Cramer-Rao Bound for Dipole Source Localization in Infants Using Realistic Geometry

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Abstract: Source localization of electrical activity in newborn infants is important from two standpoints. From an academic standpoint such insights can enable better understanding of brain development and from clinical standpoint localization of electrical activity can identify regions of the brain with higher than usual activity and possibly improve possible treatment outcomes. The electrical activity and the corresponding electroencephalography (EEG) measurements are dependant on electrical properties of brain and skull tissue i.e. corresponding conductivities and geometry. In this paper we investigate effects of realistic geometry in newborn infants by accounting for soft spots (fontanels) that are present in newborn infants. These structures have larger conductivity than regular bone tissue and hence the estimation accuracy can potentially be improved by optimally positioning EEG sensors on the surface of the skull. We generate forward model using realistic geometry and finite-element model generated by COMSOL. We utilize simplified source model consisting of single dipole source and calculate corresponding Cramer-Rao bound as a function of source intensity and locations.

1 INTRODUCTION

Neonatal convulsions are one of the most common emergency neurological events in the early period after birth with the frequency of 1.5 to 3 in 1000 live births (Volpe, 2001). Consequently, neonatal intensive care units (NICU) continuously monitor electrical activity of preterm infants for both short-term and long-term interventions and/or treatments (Shellhaas and Clancy, 2007) These techniques commonly utilize only detection algorithms whose main purpose is to detect events in electroencephalography (EEG) recordings. In addition to those, estimation techniques can potentially provide insight into the brain development and indicate regions of higher convulsion rate. The estimation of electrical activity of the brain in adults has been a subject of considerable research interest in adults (Asadzadeh et al., 2020). Most of the existing solutions utilize combination of EEG (excellent temporal resolution and poor spatial resolution) as a source of electrical activity information and magnetic resonance imaging (MRI, excellent spatial resolution and poor temporal resolution) as a source of geometry information and combine them in so called inverse models that are then used in order to estimate the unknown parameters (usually some type of constrained spatial source models such as distributed dipoles). In infants, however, accurately describing the anatomy of the head remains a challenge due to the complexity of the infant skull from the electromagnetic point of view. The most significant anatomical difference with respect to adult anatomy in addition to volume is the existence of fontanels. soft tissue between incompletely formed cranial bones (Cornette et al., 2002).

To this purpose in this paper we investigate the effect of the fontanelle structure on the estimation accuracy by evaluating Cramer-Rao lower bound (CRLB) for a realistic geometry of the infant brain that is the lowest attainable variance that can be achieved using unbiased estimators. The effect of fontanels on EEG field has been studied in several recently published reports e.g. (Gargiulo and Belfiore, 2015) using forward models. On the other hand, source localization requires inverse models and consequently estimation of the source parameters such as location. The CRLB is a commonly used indicator of how far any proposed inverse/estimation solution is from the theoretically best possible performance. To this purpose our results can be used for benchmarking subsequent ma-

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chine learning (semi-supervised and/or unsupervised) solutions once the sufficiently large training datasets are obtained.

To model the electrical activity of the brain we use two dipole structure: low power dipoles that model the background noise/activity of the brain and single high power dipole whose location we aim to estimate. We reiterate that our main goal is not to develop the accurate model of electrical activity but rather to show the accuracy dependance on the modelling of fontanelles. To this purpose we believe that a simplified model is a good preliminary approach to investigate numerically to which extent the fontanelle structure affects the estimation accuracy. We calculate the corresponding field using AC and Medical Imaging toolboxes in COMSOL software as well as 3D slicer for the infant brain segmentation. Using the model predicted values we estimate the corresponding parameters using numerical optimization techniques discussed in Section 2 and calculate the corresponding CRLB . In Section 3 we present our results for various parameters. In Section 4 we present conclusions and directions for future research.

2 MATHEMATICAL MODEL

We model the electrical field on the surface of the head using a volume conductor approach (Malmuvio, 1995) in which the electrical activity in the cortex is modelled using generic current density representation $J(\vec{r},t$. The electrical field is then obtained by solving Maxwell equation and the corresponding solution is represented by well known Geselowitz equation (Gulrajani, 1998) that using a piecewise homogeneous head model consisting of the multiple closed surfaces (skull, brain, etc.) Due to the fact that the geometry is inherently irregular the solution of these equations can only be obtained by using a numerical method such as finite-element method. We use realistic geometry of the 9 months old infant obtained at The University Children Hospital, University of Belgrade, Serbia. MRI images consisted of 110 axial MR slices with 256x256 size and field of view of 240 mm. The segmentation and meshing was done using software packages Slicer and Meshlabs that were then imported as STL files in COMSOL finite-element solver.

