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Improving the accuracy of Laplacian estimation with novel multipolar concentric ring electrodes

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ABSTRACT

Conventional electroencephalography with disc electrodes has major drawbacks including poor spatial resolution, selectivity and low signal-to-noise ratio that are critically limiting its use. Concentric ring electrodes, consisting of several elements including the central disc and a number of concentric rings, are a promising alternative with potential to improve all of the aforementioned aspects significantly. In our previous work, the tripolar concentric ring electrode was successfully used in a wide range of applications demonstrating its superiority to conventional disc electrode, in particular, in accuracy of Laplacian estimation. This paper takes the next step toward further improving the Laplacian estimation with novel multipolar concentric ring electrodes by completing and validating a general approach to estimation of the Laplacian for an $(n+1)$-polar electrode with n rings using the $(4n+1)$-point method for $n \geqslant 2$ that allows cancellation of all the truncation terms up to the order of $2n$. An explicit formula based on inversion of a square Vandermonde matrix is derived to make computation of multipolar Laplacian more efficient. To confirm the analytic result of the accuracy of Laplacian estimate increasing with the increase of n and to assess the significance of this gain in accuracy for practical applications finite element method model analysis has been performed. Multipolar concentric ring electrode configurations with n ranging from 1 ring (bipolar electrode configuration) to 6 rings (septapolar electrode configuration) were directly compared and obtained results suggest the significance of the increase in Laplacian accuracy caused by increase of n.

1. Introduction

Electroencephalography (EEG) is an essential tool for brain and behavioral research and is used extensively in neuroscience, cognitive science, cognitive psychology, and psychophysiology. EEG is also one of the mainstays of hospital diagnostic procedures and pre-surgical planning. Despite scalp EEG's many advantages end users struggle with its poor spatial resolution, selectivity and low signal-to-noise ratio, which are EEG's biggest drawbacks critically limiting the research discovery and diagnosis [1–3].

EEG's poor spatial resolution is primarily due to (1) the blurring effects of the volume conductor with disc electrodes; and (2) EEG signals having reference electrode problems as idealized references are not available with EEG [2]. Interference on the reference electrode contaminates all other electrode signals [2]. The application of the surface Laplacian (the second spatial derivative of the potentials on the body surface) to EEG has been shown to alleviate the blurring effects enhancing the spatial resolution and selectivity, and reduce the reference problem [4–6].

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While several methods were proposed for estimation of the surface Laplacian through interpolation of potentials on a surface and then estimating the Laplacian from an array of disc electrodes [5–9], concentric ring electrodes (CRE) have shown more promise. The CREs can resolve the reference electrode problems since they act like closely spaced bipolar recordings [2]. CREs are symmetrical alleviating electrode orientation problems [10]. They also act as spatial filters reducing the low spatial frequencies and increasing the spatial selectivity [10,11]. Finally, even bipolar CREs, consisting of just two elements including a single ring and the central disc, improve the radial attenuation of the conventional disc electrode from $1/r^3$ to $1/r^4$ with larger numbers of poles having the potential to enhance radial attenuation even further [12].

Tripolar CREs (TCRE; the largest number of CRE poles currently used), consisting of three elements including the outer ring, the middle ring, and the central disc (Fig. 1B), are distinctively different from conventional disc electrodes that have a single element (Fig. 1A). TCREs have been shown to estimate the surface Laplacian directly through the nine-point method (NPM), an extension of the five-point method (FPM) used for bipolar CREs, and significantly better than other electrode systems including bipolar and quasi-bipolar CREs [13,14]. Compared to EEG with conventional disc electrodes Laplacian via TCREs have been shown to have significantly better spatial selectivity (approximately 2.5 times higher), signal-to-noise ratio (approximately 3.7 times higher), and mutual information (approximately 12 times lower) [15]. TCREs also have very high common mode noise rejection providing automatic artifact attenuation, −100 dB one radius from the electrode [14]. Because of such unique capabilities TCREs have found numerous applications in a wide range of areas including brain–computer interface [16,17], seizure onset detection [18,19], seizure attenuation using transcranial focal stimulation applied via TCREs [20–23], detection of high-frequency oscillation and seizure onset zones [24], etc. These applications suggest experimental practicality of further increasing the number of poles in noninvasive electrophysiological electrodes.

Taking a first, preliminary step toward development of multipolar CREs, the Laplacian has been derived for a general case of $(n+1)$-polar CRE with n rings using the $(4n+1)$-point method for $n \geqslant 2$ demonstrating how the accuracy of the Laplacian estimate increases with the increase of n due to elimination of higher order truncation terms [25]. This approach allows canceling all the truncation terms up to the order of $2n$ which has been shown to be the highest order achievable for a CRE with n rings [25]. Furthermore, the proposed general approach has been illustrated with two examples numerically deriving the Laplacian estimates for TCRE and [13–24], for the first time, quadripolar CRE (QCRE) [25].

