate modeling of the electromagnetic fields, i.e., the electric field is not dependent upon temporal variations of the magnetic field and vice versa:

$$\nabla \circ \mathbf{E} = \rho / \varepsilon \tag{1}$$

$$\nabla \times \mathbf{E} = 0 \Leftrightarrow \mathbf{E} = -\nabla \mathbf{V} \tag{2}$$

$$\nabla \circ \mathbf{B} = 0 \Leftrightarrow \mathbf{B} = \nabla \times A \tag{3}$$

$$\nabla \times \mathbf{B} = \mu \mathbf{J} \Rightarrow \nabla \circ \mathbf{J} = 0 \tag{4}$$

The total current emerging in biological tissue can be split into two terms: a primary and neurophysiologically driven current (J_p), and the volume or secondary current (σ**E,** i.e. **J**= J_p +σ**E**). From equation (4) derives that the divergence of total current (**J**) is zero, which when combined with previous current decomposition, and equation (2) yields Poisson's equation for the electric potential field:

$$\nabla \circ (\sigma \nabla V) = \nabla \circ J_p \tag{5}$$

This equation establishes that the actual generators of potential V are determined by the sources and the sinks obtained from the divergence of the primary current. This is mathematically identical to the Laplacian of the intracranial fields or the current source density (CSD).
Denoting by Q the brain region and using the Green function ψ associated to the solution of (5) we can rewrite it as a (first kind) Fredholm linear integral equation:

$$V(s) = -\int_Q \nabla \circ J_p(r) \psi(s,r) dQ \tag{6}$$

Designating the (vector) lead field by $L(s,r) = \nabla_r \psi(s,r)$ and noting that the primary current source distribution is bounded to the brain, it results the standard formulation of the neuro-electromagnetic inverse problem:

$$V(s) = \int_Q L(s,r) \bullet J_p(r) dr \tag{7}$$

denoting the relationship between the data measured at the external point, *V(s)*, and the superposition of the contribution of the unknown current source density distribution J_p at locations *r* inside the brain (Grave de Peralta Menendez, et al. 2004; Greenblatt 1993; M. Hämäläinen 1993; Sarvas 1987). The symbol "•" denotes the scalar or the vector product for the electric or magnetic case respectively. For the derivation of the magnetic lead field see Grave de Peralta Menendez et al. 2004.

Several (theoretical) source models have been used to solve equation (7) and thus to describe the sources of the electromagnetic activity of the brain, e.g., dipoles, monopoles, current density vector. Without entering into a formal discussion about the plausibility of these mathematical models, it is important to note that except for currents, none of these theoretical source models actually exists within the brain nor is any physically measurable. Instead, real measurements are the result of quantifiable potentials at different "measurable" levels. At the microscopic (neuron) level, this is the membrane potential. At the macroscopic (region) level, this is the local field potential (LFP). Through volume conduction, the effect of these potentials arrives at the scalp where they are measured as the Electroencephalogram (EEG). It is then natural to question whether potentials inside the brain can be related to and thus computed from potentials measured at the scalp.

A positive answer to this question can be given if we notice that, as discussed in previous section, macroscopic primary sources, i.e. the generators of the EEG, are dominated by microscopic secondary (volume) currents or in Plonsey words (Plonsey 1982) that "the fields measured do not even arise from J_p [the current source density vector field] but rather from secondary sources only. These secondary sources, in turn, depend on both the electrical field and the interfaces, and hence are related to divergence of J_p and the geometry". This kind of source corresponds to a potential distribution inside the brain.

A definitive theoretical argument can be obtained if we note that, according to the Helmholtz theorem, the current density vector field can be written as the sum of a solenoidal vector field plus an irrotational vector field plus the gradient of a harmonic function. That is,

$$J_p = J_s + J_i + J_h \tag{8}$$

where $J_h = \nabla\Omega$ with Ω harmonic in the brain region and $\nabla \circ J_s \equiv \nabla x J_i \equiv \nabla^2\Omega \equiv 0$. Here zero denotes the neutral for the addition of functions of each space.