Since our main goal is to investigate the effect of fontanel on the accuracy of inverse model we propose to use simplified forward model i.e. scalp EEG generator. In (Gargiulo and Belfiore, 2015) the authors utilized large scale computational model using large number of dipoles to simulate EEG signal measured on the scalp. The inverse models have to rely on much smaller number of parameters due to the fact the number of EEG electrodes that can be placed on infant heads is limited due to the small area. Furthermore, EEG signals from spatially close electrodes is known to be highly correlated and thus of limited use in inverse EEG models.

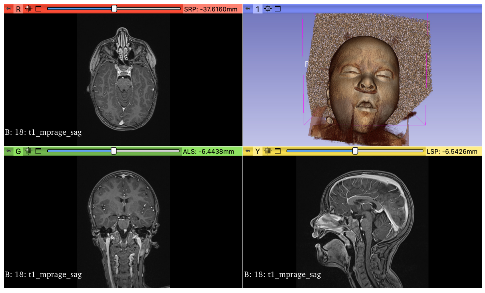
Figure 1: MRI of Infant Head.

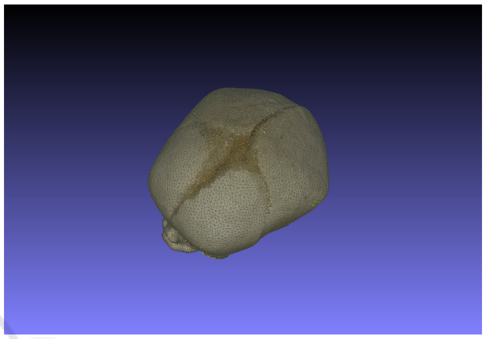
Figure 2: Fontanel Structure.

To this purpose we propose to use the following model: a) the regular brain activity is modelled using 256 Gaussian dipoles placed in the cortical layer that represent background noise in the EEG signal measured on the scalp distributed in the circular pattern under the centre of fontanel and b) single current dipole model with high power current dipole described by three parameters (J_x, J_y, J_z).

Using the finite-element solver in we calculated the corresponding EM field so that the measurement model is then given by

$$y_{ij} = \vec{f}(\vec{r}_i, t_j, \vec{\theta}) + e_{ij} \tag{1}$$

where y_{ij} represents electric potential on the scalp measured on the ith EEG sensor at timet_j, f represents the solution of FE solver at location $\vec{r}_i$ and time t_j and e_{ij} represents the measurements noise/residual model error. The parameters of the model $\vec{\theta}$ are defined by dipole moment and location that are treated as unknown parameters. As a preliminary approach we assume that the measurement noise is zero-mean Gaussian and spatiotemporally uncorrelated. We then estimate the unknown parameters using maximum likelihood estimation which in this scenario results

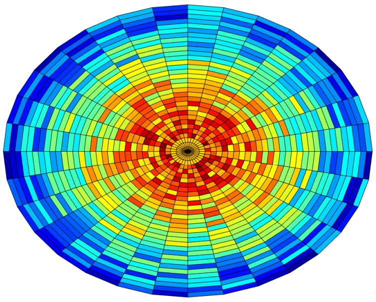

Figure 3: Random instance of dipole moments.

in least-squares estimate by minimizing the error between measured (simulated and model predicted values).

$$\vec{\hat{\theta}}_{LS} = \text{argmin} = \|\vec{y} - \vec{f}\| \tag{2}$$

where $\vec{y}$ is the lumped vector of all the measurements and $\vec{f}$ is lumped vector of all the model predicted values. The measurements consist of n spatial measurements and m temporal measurements assuming that the dipole source is not changing with time.

To evaluate the performance of the proposed algorithms we calculate Cramer-Rao bound which represents the lower bound on the variance of unbiased estimators. This bound is a theoretical limit of the lowest possible variance of the unbiased estimator and hence it is desirable to have the smallest possible value as it is a value to which the variance of the proposed estimator will converge if the number of measurements is sufficiently high. The Cramer-Rao bound is calculated using the Fischer information matrix given by

$$T_{ij}(\vec{\theta}) = -E\left(\frac{\partial \ln p_y(\vec{y},\vec{\theta})}{\partial \theta_i}\frac{\partial \ln p_y(\vec{y},\vec{\theta})}{\partial \theta_j}\right) \tag{3}$$

where $p(\vec{y},\vec{\theta})$ is the probability density function of the measurement vector calculated using FEM solver for a given $\vec{\theta}$. The analytical expression for the Gaussian case can be obtained following (Kay, 1993) using the Gaussian distribution with a nonlinear parametric mean.