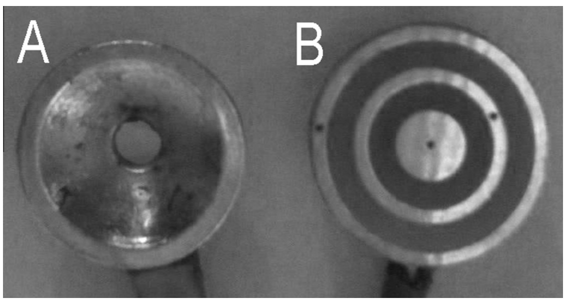

Fig. 1. Conventional disc electrode (A) and tripolar concentric ring electrode (B).

This preliminary study had two fundamental shortcomings. First, for any $n \geqslant 2$ the Laplacian estimates in the form of the null space vectors could be calculated numerically through finding the column echelon form of the matrix using methods like Bareiss algorithm which for exactly given integer matrices have been shown to be more efficient than the standard Gaussian elimination [26]. However, deriving an explicit formula for Laplacian estimates as a function of n would be even more efficient in terms of its computation. Second, computer modeling was needed to confirm the analytic result of the accuracy of Laplacian estimate increasing with the increase of n and to assess the significance of this gain in accuracy for practical applications.

This paper addresses both shortcomings of the preliminary study [25]. First, explicit formula for multipolar Laplacian is derived based on the inversion of a square Vandermonde matrix completing the proposed approach to estimation of multipolar Laplacian. Second, multipolar CRE configurations with n ranging from 1 (bipolar CRE) to 6 (septapolar CRE) were directly compared in accuracy of Laplacian estimation using finite element method (FEM) model analysis with a single dipole. While FEM modeling is commonly used to assess and compare different electrode configurations [27,28], the model used in this paper was adopted from our previous studies where it was used to compare bipolar, quasi-bipolar, and tripolar CRE configurations [13,14].

This paper is organized as follows: preliminaries and notations for the proposed approach for multipolar Laplacian estimation including basic cases of FPM and NPM as well as the general approach for $(n+1)$-polar CRE with n rings are presented in the Material and Methods section. This section also contains all the details on the FEM modeling used to compare different multipolar CRE configurations as well as on statistical analysis of obtained results. Main results including derivation of the explicit formula for multipolar Laplacian estimate based on the inversion of a square Vandermonde matrix and FEM modeling results are presented in the Results section. Discussion of the obtained results and plans for future work are presented in the Discussion section followed by the overall conclusion.

2. Material and methods

2.1. Notations and preliminaries

2.1.1. Five-point method (bipolar CRE)

As shown in Fig. 2 v_0 through $v_{nr,4}$ are the potentials at points p_0 through $p_{nr,4}$, respectively. To simplify the narrative, v_0 through $v_{nr,4}$ may also signify points p_0 through

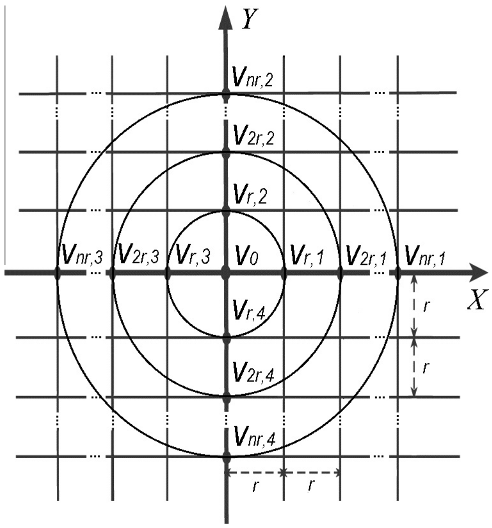

Fig. 2. Regular plane square grid with interpoint distance equal to r.

$p_{nr,4}$. v_0, $v_{r,1}$, $v_{r,2}$, $v_{r,3}$ and $v_{r,4}$, with a spacing of r are applied in the FPM (a bipolar CRE configuration Laplacian estimate) following Huiskamp's calculation of the Laplacian [29]. The Laplacian potentials at point p_0 are calculated using Taylor expansion:

$$\Delta v_0 = \frac{\partial^2 v}{\partial x^2} + \frac{\partial^2 v}{\partial y^2} = \frac{1}{r^2}\left(\sum_{i=1}^{4} v_{r,i} - 4v_0\right) + O(r^2) \tag{1}$$

where $O(r^2) = \frac{r^2}{4!}\left(\frac{\partial^4 v}{\partial x^4} + \frac{\partial^4 v}{\partial y^4}\right) + \frac{r^4}{6!}\left(\frac{\partial^6 v}{\partial x^6} + \frac{\partial^6 v}{\partial y^6}\right) + \ldots$

is the truncation error. Expression (1) can be generalized by taking the integral along the circle of radius r around p_0 of the Taylor expansion. Defining $x = r\cos(\theta)$ and $y = r\sin(\theta)$ as in Huiskamp we have [29]:

$$\frac{1}{2\pi}\int_0^{2\pi} v(r,\theta)d\theta - v_0 = \frac{r^2}{4}\Delta v_0 + \frac{r^4}{4!}\int_0^{2\pi}\sum_{j=0}^{4}\sin^{4-j}(\theta) \times \cos^j(\theta)d\theta\left(\frac{\partial^4 v}{\partial x^{4-j}\partial y^j}\right) + \ldots \tag{2}$$

where $\frac{1}{2\pi}\int_0^{2\pi} v(r,\theta)d\theta$ is the average potential on the ring of radius r and v_0 is the potential on the central disc of the bipolar CRE.