Substitution of decomposition (8) in equation (6) yields:

$$V(s) = -\int_Q \nabla \circ J_s(r)\psi(s,r)dQ - \int_Q \nabla \circ J_i(r)\psi(s,r)dQ - \int_Q \nabla^2\Omega(r)\psi(s,r)dQ \tag{9}$$

Based on Green identities, it follows that only the second integral, corresponding to the irrotational current contributes to the measured potentials (EEG). In mathematical parlance, it means that the EEG generators fulfill:

$$\nabla x\, J_p = 0 \Leftrightarrow J_p = \nabla\varphi \tag{10}$$

where φ is a potential field within the brain. Assuming piece-wise constant conductivities σ, substitution of (10) into Poisson's equation (5) shows that φ has the same sources and sinks as the EEG potential V, i.e.:

$$\sigma\nabla \circ (\nabla V) = \nabla \circ (\nabla\varphi) \tag{11}$$

Note that, plotting the modulus of the estimated primary current obtained by solving (7), which we would note has thus far been the common procedure used to depict inverse solutions results, does not reflect the actual generators. Instead, the actual generators are determined by the sources and the sinks obtained from the Laplacian of potential field φ or $\nabla \circ J_p$ (the divergence of the primary current density vector).

The irrotational source model corresponds to the solution of the following equation

$$V(s) = \int_Q \nabla\varphi(r') \circ \nabla\psi(s,r')dQ = \int_Q \nabla \circ J_p(r')\psi(s,r')dQ \tag{12}$$

with respect to one of the following magnitudes: 1) The estimation of an irrotational current density vector $J_p = \nabla\varphi$ with the vector lead field $L = \nabla\psi$. 2) The estimation of a scalar field, the current source density (CSD), $\nabla \circ J_p = I$ with the scalar lead field ψ. 3) The estimation of a scalar field, the potential distribution φ in Q with a transformed scalar lead field $\nabla\psi \circ \nabla$.

Using the vector lead field, the third alternative relating the potential distribution inside the brain with the potential distribution on the scalp (EEG) can be written as:

$$V(s) = \int_Q L(s,r') \circ \nabla\varphi(r')dQ \tag{13}$$

In real conditions, neither the measurements nor the lead field functions are known for arbitrary surface/brain locations, but rather only at restricted discrete sites. Thus, it is reasonable to introduce a discrete formalism where the integral equation in (13) is approximated by a discrete sum, which leads to the following underdetermined system of linear equations:

$$v=Lf \tag{14}$$

Vectors **v** and **f** and matrix **L** represent the discretization of the continuous functions, i.e., $\mathbf{v_k}=V(s_k)$ for k=1 to Numbers of sensors, $\mathbf{f_m}=\mathbf{f}(r_m)$ for m=1 to Number of solution points, and $\mathbf{L}_{km}=w_{km}\,\mathbf{L}(s_k,r_m)\,°\nabla$ and w_{km} are the quadrature weights.

Unfortunately, the restriction of the source model is not enough to ensure a unique solution to equations (13)-(14). For that reason, additional information (independent of the measured data) should be included in the solution. In principle, any mathematical method proposed

for the solution of ill-posed problems can be considered. For reviews see (Menke 1989; Tikhonov and Arsenin 1977). While there is a wide range of solutions, we would like to caution the reader about the selection of a method based on figures of merit obtained from the localization of single sources, such as the so-called "zero dipole localization" or "location bias". We have previously demonstrated that these measures are neither necessary nor sufficient for assessing the performance of inverse solutions (Grave de Peralta Menendez and Gonzalez Andino 2000; Grave de Peralta-Menendez and Gonzalez-Andino 1998).