3 NUMERICAL RESULTS

To simulate the background EEG signal we use circular grid of 32x32 dipoles with randomly generated dipole intensities so that in the fontanel region the background noise dipole density has expected value of $20\mu A/cm^2$ and standard deviation of $100\mu A^2/cm^4$. In the outer region of the cortex the background EEG dipoles have expected value of $10\mu A/cm^2$ and standard deviation of $100\mu A^2/cm^4$. For the source we are trying to estimate/localize we use a dipole with density of $40\mu A/cm^2$. Following the values used in (Gargiulo and Belfiore, 2015) we vary the conductivity of the fontanel region from 0.01 to 1.51 S/m to evaluate its effect on the Cramer-Rao bound.

Since in our model the measurement noise is assumed to be Gaussian the Fischer information matrix and consequently CRLB depend only on the gradient of the model predicted solution $\vec{f}$ with respect to the unknown parameters $\vec{\theta}$. We calculate the corresponding gradients using finite difference approximation in the parameter space. Note that if parameters of interest can be modelled as random variables the calculation of CRLB would require Monte-Carlo simulations. We use the multichannel EEG sensor model consisting of 4 sensors distributed on the fontanel periphery. The distance of the source is measured with respect to the centre of the fontanel structure as illustrated in Figure 4.

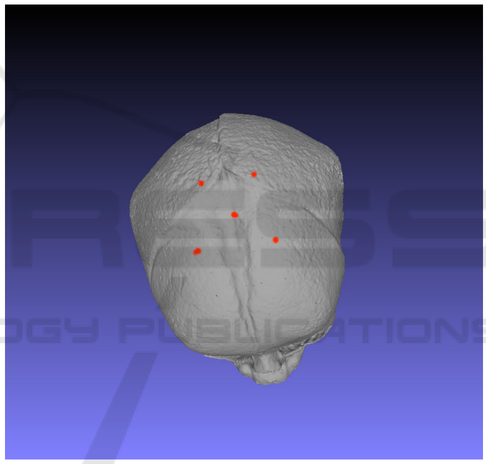

Figure 4: EEG sensor locations.

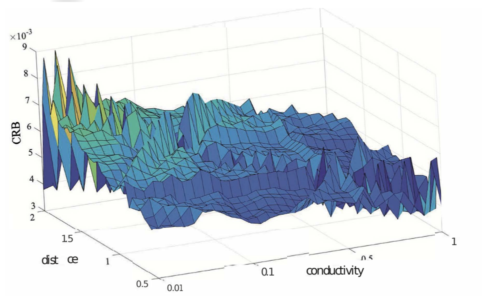

Figure 5: Source localization CRB.

In Figure 5 we illustrate the CRB as a function of distance of the high activity dipole source from the centre of the fontanel and conductivity. As expected for larger conductivity values we obtain the lower CRLB which improves our ability to estimate the source location accurately. In Figure 6 we illus-

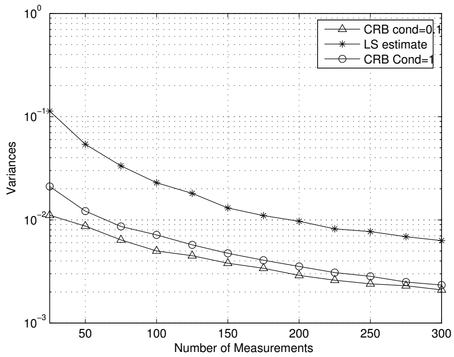

Figure 6: Source localization CRB as a function of time.

trate the CRLB and mean square error as a function of number of measurements. For illustration purposes we calculate two CRLB for different conductivity values of 0.1 and 1 and mean square error of LS estimator using 1000 runs. Note that in this example we assume that the dipole intensity is fixed during the measurement interval which may not be valid in realistic scenario due to the fact that EEG activity epochs are quite dynamic with respect to time. As expected the estimator variance decreases with the number of measurements and is expected to asymptotically approach CRB.

4 CONCLUSIONS

We proposed a computational framework for calculating theoretical bound for localization of single dipole source in an infant head using single dipole model and realistic geometry. The proposed framework enables us to calculate the lowest possible variance that can be obtained for a given geometry. Our preliminary results indicate that the ability to localize single dipole depends on the conductivity as well as geometry of the subject as well as the conductivity of fontanel. Therefore an effort should be place on improving our ability to estimate the conductivity jointly with source localization. In addition, an effort should be made to investigate the accuracy of the model with respect to signal-to-noise ratio. Although this analysis is important it is left for future studies as the CRB of power is significantly dependent on the conductivity and thus may require improved knowledge on conductivity values of the fontanels. Furthermore, based on the aforementioned CRB studies the performance can be significantly increased if we position the EEG sensors in a such way to minimize CRLB at the largest possible number of possible source (regions of high activity) instances. Our results indicate that an adequate localization error can be achieved using inverse EM modelling approach although it may require advanced signal processing algorithms.

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