2.1.2. Nine-point method (TCRE)

To derive the Laplacian for the TCRE using NPM we add another FPM applying the integral along a circle of radius $2r$ (v_0, $v_{2r,1}$, $v_{2r,2}$, $v_{2r,3}$ and $v_{2r,4}$ on Fig. 2) around point p_0 [13,14]. The following is obtained for the average potential on the ring of radius $2r$ and disc:

$$\frac{1}{2\pi}\int_0^{2\pi} v(2r,\theta)d\theta - v_0 = \frac{(2r)^2}{4}\Delta v_0 + \frac{(2r)^4}{4!}\int_0^{2\pi}\sum_{j=0}^{4}\sin^{4-j}(\theta)\cos^j(\theta)d\theta\left(\frac{\partial^4 v}{\partial x^{4-j}\partial y^j}\right) + \ldots \tag{3}$$

Next, we multiply (2) by 16 and subtract (3) canceling the fourth-order truncation term and resulting in the Laplacian estimate:

$$\Delta v_0 \cong \frac{1}{3r^2}\left[16\left(\frac{1}{2\pi}\int_0^{2\pi} v(r,\theta)d\theta - v_0\right) - \left(\frac{1}{2\pi}\int_0^{2\pi} v(2r,\theta)d\theta - v_0\right)\right] \tag{4}$$

where $\frac{1}{2\pi}\int_0^{2\pi} v(2r,\theta)d\theta$ is the average potential on the outer ring of radius $2r$, $\frac{1}{2\pi}\int_0^{2\pi} v(r,\theta)d\theta$ is the average potential on the middle ring of radius r, and v_0 is the potential on the central disc of the TCRE [13,14]. In practice, (4) is computed using custom preamplifier boards that for each TCRE combine potentials from two concentric rings and central disc into surface Laplacian estimation signal (termed tEEG for electroencephalography via TCREs). This surface Laplacian estimate is the only signal sent to the amplifier from each TCRE.

2.1.3. General (4n + 1)-point method for (n + 1)-polar CRE with n rings

Generalizing (2) and (3) for a case of CRE with n rings ($n \geqslant 2$) we obtain a set of n FPM equations, one for each ring with radii ranging from r to nr (v_0, $v_{nr,1}$, $v_{nr,2}$, $v_{nr,3}$ and $v_{nr,4}$ on Fig. 2) around point p_0 for which we have:

$$\frac{1}{2\pi}\int_0^{2\pi} v(nr,\theta)d\theta - v_0 = \frac{(nr)^2}{4}\Delta v_0 + \frac{(nr)^4}{4!}\int_0^{2\pi}\sum_{j=0}^{4}\sin^{4-j}(\theta)\cos^j(\theta)d\theta\left(\frac{\partial^4 v}{\partial x^{4-j}\partial y^j}\right) + \frac{(nr)^6}{6!}\int_0^{2\pi}\sum_{j=0}^{6}\sin^{6-j}(\theta)\cos^j(\theta)d\theta\left(\frac{\partial^6 v}{\partial x^{6-j}\partial y^j}\right) + \ldots \tag{5}$$

To estimate the Laplacian for this general case the n equations are combined in a way that cancels all the truncation terms up to the highest order that can be achieved for n rings increasing the accuracy of the Laplacian estimate. In order to find such a combination we arrange the coefficients l^k of the truncation terms with the general form $\frac{(lr)^k}{k!}\int_0^{2\pi}\sum_{j=0}^{k}\sin^{k-j}(\theta)\cos^j(\theta)d\theta\left(\frac{\partial^k v}{\partial x^{k-j}\partial y^j}\right)$ for order k ranging in increments of 2 from 4 to some even positive integer m ($m \geqslant 4$) and ring radius multiplier l ranging from 1 (Eq. (2)) to n (Eq. (5)) into the $(m-2)/2$ by n matrix A as follows:

$$A = \begin{pmatrix} 1^4 & 2^4 & \cdots & n^4 \\ 1^6 & 2^6 & \cdots & n^6 \\ \vdots & \vdots & \ddots & \vdots \\ 1^m & 2^m & \cdots & n^m \end{pmatrix} = \begin{pmatrix} 1 & 2^4 & \cdots & n^4 \\ 1 & 2^6 & \cdots & n^6 \\ \vdots & \vdots & \ddots & \vdots \\ 1 & 2^m & \cdots & n^m \end{pmatrix} \tag{6}$$

A matrix equation of the form:

$$A\bar{x} = \bar{0} \tag{7}$$

is equivalent to a homogeneous system of linear equations where $\bar{0}$ is the $(m-2)/2$-dimensional zero vector and $\bar{x}$ is the n-dimensional vector that allows the cancellation of all the truncation terms up to the order of m by setting the linear combination of n coefficients l^k corresponding to all ring radii for each order k equal to 0 [25].