Since our goal of additional information is to better imitate the behavior of real sources in the head, we prefer to use additional information derived from biophysical laws. Therefore, we copy the spatial structure of a well- known potential field generated by an irrotational (dipolar) source, i.e., (Grave de Peralta Menendez, et al. 2004):

$$\phi(r) = M.\frac{r-r'}{|r-r'|^3} = \frac{|M|\cos\theta}{|r-r'|^2} \tag{15}$$

expressing that the potential field at given point r depends upon the activity at another brain site r' according to a square inverse law. While this law relates one solution point with all the others, in our current implementation (see next section) we use only neighborhoods with no more than 26 points. This range is enough to compute the local autoregressive average (LAURA) regularization operator (Grave de Peralta Menendez, et al. 2001, 2004). We would note that this is not the same exponent we use for vector fields where we consider a cubic inverse distance instead.

In summary, the main advantages of the irrotational source model are:

1. Reduction of the number of unknowns. Since we need to estimate only a scalar field instead of a vector field, the number of unknowns is reduced three-fold. Given that the ratio between the number of unknowns and the number of sensors is a measure of uncertainty, we can say that the inverse problem with irrotational sources (13) is better determined than the unrestricted (arbitrary current density vector) estimation problem (7). In practice this results in images with rather detailed patterns (see Grave de Peralta Menendez, et al. 2000 for examples of visual evoked potentials).
2. The use of a scalar magnitude facilitates the inclusion of additional *a priori* information from other modalities of images (e.g., fMRI, PET, SPECT) brain images and reduces the computational load. In addition, post-processing of the single time series associated to each solution point might be easier than the analysis of three time series of the current density vector model.
3. Unquestionable constraints. The existence of irrotational sources is a condition necessary and sufficient for the existence of EEG. More simply, EEG recorded at the scalp surface is due to, and only due to, the presence of irrotational sources inside the brain. This constraint is independent of the data.
4. Experimentally verifiable model. Although defined up to a sign change, the potential distribution produced by this source model can be directly compared with intracranial measures (e.g. spectrum, energy, etc) derived from them. Related to this point, these estimated LFPs could also be compared with similar measurements from other species.

2.3 Practical aspects of LFP computation

The general solution of equation (14) can be obtained as the solution of the following variational problem (Grave de Peralta-Menendez and Gonzalez-Andino 1998; Menke 1989):

$$\min\ (\mathbf{Lf}-\mathbf{v})^t\mathbf{W}_v(\mathbf{Lf}-\mathbf{v})+\lambda^2(\mathbf{f}-\mathbf{f}_p)^t\mathbf{W}_f(\mathbf{f}-\mathbf{f}_p) \tag{16}$$

Where $\mathbf{W}_v$ and $\mathbf{W}_f$ are symmetric (semi) positive definite matrices representing the (pseudo) metrics associated with the measurement space and the source space, respectively. Vector $\mathbf{f}_p$ denotes any available *a priori* value of the unknown, e.g., from other varieties of brain functional images. The regularization parameter is denoted by λ. Independently of the rank of **L**, the solution to (16) is unique if and only if the null spaces of $\mathbf{W}_f$ and $\mathbf{L}^t\mathbf{W}_v\mathbf{L}$ intersect trivially, i.e., $\mathrm{Ker}(\mathbf{W}_f)\cap\mathrm{Ker}(\mathbf{L}^t\mathbf{W}_v\mathbf{L})$ is the empty set. In this case, the estimated solution vector **f** can be obtained using the change of variable $\mathbf{f}=\mathbf{f}_p+\mathbf{h}$ and solving the resulting problem for **h**, i.e.:

$$\mathbf{f}=\mathbf{f}_p+[\mathbf{L}^t\mathbf{W}_v\mathbf{L}+\lambda^2\mathbf{W}_f]^{-1}\mathbf{L}^t\mathbf{W}_v[\mathbf{v}-\mathbf{L}\mathbf{f}_p]=\mathbf{f}_p+\mathbf{G}[\mathbf{v}-\mathbf{L}\mathbf{f}_p] \tag{17}$$

If and only if matrices $\mathbf{W}_f$ and $\mathbf{W}_v$ are positive and definite, equation (17) is equivalent to:

$$\mathbf{f}=\mathbf{f}_p+\mathbf{W}_f^{-1}\mathbf{L}^t[\mathbf{L}\mathbf{W}_f^{-1}\mathbf{L}^t+\lambda^2\mathbf{W}_v^{-1}]^{-1}[\mathbf{v}-\mathbf{L}\mathbf{f}_p]=\mathbf{f}_p+\mathbf{G}[\mathbf{v}-\mathbf{L}\mathbf{f}_p] \tag{18}$$

The latter equation might be used when the same head model is used with several electrode configurations. Storing the inverse of the metric $\mathbf{W}_f$ and $\mathbf{W}_v$, we can repeatedly use equation (18) that only requires the inversion of a matrix of size equal to the number of sensors.

