Analysis of Variance to Assess Statistical Significance of Laplacian Estimation Accuracy Improvement due to Novel Variable Inter-Ring Distances Concentric Ring Electrodes*

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***Abstract*— Concentric ring electrodes have shown promise in non-invasive electrophysiological measurement demonstrating their superiority to conventional disc electrodes, in particular, in accuracy of Laplacian estimation. Recently, we have proposed novel variable inter-ring distances concentric ring electrodes. Analytic and finite element method modeling results for linearly increasing distances electrode configurations suggested they may decrease the truncation error resulting in more accurate Laplacian estimates compared to currently used constant inter-ring distances configurations. This study assesses statistical significance of Laplacian estimation accuracy improvement due to novel variable inter-ring distances concentric ring electrodes. Full factorial design of analysis of variance was used with one categorical and two numerical factors: the inter-ring distances, the electrode diameter, and the number of concentric rings in the electrode. The response variables were the Relative Error and the Maximum Error of Laplacian estimation computed using a finite element method model for each of the combinations of levels of three factors. Effects of the main factors and their interactions on Relative Error and Maximum Error were assessed and the obtained results suggest that all three factors have statistically significant effects in the model confirming the potential of using inter-ring distances as a means of improving accuracy of Laplacian estimation.**

I. INTRODUCTION

Electroencephalography (EEG) is an essential tool for brain and behavioral research as well as 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 that are critically limiting the research discovery and diagnosis [1]–[3]. In particular, 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 and 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 scalp surface) to EEG has been shown to alleviate the blurring effects enhancing the spatial resolution and selectivity, and reduce the reference problem [4]–[6].

Noninvasive concentric ring electrodes (CREs) can resolve the reference electrode problems since they act like closely spaced bipolar recordings [2]. Moreover, CREs are symmetrical alleviating electrode orientation problems [7]. They also act as spatial filters reducing the low spatial frequencies and increasing the spatial selectivity [7], [8]. Most importantly, tripolar CREs (TCREs; Fig. 1B) have been shown to estimate the surface Laplacian directly through the nine-point method, an extension of the five-point method used for bipolar CREs, and significantly better than other electrode systems including bipolar and quasi-bipolar CRE configurations [9], [10]. Compared to EEG with conventional disc electrodes (Fig. 1A) Laplacian EEG via TCREs (tEEG) 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) [11]. Because of such unique capabilities TCREs have found numerous applications in a wide range of areas including brain–computer interface [12], [13], seizure onset detection [14], [15], detection of high-frequency oscillations and seizure onset zones [16], etc.

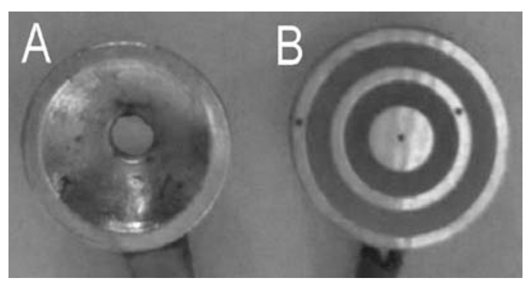

Figure 1. Conventional disc electrode (A) and tripolar concentric ring electrode (B).

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In [17] we have shown that accuracy of Laplacian estimation can be improved with multipolar CREs. General approach to estimation of the Laplacian for an $(n + 1)$-polar electrode with n rings using the $(4n + 1)$-point method for $n \geq 2$ has been proposed. This approach allows cancellation of all the Taylor series truncation terms up to the order of $2n$ which has been shown to be the highest order achievable for a CRE with n rings [17]. The multipolar approach was validated using finite element method (FEM) modeling. Multipolar CRE configurations with n ranging from 1 ring (bipolar configuration) to 6 rings (septapolar configuration) were compared and obtained results suggested statistical significance of the increase in Laplacian accuracy caused by increase in the number of rings n [17].

Most recently, in [18] the next fundamental step toward further improving the Laplacian estimation accuracy was taken by proposing novel variable inter-ring distances CREs. Laplacian estimates for linearly increasing and linearly decreasing inter-ring distances TCRE ($n = 2$) and quadripolar CRE (QCRE; $n = 3$) configurations were derived using a modified $(4n + 1)$-point method from [17] and directly compared to their constant inter-ring distances counterparts using Laplacian estimation errors obtained via FEM modeling. The obtained results suggested that increasing inter-ring distances CRE configurations may offer more accurate Laplacian estimates compared to respective constant inter-ring distances CRE configurations.