The existence of nontrivial solution ($\bar{x} \neq \bar{0}$) of equation (7) depends on the relationship between the number of rows $(m-2)/2$ and the number of columns n of matrix A. It is known that for homogeneous systems nontrivial solutions exist only when the system is underdetermined, i.e. $(m-2)/2 < n$ [30]. Moreover, if A is real as in our case, a real nontrivial solution exists. The largest number of rows the matrix A from (6) may have to stay underdetermined is $n-1$, so in order to find the highest truncation term order m that can be canceled with n rings CREs we solve $(m-2)/2 = n-1$ which yields $m = 2n$. Therefore, matrix A can be rewritten as an $n-1$ by n matrix A' that is a function only of the number of the rings n:

$$A' = \begin{pmatrix} 1 & 2^4 & \cdots & n^4 \\ 1 & 2^6 & \cdots & n^6 \\ \vdots & \vdots & \ddots & \vdots \\ 1 & 2^{2n} & \cdots & n^{2n} \end{pmatrix} \tag{8}$$

Equivalently to substituting A' for A into (7) it can be observed that the same nontrivial solutions are given by the null space (or kernel) of matrix A' [30]. It should be noted that null space vectors used for Laplacian estimates are not unique. From the properties of matrix multiplication it is known that for any vector $\bar{x}$ that belongs to the null space of matrix A and a scalar c the scaled vector $c\bar{x}$ also belongs to the null space of the same matrix A since $(cA)\bar{x} = c(A\bar{x})$. Therefore, any scaled version of given null space vector would also be a null space vector.

2.2. FEM modeling

All the FEM modeling was performed using Matlab (Mathworks, Natick, MA). The modeling scripts are available from the authors (OM) upon request. To compare the discrete Laplacian estimates including the bipolar (number of rings $n = 1$), tripolar ($n = 2$), quadripolar ($n = 3$), quintopolar ($n = 4$), sextopolar ($n = 5$), and septapolar ($n = 6$) multipolar CRE configurations directly a FEM computer model was developed with a 1700×1700 evenly spaced mesh located in the first quadrant of the X–Y plane above a unit charge dipole projected to the center of the mesh and oriented toward the positive direction of the Z axis as shown in Fig. 3. The dipole was moved along the Z axis to evaluate the effect of depth on accuracy of Laplacian estimates.

At each point of the mesh, the electric potential ϕ generated by a unity dipole was calculated with the formula for electric potential due to a dipole in a homogeneous medium of conductivity σ [31]:

$$\phi = \frac{1}{4\pi\sigma}\frac{(\bar{r}_p - \bar{r})\cdot\bar{p}}{|\bar{r}_p - \bar{r}|^3} \tag{9}$$

where $\bar{r} = (x, y, z)$ and $\bar{p} = (p_x, p_y, p_z)$ represent the location and the moment of the dipole and $\bar{r}_p = (x_p, y_p, z_p)$ represents the observation point. The conductivity σ of the medium was taken to be 7.14 mS/cm to emulate biological tissue [32]. For this FEM model it was assumed that the medium was homogeneous and $\bar{p} = (0, 0, 1)$ making the term $\bar{p}/4\pi\sigma$ in (9) constant. The analytical Laplacian was then calculated at each point of the mesh, by taking the second derivative of the electric potential ϕ [31]:

$$L = \Delta\phi = \frac{\partial^2\phi}{\partial x^2} + \frac{\partial^2\phi}{\partial y^2} \tag{10}$$

According to He and Wu [31], this results in:

$$L = \frac{3}{4\pi\sigma}\left[5(z_p - z)^2\frac{(\bar{r}_p - \bar{r})\cdot\bar{p}}{|\bar{r}_p - \bar{r}|^7} - \frac{(\bar{r}_p - \bar{r})\cdot\bar{p} + 2(z_p - z)p_z}{|\bar{r}_p - \bar{r}|^5}\right] \tag{11}$$

Laplacian estimates for six multipolar CRE configurations ranging from bipolar to septapolar were computed at each point of the mesh where appropriate boundary conditions could be applied. In order to show that there is no inherent increase in the size of CREs due to the number of poles we ensured that all modeled multipolar CREs have the same dimensions despite having different numbers of rings. The largest ring radius for all the CRE configurations was selected to be equal to $60r$ since 60 is the least common multiple of all the integers from 1 to 6. Moreover, the process was repeated for different interpoint distances using integer multiples of r ranging from 1 to 10. Therefore, in the worst case scenario of a CRE being modeled with the interpoint distance using a multiple value equal to 10 the number of points on the mesh where appropriate boundary conditions could be applied to compute Laplacian estimates was equal to 500×500 (since for each dimension of the mesh $1700 - 2 * 60 * 10 = 500$). Correspondingly, in the best case scenario for a multiple value equal to 1 the number of points on the mesh where Laplacian estimates were computed was equal to 1580×1580 ($1700 - 2 * 60 * 1 = 1580$). The model was tied to the physical dimensions (in cm) through the target physical size of the multipolar CREs. The smallest CRE diameter was equal to 0.5 cm (multiple of r equal to 1) and the largest was equal to 5 cm (multiple of r equal to 10). The dipole depth ranged from 1 cm to 5 cm.