The definition of the metric matrices and the a priori vector $\mathbf{f}_p$ vary according to the data available. For example, when dealing with average event-related potentials or another EEG window we could define $\mathbf{W}_v$ as the inverse of the covariance matrix. If we use all the single trials of one experiment, we can build a covariance matrix for each time point. In the following, we will assume that we have no information about matrix $\mathbf{W}_v$ and vector $\mathbf{f}_p$. That is, we will use $\mathbf{W}_v$ =Identity and $\mathbf{f}_p$=0.

To compute the metric of the source space, consider the auxiliary matrix A associated to the autoregressive averages with coefficients according to the square inverse law (equation 15):

$$A_{ii}=\frac{N}{N_i}\sum_{k\subset V_i}d_{ki}^{-2},\ A_{ik}=-d_{ki}^{-2} \tag{19}$$

Where V_i denotes the vicinity of each solution point, defined as the hexaedron centered at the point and comprising at most N=26 neighbors. N_k is the number of neighbors of point k and d_{ki} stands for the Euclidean distance from point k to point i.

Then, we can define the metric of the source space as:

$$\mathbf{W}_f=\mathrm{A}^t\mathrm{A} \tag{20}$$

For the computation of the regularization parameter we use the generalized cross validation method as described in (Davies 1992), i.e., we look for the value of λ that minimizes the following expression:

$$\frac{\frac{1}{N}\left\|\{\mathbf{I}-R(\lambda)\}\mathbf{v}\right\|^2}{\left[\frac{1}{N}Trace[\mathbf{I}-R(\boldsymbol{\lambda})]\right]^2} \tag{21}$$

where **R**(λ) is the influence matrix, also called the data resolution matrix (Menke 1989), defined as the product of the lead field matrix and the inverse matrix. That is, **R**(λ)=**L***G(λ) and **G**(λ) is the inverse defined by equations (17) or (18) for a particular value of λ.
In summary, the computation of LFPs comprises the following steps:

1. Compute the scalar lead field matrix (equation 14) of your head model as the product of the vector lead field matrix times the gradient operator matrix.
2. Compute the metric of the source space as described in equations (19) and (20). Select the metric on the data space according the information available as well as the a priori source value $\mathbf{f}_{p.}$
3. Compute the inverse defined by equations (16) or (17) using a regularization parameter obtained by minimizing equation (20).

To obtain local field potentials, apply the inverse matrix **G** to your data.
Finally note that, in all derivations in equations 14-21, we assumed that the lead field matrix **L** and the data **v** have the same electrical reference (e.g. reference electrode). If it is not the case, you can pre-multiply both, the lead field and the EEG data, by the centering matrix that transforms column vectors to common average reference vectors (i.e. zero sum vectors).

3. Comparison of EEG, eLFP and IR in real experimental conditions

3.1 Experiment and data recording

We recorded scalp EEG data and intracranial data in 4 subjects and two patients performing a simple visuo-motor reaction time task. Subjects were asked to fixate a central cross that also served as a warning signal and to respond as fast as possible with the right or left index finger to visual stimuli appearing 3-4 s following the onset of the cross. Stimuli were presented for 60 ms in random order either in the left visual field (LVF) or in the right visual field (RVF) (4° horizontal eccentricity). Reaction times (RT) to stimuli were measured using an external device. Subjects had to give manual responses independent of stimulus location (simple RT task) with only the left or the right hand, in two separate blocks. Each block consisted of 120 trials and was preceded by a training session. The position of the head was stabilized by means of a head and chin rest and the hand of the subjects rested over the response device throughout the experiment.
EEG recording: The electroencephalogram (EEG) was continuously monitored at 500 Hz during the whole experiment from 125 scalp electrodes (Electric Geodesic Inc. system, USA). Recordings were done using a cephalic reference placed at the vertex. Off-line processing of the data consisted of (1) Transformation of the EEG data to the common average reference, (2) rigorous rejection of trials contaminated by ocular or movement artifacts through careful