While in [17] the analysis of variance (ANOVA) has been performed for multipolar CREs to confirm the statistical significance of obtained FEM results, no such analysis has been performed in [18] for variable inter-ring distances CREs. Instead, a connection was established between the analytic truncation term coefficient ratios from the Taylor series used in $(4n + 1)$-point method and respective ratios of Laplacian estimation errors computed using the FEM model [18]. The purpose of this study is to address this limitation of [18] using full factorial ANOVA to assess statistical significance of Laplacian estimation accuracy improvement due to novel variable inter-ring distances concentric ring electrodes.

II. Methods

A. Preliminaries and Notations

In [17] general $(4n + 1)$-point method for constant inter-ring distances $(n + 1)$-polar CRE with n rings was proposed. It was derived using a regular plane square grid with all inter-point distances equal to r (Fig. 2). Based on the general method surface Laplacian estimates were derived for the constant inter-ring distances [17] as well as, after the $(4n + 1)$-point method modification, for novel variable (linearly increasing and decreasing) inter-ring distances (Fig. 2) [18].

In order to directly compare those surface Laplacian estimates for the previously proposed constant inter-ring distances TCRE and QCRE configurations to their counterparts with variable inter-ring distances a FEM model [17], [18] was used with an evenly spaced square mesh size of 600 x 600 located in the first quadrant of the X-Y plane above a unit charge dipole projected to the center of the mesh and oriented towards the positive direction of the Z axis as shown in Fig. 3. In particular, comparisons to the linearly increasing and linearly decreasing variable inter-ring distances TCRE and QCRE configurations respectively were drawn. All the FEM modeling was performed using Matlab (Mathworks, Natick, MA).

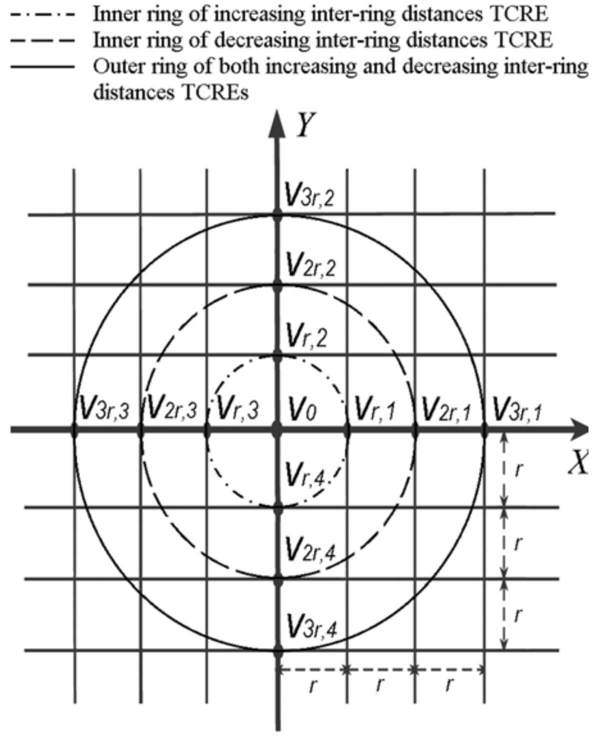

Figure 2. Linearly increasing and linearly decreasing inter-ring distances TCREs.

At each point of the mesh, the electric potential was generated by a unity dipole at depth equal to 5 cm. For this FEM model it was assumed that the medium was homogeneous and the conductivity of the medium was equal to 7.14 mS/cm to emulate biological tissue [19]. The analytical Laplacian was then calculated at each point of the mesh, by taking the second derivative of the electric potential. Laplacian estimates for six CRE configurations were computed at each point of the mesh where appropriate boundary conditions could be applied for different CRE diameters. These six Laplacian estimates including three for TCREs (decreasing, constant, and increasing inter-ring distances respectively) and three for QCREs 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 [17], [18]:

$$\text{Relative Error}^i = \sqrt{\frac{\sum(\Delta v - \Delta^i v)^2}{\sum(\Delta v)^2}} \tag{1}$$

$$\text{Maximum Error}^i = \max\left|\Delta v - \Delta^i v\right| \tag{2}$$

where i represents the six Laplacian estimation methods used to approximate the Laplacian potential $\Delta^i v$ and Δv represents the analytical Laplacian potential.

Resulting Relative and Maximum Errors computed using (1) and (2) respectively are presented on a semi-log scale in Fig. 4 for CRE diameters ranging from 0.5 cm to 5 cm.