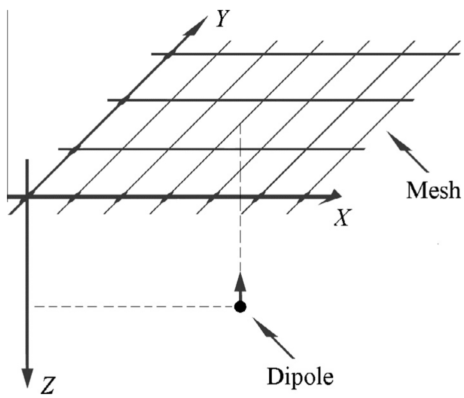

Fig. 3. Schematic of the finite element method computer model with a square mesh of size 1700×1700 used to assess and compare the accuracy of Laplacian estimates for multipolar concentric ring electrode configurations ranging from bipolar to septapolar.

Derivation of Laplacian estimate coefficients for multipolar CRE configurations was performed using the approach proposed in this paper. The following sets of coefficients were used: (16, −1) for tripolar, (270, −27, 2) for quadripolar [25], (8064, −1008, 128, −9) for quintopolar, (42,000, −6000, 1000, −125, 8) for sextopolar, and (1,425,600, −222,750, 44,000, −7425, 864, −50) for septapolar multipolar CRE configurations. For example, for the case of TCRE, (16, −1) is one of the integer vectors of the null space of matrix A' from (8) for $n = 2$. It was used to estimate the surface Laplacian for TCRE in (4) as well as in [13–24] and other works utilizing TCREs. In a similar way, null space of matrix A' from (8) can be calculated offline for any given n with the null space vector becoming the coefficients of the linear combination of differences of potentials from each of the n rings and the central disc respectively to produce Laplacian estimate similar to the one derived in (4) for TCRE. Preamplifier boards for multipolar CREs can be designed in a similar way to the ones currently used for TCREs. Single preamplifier board is needed for each multipolar CRE to estimate surface Laplacian to be sent to the amplifier.

These six estimates were then compared with the calculated analytical Laplacian for each point of the mesh where corresponding Laplacian estimates were computed using Relative Error and Maximum Error measures [13,14,29]:

$$\text{Relative Error}^i = \sqrt{\frac{\sum\left(\Delta v - \Delta^i v\right)^2}{\sum(\Delta v)^2}} \tag{12}$$

$$\text{Maximum Error}^i = \max|\Delta v - \Delta^i v| \tag{13}$$

where i represents the Laplacian estimation method (bipolar, tripolar, quadripolar, quintopolar, sextopolar or septapolar) used to approximate the Laplacian potential $\Delta^i v$ and Δv represents the analytical Laplacian potential.

Statistical analysis of FEM modeling results was performed using Design-Expert software (Stat-Ease Inc., Minneapolis, MN, USA). Full factorial design of analysis of variance (ANOVA) was used with three numerical factors [33]. The first factor (A) was the dipole depth presented at five levels uniformly distributed in the range from 1 cm to 5 cm. The second factor (B) was the CRE diameter presented at ten levels uniformly distributed in the range from 0.5 cm to 5 cm. The third factor (C) was the number of rings in the multipolar CRE configuration presented at six levels ranging from one (bipolar CRE) to six (septapolar CRE). Two response variables were the Relative Error and Maximum Error computed for each of the $5 * 10 * 6 = 300$ combinations of levels of three factors.

3. Results

3.1. Explicit formula for multipolar Laplacian estimate for (n + 1)-polar CRE with n rings

In order to derive the explicit formula for the null space vectors of $n-1$ by n matrix A' from (8) as a function of n we will turn A' into a square Vandermonde matrix and use the explicit formula for the inversion of such matrix that has been derived by Knuth [34].

We want to solve $A'\bar{x} = \bar{0}$ that can be re-written as:

$$\begin{pmatrix} 1 & 2^4 & \cdots & n^4 \\ 1 & 2^6 & \cdots & n^6 \\ \vdots & \vdots & \ddots & \vdots \\ 1 & 2^{2n} & \cdots & n^{2n} \end{pmatrix} \begin{bmatrix} x_1 \\ x_2 \\ \vdots \\ x_n \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix} \tag{14}$$

where $\bar{0}$ is the $(n-1)$-dimensional zero vector and $\bar{x} = [x_1, \ldots, x_n]^T$.

Without loss of generality, we can divide both sides of (14) by x_1 resulting in:

$$\begin{pmatrix} 1 & 2^4 & \cdots & n^4 \\ 1 & 2^6 & \cdots & n^6 \\ \vdots & \vdots & \ddots & \vdots \\ 1 & 2^{2n} & \cdots & n^{2n} \end{pmatrix} \begin{bmatrix} 1 \\ x_2/x_1 \\ \vdots \\ x_n/x_1 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix} \tag{15}$$

or, equivalently:

$$\underbrace{\begin{pmatrix} 2^4 & 3^4 & \cdots & n^4 \\ 2^6 & 3^6 & \cdots & n^6 \\ \vdots & \vdots & \ddots & \vdots \\ 2^{2n} & 3^{2n} & \cdots & n^{2n} \end{pmatrix}}_{A''} \begin{bmatrix} x_2/x_1 \\ x_3/x_1 \\ \vdots \\ x_n/x_1 \end{bmatrix} = \begin{bmatrix} -1 \\ -1 \\ \vdots \\ -1 \end{bmatrix} \tag{16}$$