visual inspection, and (3) bad channel selection and interpolation. Fourteen electrodes from the lowest circle on the electrode array, i.e., closest to neck and eyes, were excluded a posteriori because of their likeliness to pick up muscular artifacts. A final configuration of 111 electrodes was used for all the analysis.
eLFP estimation: EEG recordings obtained from previous step were transformed into Local Field potential estimates (eLFP) using the inverse matrix associated to the irrotational source model (ELECTRA) described in previous sections. This yielded LFP estimates for 4024 brain "electrodes" distributed all over the gray matter of a realistic head model.
Intracranial recording: Two patients that underwent intracranial recordings (IR) for presurgical epilepsy evaluation performed the same visuo-motor reaction time task as used in the healthy subjects. IR were recorded at 200 Hz from subdural electrodes covering motor cortex and parietal and temporal areas of one hemisphere. The covering of motor areas was assessed by direct electrical cortical stimulation. The local ethical committee approved the experiments, and written informed consent was obtained in all cases.

3.2 Data analysis methods

Analysis window: For the analysis of the 111 EEG channels and the 4024 eLFP estimated channels, we selected a stimulus-locked time window of duration equal to the subject's fastest response. This period was chosen because it is very unlikely to be contaminated by electromyographic activity as this period precedes the actual movement onset for each single trial. Since the IC recordings are unlikely to be contaminated by electromyographic activity, the duration of the analysis window was selected as the mean reaction time (what could favor this modality).
Features extraction: For each data set, the power spectral density (PSD) was computed for all electrodes and single trials during the analysis window using a multitaper method with seven sleepian data tapers. All computations were done in Matlab. For the healthy subjects, the whole analysis covered the frequency range from 0 to 250 Hz, i.e. half of the frequency sampling, while for patients it was limited to the 0 to 100 Hz range, defined by the frequency sampling set to 200 Hz.
Classification details: For all modalities (i.e. EEG, eLFP and IC) the whole data set was divided in two halves. The first half was used as a learning set and the second one as the test set. Classification was based on the linear OSU-SVM and the performance was evaluated with the leave-one-out method on the test set using the features selected on the learning set. Leave-one-out (LOO) cross-validation is a special case of the cross-validation technique used to estimate the predictive accuracy of a classifier. Given n trials available in the test set, a classifier is trained on (n-1) trials, and then is tested on the trial that was left out. This process is repeated n times until every trial in the test set, has been included once as a cross-validation instance. The results are averaged across the n trials to estimate the classifier's prediction performance.
Discriminative Power (DP): The DP reflects the separation between the left and right hand responses in terms of their power spectral density (PSD) for each individual frequency and each electrode. It is graded between 0 and 100, with zero representing complete overlap between both PSD distributions (no discrimination between movements is possible) and 100 representing the perfect separation between them. The DP provides an estimate of how many trials can be unambiguously classified as pertaining to right or left movements on the basis of a single feature. This measure provides an estimate of the percentage of true

positives that can be obtained classifying with each single feature given that the number of false positive is set to zero. For a detailed description see (Gonzalez Andino et al. 2006)
Feature selection: Features were selected according to their DP on the learning set. That is, for each data set the best 150 features, with highest DP, were selected from all possible electrodes and frequencies over the trials on the learning set.

3.3 Data analysis results

The results obtained for the 4 normal subjects and the two patients are summarized in table 1. As a figure of merit we used the percentage of correct classification (CC%) computed from the leave one out results on the test set. Healthy subjects are referred as S1 to S4 and the two patients by P1 and P2.