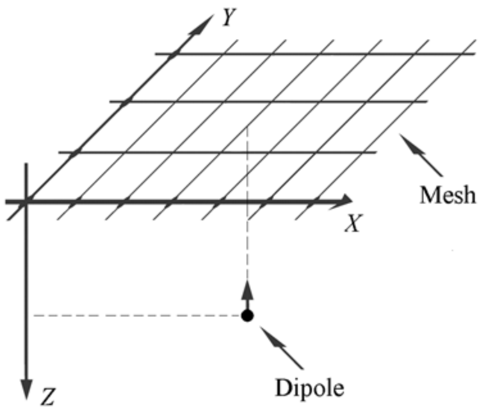

Figure 3. Schematic of the FEM model with an evenly spaced square mesh size of 600 x 600 used to assess and compare the accuracy of Laplacian estimates for constant and variable inter-ring distances CRE configurations.

B. *Statistical Analysis*

Statistical analysis of FEM modeling results from Fig. 4 was performed using Design-Expert software (Stat-Ease Inc., Minneapolis, MN, USA). Full factorial ANOVA was used with one categorical and two numerical factors (Table I) [20]. Since the data for this study was collected in [18] the Historical Data Response Surface design of ANOVA was used [20]. The categorical factor (A) was the inter-ring distances of the CRE presented at three levels corresponding to electrodes with decreasing inter-ring distances, constant inter-ring distances, and increasing inter-ring distances respectively. The first numerical factor (B) was the number of concentric rings in the CRE presented at two levels corresponding to currently used TCRE (two rings) and the next generation QCRE (three rings) configurations. The second numerical factor (C) was the CRE diameter presented at ten levels uniformly distributed in the range from 0.5 cm to 5 cm. One possible nuisance factor is the type of the FEM model used in this study which is known but uncontrollable [20]. Two response variables were the Relative Error and Maximum Error of Laplacian estimation computed using (1) and (2) respectively for each of the 3*2*10 = 60 combinations of levels for the three factors. Assumptions of ANOVA including normality, homogeneity of variance, and independence of observations were verified ensuring the validity of the analysis with no studentized residuals being outliers (falling outside of the [-3, 3] range) [20]. Due to the use of the Historical Data Response Surface ANOVA design and deterministic nature of the FEM model randomizing the order of runs and adding replications were not feasible.

TABLE I. ANOVA FACTORS

	Factors			
	Description/type (units)	***NL[a]***	***High level***	***Low level***
A	Inter-ring distances/categorical	3	Increasing	Decreasing
B	Number of rings/numerical	2	3	2
C	CRE diameter/numerical (cm)	10	5	0.5

a. Number of levels.

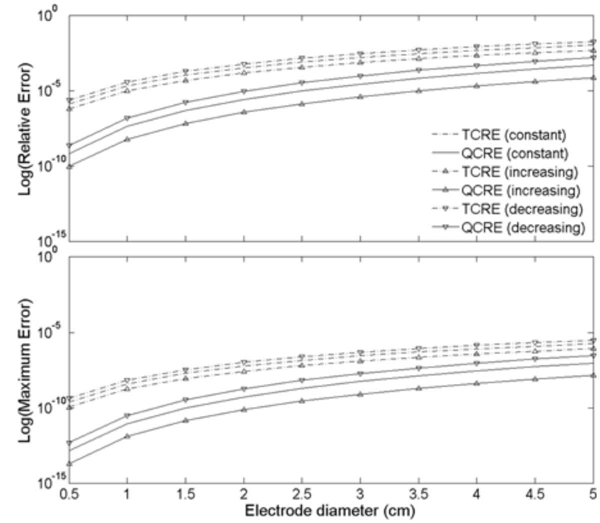

Figure 4. Relative (top panel) and Maximum (bottom panel) Errors for six Laplacian estimates corresponding to TCRE and QCRE configurations.

III. RESULTS

The effect of factors A (inter-ring distances), B (CRE diameter), and C (number of rings) along with the effect of all possible two- and three-factor interactions 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. = 11, $F = 62.31$, $p < 0.0001$; Maximum Error: d.f. = 11, $F = 212.71$, $p < 0.0001$) for the optimal transform being logarithmic function (lambda = 0 for both the Relative Error and the Maximum Error) as determined using the Box-Cox procedure [20]. The effects of the main factors were: A (Relative Error: d.f. = 2, $F = 16.94$, $p < 0.0001$; Maximum Error: d.f. = 2, $F = 63.09$, $p < 0.0001$), B (Relative Error: d.f. = 1, $F = 224.41$, $p < 0.0001$; Maximum Error: d.f. = 1, $F = 767.61$, $p < 0.0001$), and C (Relative Error: d.f. = 1, $F = 405.11$, $p < 0.0001$; Maximum Error: d.f. = 1, $F = 1074.25$, $p < 0.0001$). Out of the four two- and three-factor interactions assessed the only one with statistically significant effect for both response variables was the interaction between factors B and C (Relative Error: d.f. = 1, $F = 16.51$, $p = 0.0002$; Maximum Error: d.f. = 1, $F = 300.41$, $p < 0.0001$).