where A'' is the $n-1$ by $n-1$ square matrix. To turn A'' into a Vandermonde matrix we re-write (16) as:

$$\begin{pmatrix} 2^4/2^4 & 3^4/3^4 & \cdots & n^4/n^4 \\ 2^6/2^4 & 3^6/3^4 & \cdots & n^6/n^4 \\ \vdots & \vdots & \ddots & \vdots \\ 2^{2n}/2^4 & 3^{2n}/3^4 & \cdots & n^{2n}/n^4 \end{pmatrix} \begin{bmatrix} 2^4x_2/x_1 \\ 3^4x_3/x_1 \\ \vdots \\ n^4x_n/x_1 \end{bmatrix} = -\begin{bmatrix} 1 \\ 1 \\ \vdots \\ 1 \end{bmatrix} \tag{17}$$

Then we let $y_i = \frac{(i+1)^4 x_{i+1}}{x_i}$ for $i = 1, \ldots, n-1$ in (17) resulting in:

$$\underbrace{\begin{pmatrix} 1 & 1 & \cdots & 1 \\ 2^2 & 3^2 & \cdots & n^2 \\ \vdots & \vdots & \ddots & \vdots \\ 2^{2(n-2)} & 3^{2(n-2)} & \cdots & n^{2(n-2)} \end{pmatrix}}_{A'''} \underbrace{\begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_{n-1} \end{bmatrix}}_{\bar{y}} = -\underbrace{\begin{bmatrix} 1 \\ 1 \\ \vdots \\ 1 \end{bmatrix}}_{\bar{1}} \tag{18}$$

The transpose of A''' in (18) follows the classical form of the square Vandermonde matrix as defined by Knuth [34]:

$$B = (A''')^T = \begin{pmatrix} 1 & 2^2 & \cdots & 2^{2(n-2)} \\ 1 & 3^2 & \cdots & 3^{2(n-2)} \\ \vdots & \vdots & \ddots & \vdots \\ 1 & n^2 & \cdots & n^{2(n-2)} \end{pmatrix} \equiv \begin{pmatrix} 1 & \alpha_0 & \cdots & \alpha_0^{n-2} \\ 1 & \alpha_1 & \cdots & \alpha_1^{n-2} \\ \vdots & \vdots & \ddots & \vdots \\ 1 & \alpha_{n-2} & \cdots & \alpha_{n-2}^{n-2} \end{pmatrix} \tag{19}$$

where $\alpha_i = (i+2)^2$ for $i = 0, \ldots, n-2$.

Therefore, substituting B from (19) into the transpose of (18) we have:

$$\bar{y}^T = -\left(\left(A'''\right)^{-1}\bar{1}\right)^T = -\bar{1}^T\left(\left(A'''\right)^{-1}\right)^T = -\bar{1}^T\left(\left(A'''\right)^T\right)^{-1} = -\bar{1}^T B^{-1} \tag{20}$$

This ultimately gives us:

$$\bar{y} = -\left(\bar{1}^T B^{-1}\right)^T = -\left(B^{-1}\right)^T \bar{1} \tag{21}$$

where $\bar{1}$ is a column vector of all ones from (18) and explicit formula for B^{-1} as a function of n has been derived by Knuth [34].

3.2. FEM modeling

Two error measures were computed for six Laplacian estimation methods corresponding to the bipolar, tripolar, quadripolar, quintopolar, sextopolar, and septapolar CRE configurations using (12) and (13). Resulting Relative and Maximum Errors are presented for multipolar CRE diameters ranging from 0.5 cm to 5 cm and dipole depth ranging from 1 cm to 5 cm on a semi-log scale in Figs. 4 and 5 respectively.

The effect of factors A (dipole depth), B (CRE diameter), and C (number of rings) on Relative and Maximum Errors was assessed and the ANOVA results suggest that all three factors have statistically significant effects in the model (Relative Error: d.f. = 3, $F = 146.72$, $p < 0.0001$; Maximum Error: d.f. = 3, $F = 228.32$, $p < 0.0001$) for the optimal power transformations (Relative Error: lambda = -1.01; Maximum Error: lambda = -2.11) determined using the Box-Cox procedure [33]. The effects of the main factors were: A (Relative Error: d.f. = 1, $F = 71.37$, $p < 0.0001$; Maximum Error: d.f. = 1, $F = 233.83$, $p < 0.0001$), B (Relative Error: d.f. = 1, $F = 135.27$, $p < 0.0001$; Maximum Error: d.f. = 1, $F = 103.15$, $p < 0.0001$), and C (Relative Error: d.f. = 1, $F = 233.52$, $p < 0.0001$; Maximum Error: d.f. = 1, $F = 347.97$, $p < 0.0001$).