Subject	EEG or IC electrodes	eLFP estimated from EEG
P1	91	--------
P2	94	--------
S1	97	98
S2	91	93
S3	85	91
S4	97	99

Table 1. Classification results for the two patients (P1 and P2) and the four healthy subjects (S1-S4) for the direct measurements (EEG or IC) or eLFP estimated from the EEG

4. Discussion and Conclusions

This chapter shows that there is a mathematical relationship between potentials measured at the scalp (EEG) and a scalar field inside the brain. This scalar field is a potential field for the current source density vector sharing the same sources and sinks of the intracranial potential measured inside the brain volume. The estimation of this potential field is mathematically equivalent to the use of the irrotational source model of ELECTRA inverse solution and for that reason it is denoted as eLFP. Extensive theoretical and practical elements needed to understand and implement the estimation of eLFP are also included.
The simulations presented shed some light on the basic questions that can arise in front of these estimates, i.e., how much information can be obtained from the eLFP in comparison with the EEG used for their to estimation and in comparison with invasive intracranial recordings.
As described in Table I, the range of CC (in %) values observed for the eLFP estimated from the EEG in healthy subjects (91-98) are not lower than the CC values (91 and 94) obtained from invasive recordings in two patients. This could be because intracranial electrodes are not located to optimize classification but to study the neurological conditions of the patients. However, it could be also an evidence for the use of the non-invasive method proposed to guide the positioning of intracranial electrodes. Further investigation will be needed to confirm that.

From a theoretical point of view it is not surprising that eLFP performs better than EEG if we consider all the elements included in their estimation and not available "per se" on the scalp EEG data. Clear examples are the information about the geometry and the conductivities included in the lead field, the irrotational property of the source model (ELECTRA) and the spatial structure induced by the regularization operator (LAURA). Nevertheless, we would note that the eLFP results reported here are just slightly better than the EEG for the same task. In fact we have found using a larger set of experimental conditions (unpublished data) that for some simple tasks, as the self paced finger tapping or the reaction time task discussed here, the use of the EEG or the eLFP yield very similar results. In contrast, for more complex tasks (e.g. cognitive processing of words or emotional images or the determination of the hand movement direction) the eLFP produces systematically much better results than the EEG and still comparable with the intracranial recordings (Grave de Peralta Menendez et al. 2005, and Grave de Peralta Menendez and Gonzalez Andino 2006). For other applications to the so called "mind reading" problem or prediction of response speed based on non invasive eLFP see Gonzalez Andino et al. 2005 and 2007.

As for a conclusion we can say that as shown by the experimental results, this non-invasively estimated field (eLFP) performs, for the classification task discussed here, better than the EEG and at least as well as the IR obtained with invasive methods. This suggests that eLFP is a worthy alternative to explore that might be considered as a safe and efficient alternative for the development of direct non invasive BCIs.

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Medical Robotics

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The first generation of surgical robots are already being installed in a number of operating rooms around the world. Robotics is being introduced to medicine because it allows for unprecedented control and precision of surgical instruments in minimally invasive procedures. So far, robots have been used to position an endoscope, perform gallbladder surgery and correct gastroesophogeal reflux and heartburn. The ultimate goal of the robotic surgery field is to design a robot that can be used to perform closed-chest, beating-heart surgery. The use of robotics in surgery will expand over the next decades without any doubt. Minimally Invasive Surgery (MIS) is a revolutionary approach in surgery. In MIS, the operation is performed with instruments and viewing equipment inserted into the body through small incisions created by the surgeon, in contrast to open surgery with large incisions. This minimizes surgical trauma and damage to healthy tissue, resulting in shorter patient recovery time. The aim of this book is to provide an overview of the state-of-art, to present new ideas, original results and practical experiences in this expanding area. Nevertheless, many chapters in the book concern advanced research on this growing area. The book provides critical analysis of clinical trials, assessment of the benefits and risks of the application of these technologies. This book is certainly a small sample of the research activity on Medical Robotics going on around the globe as you read it, but it surely covers a good deal of what has been done in the field recently, and as such it works as a valuable source for researchers interested in the involved subjects, whether they are currently “medical roboticists” or not.

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