4. Discussion

The contribution of this paper is twofold. First, the proposed general approach to estimation of surface Laplacian for novel multipolar CREs with any given number of rings was completed by deriving an explicit formula based on the inversion of a square Vandermonde matrix. Second, accuracies of Lapacian estimates corresponding to multipolar CRE configurations ranging from bipolar to septapolar were directly compared using FEM model analysis. FEM modeling was used as a measure to demonstrate the practical usefulness of the approach taking it beyond the preliminary, conceptual stage [25]. FEM modeling results obtained in this paper are consistent with the previous FEM modeling results obtained for bipolar and tripolar CRE configurations only [13,14] and confirm the theoretical results stemming from the mathematical derivation of Laplacian for multipolar CREs [25]. Therefore, this paper provides a comprehensive theoretical basis for novel multipolar CREs as well as validation of analytic results via FEM modeling for CRE configurations up to the septapolar one. Biomedical significance of CREs is related to the fact that they allow estimating surface Laplacian directly at the electrode instead of combining the data from an array of conventional disc (single pole) electrodes, so further improving the accuracy of Laplacian estimate recorded via multipolar CREs may be critical to advancement of noninvasive electrophysiological electrode design with application areas not limited to electroencephalography, electrocardiography, and electromyography. Moreover, other potential advantages of multipolar CREs with higher numbers of poles need to be investigated including, for example, improved control of the electric field used for seizure attenuation compared to the one that current transcranial focal stimulation applied via TCREs can offer [20–23].

The ANOVA results for comparison of global Lapacian estimates corresponding to different multipolar CRE configurations have showed the significance of all three factors included in this FEM model. While it was important to confirm that the accuracy of Laplacian estimation increases (Relative and Maximum Errors decrease) with an increase of the dipole depth (factor A) and decreases (Relative and Maximum Errors increase) with an increase of the CRE diameter (factor B), the most important result is that, for the case of the factor C, the multipolar Laplacian estimates for larger numbers of rings are significantly better than the ones for smaller numbers of rings at approximating the analytical Laplacian. This result supports the theoretical findings that for an $(n+1)$-polar CRE with n rings the proposed general Laplacian estimation approach allows cancellation of all the truncation terms up to the order of $2n$ increasing the estimation accuracy.

However, even though the statistical analysis showed that, in general, both Relative and Maximum Errors were decreasing significantly with the increase in the number of CRE rings, using a realistic FEM model also revealed that for dipoles at larger depths and for smaller sizes of CREs the difference between the multipolar CRE configurations with large (4–6) numbers of rings becomes negligible. This can be seen from Figs. 4 and 5 at dipole depth of 3 cm and larger (panels C–E) and the CRE diameter of 1 cm and smaller. This is an intuitive result suggesting the existence of an upper bound on the maximum practical number of rings to include in the multipolar CRE. Larger number of rings means larger number of independently computed samples of the potentials to include into the Laplacian estimate providing a closer approximation of the analytical Laplacian. However, decreasing the distance between rings/samples by decreasing the size of the CRE and/or decreasing the difference between the potentials to sample by increasing the depth of the source makes the effect of additional independently computed samples negligible. Existence of an upper bound on the maximum practical number of rings also suggests the possibility of optimizing the design of a multipolar CRE for specific applications taking into account the requirements on the CRE size and expected maximum depth of the sources to record from. For example, currently used TCREs have a diameter of 1 cm [13–24]. For EEG applications it is not unrealistic to assume possibility of detectable sources at depths of up to 5 cm from the scalp. Based on the FEM modeling results presented in Figs. 4 and 5 (panel E) the optimal multipolar CRE configuration for this CRE size and source depth would be a sextopolar CRE while a septapolar CRE would not result in significant

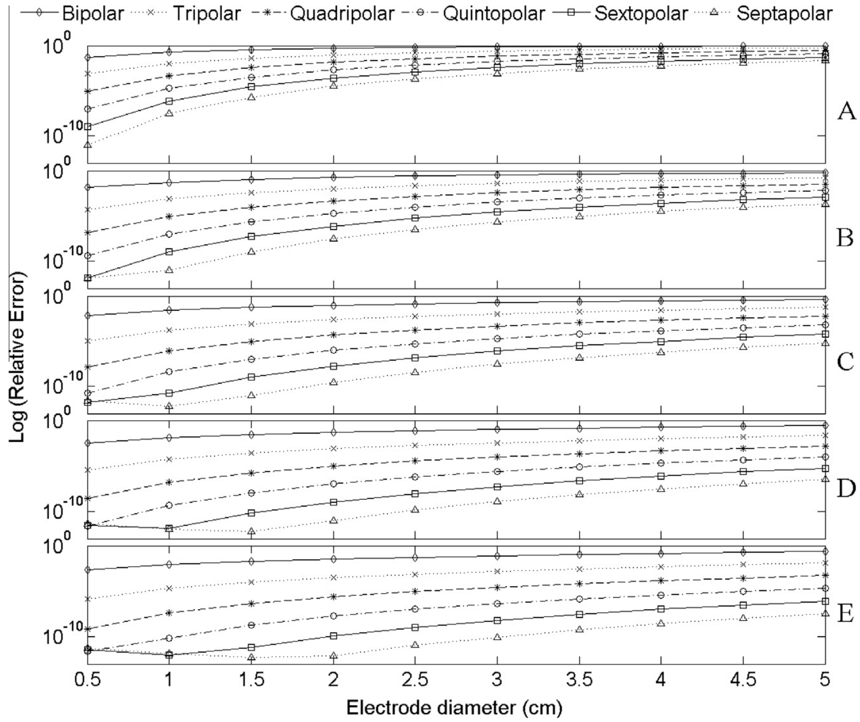

Fig. 4. Relative Error of six Laplacian estimates corresponding to the bipolar, tripolar, quadripolar, quintopolar, sextopolar, and septapolar CRE configurations for multipolar CRE diameters ranging from 0.5 cm to 5 cm. Panels A–E correspond to dipole depth ranging from 1 cm to 5 cm respectively.

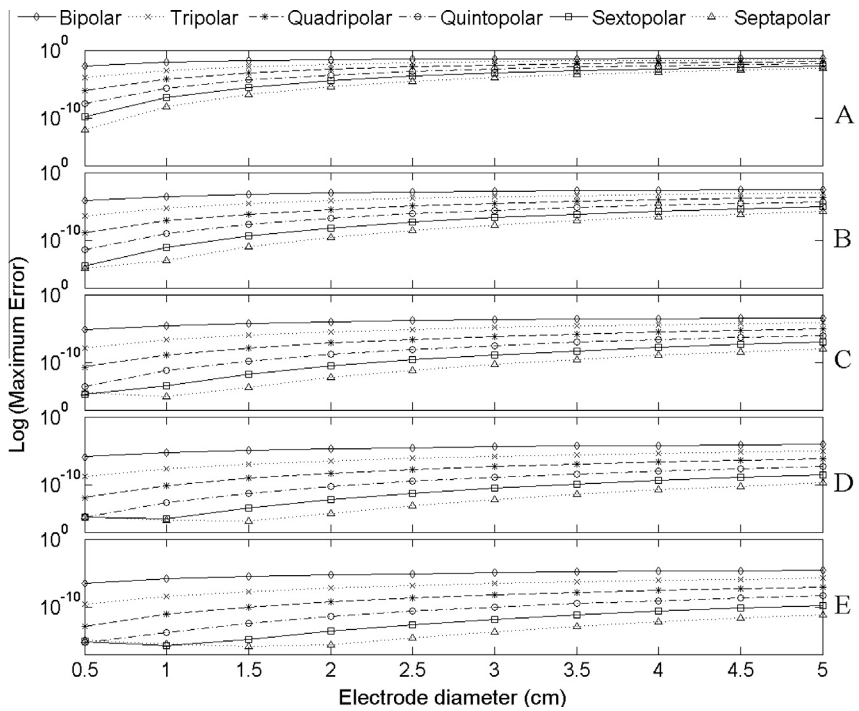

Fig. 5. Maximum Error of six Laplacian estimates corresponding to the bipolar, tripolar, quadripolar, quintopolar, sextopolar, and septapolar CRE configurations for multipolar CRE diameters ranging from 0.5 cm to 5 cm. Panels A–E correspond to dipole depth ranging from 1 cm to 5 cm respectively.

improvement in accuracy of Laplacian estimation. Optimal numbers of rings and sizes of multipolar CREs may be selected in a similar way for different applications in electrocardiography, electromyography, etc. Finally, it can be seen from Figs. 4 and 5 that Relative and Maximum Errors do not always decrease with an increase of the CRE size. For example, for dipole depth of 5 cm (panel E) both errors increase with an increase of the septapolar CRE diameter from 0.5 cm to 1 cm. We believe that this effect is due to the fact that the upper bound on the maximum practical number of rings is different for CREs of different sizes. Panel E of Figs. 4 and 5 suggest that the optimal number of rings for CRE with diameter of 0.5 cm is 4 while for CRE with diameter of 1 cm it is 5 and for CRE with diameter of 1.5 cm it is 6. The question is which one of these three upper bound CRE configurations offers a more accurate Laplacian estimate. Panel E of Figs. 4 and 5 suggest that it is the septapolar CRE with diameter of 1.5 cm, i.e. that the number of rings as a factor has a greater effect on Relative and Maximum Errors than does the diameter of the CRE. This is confirmed by the results of the statistical analysis since for both errors factor C (number of rings) has larger F values than factor B (CRE diameter) for the same number of degrees of freedom equal to 1 (Relative Error: $F = 233.52$ and $F = 135.27$ for factors C and B respectively; Maximum Error: $F = 347.97$ and $F = 103.15$ for factors C and B respectively).

Further investigation is needed to confirm the obtained FEM modeling results. The plan for future work includes several directions and is based on limitations of the current study. First direction is to use realistic concentric sphere head models to confirm the modeling results obtained in this study. Second direction is to create first prototypes of multipolar CREs with 3 and more rings and test them on real life data, both phantom and from human subjects. Finally, all the multipolar CRE configurations assessed in this study have equal distances between the concentric rings. The potential of CREs with variable (increasing or decreasing with the increase of the distance to the central disc) distances between the consecutive rings to improve the accuracy of Laplacian estimation needs to be assessed.

5. Conclusions

With tripolar concentric ring electrodes (CREs) gaining increased recognition in a wide range of applications due to their unique capabilities this study assesses the potential of novel multipolar CREs. Results of mathematical analysis and finite element method modeling suggest that multipolar CREs with larger numbers of rings may offer more accurate Laplacian estimation than the ones with smaller numbers of rings further confirming the superiority of CREs as an alternative to conventional disc electrodes for applications not limited to electroencephalography.

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