IV. DISCUSSION

The contribution of this paper is two-fold. First, full factorial ANOVA was used to confirm the statistical significance of FEM results obtained in [18]. Second, additional insight into minimization of Laplacian estimation error via CREs has been obtained and is discussed below.

The ANOVA results for comparison of surface Laplacian estimates corresponding to different CRE configurations showed the significance of all three factors included in this study. While it was important to confirm that the accuracy of Laplacian estimation increases (Relative and Maximum Errors decrease) with an increase in the number of rings (factor B) and decreases (Relative and Maximum Errors increase) with an increase of the CRE diameter (factor C), which is consistent with results obtained in [17], the most important result is that, for the case of factor A (inter-ring distances), the Laplacian estimates for increasing inter-ring distances CREs are significantly more accurate than the ones for their constant and decreasing inter-ring distances counterparts. This result confirms the potential of using the distances between the rings as a means of improving the accuracy of Laplacian estimation via CREs.

The relative significance of the effect of factor A compared to the effects of factors B and C remains an open question since all three main factors yielded the same range of p-values ($p < 0.0001$). Comparison of F values suggests that the order of factors in terms of the significance of their effect (highest to lowest) may be: C, B, and A, but it has to be taken into account that, unlike factors B and C, A is a categorical factor that affects its number of degrees of freedom.

Of all the two- and three-factor interactions, the interaction between factors B and C was the only statistically significant one for both response variables. This is an intuitive result and stems from the physical implementation of CREs. While increasing the number of rings and decreasing the CRE diameter both decrease the Laplacian estimation errors, there is a practical upper bound on how many rings can be added to a CRE of a certain diameter. Beyond this bound the distances between the concentric rings become small enough for the partial shorting due to salt bridges to affect the Laplacian estimation. This practical upper bound is discussed in more detail in [17].

Further investigation is needed to confirm the obtained results. The main direction of future work is to build prototypes of increasing inter-ring distances CREs with two and more rings and test them on real life data, both phantom and from human subjects. These prototypes would allow quantifying the translation of Relative and Maximum Errors of Laplacian estimation assessed in this study into improvement of spatial selectivity, signal-to-noise ratio, source mutual information, etc. the same way it has been quantified for tEEG via TCREs compared to EEG via conventional disc electrodes in [11].

V. Conclusion

Full factorial analysis of variance has been performed to assess finite element method results obtained for novel variable inter-ring distances concentric ring electrodes. It showed statistical significance of the effect of all three factors included in the study on the estimation accuracy of surface Laplacian: the number of concentric rings, the diameter of the electrode, and the inter-ring distances, further confirming the potential of using variable inter-ring distances to optimize the concentric ring electrode design.

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References

[1] J. E. Desmedt, V. Chalklin, and C. Tomberg, “Emulation of somatosensory evoked potential (SEP) components with the 3-shell head model and the problem of ‘ghost potential fields’ when using an average reference in brain mapping,” *Electroencephalogr. Clin. Neurophysiol. Potentials Sect.*, vol. 77, no. 4, pp. 243–258, Jul. 1990.

[2] P. L. Nunez, R. B. Silberstein, P. J. Cadusch, R. S. Wijesinghe, A. F. Westdorp, and R. Srinivasan, “A theoretical and experimental study of high resolution EEG based on surface Laplacians and cortical imaging,” *Electroencephalogr. Clin. Neurophysiol.*, vol. 90, no. 1, pp. 40–57, Jan. 1994.

[3] G. Lantz, R. Grave de Peralta, L. Spinelli, M. Seeck, and C. M. Michel, “Epileptic source localization with high density EEG: how many electrodes are needed?,” *Clin. Neurophysiol.*, vol. 114, no. 1, pp. 63–69, Jan. 2003.

[4] R. Srinivasan, “Methods to Improve the Spatial Resolution of EEG,” *Int. J. Bioelectromagn.*, vol. 1, no. 1, pp. 102–111, 1999.

[5] B. He, “High-resolution source imaging of brain electrical activity,” *IEEE Eng. Med. Biol. Mag.*, vol. 17, no. 5, pp. 123–129, Sep. 1998.

[6] B. He, J. Lian, and G. Li, “High-resolution EEG: a new realistic geometry spline Laplacian estimation technique,” *Clin. Neurophysiol.*, vol. 112, no. 5, pp. 845–852, May 2001.

[7] D. Farina and C. Cescon, “Concentric-ring electrode systems for noninvasive detection of single motor unit activity,” *IEEE Trans. Biomed. Eng.*, vol. 48, no. 11, pp. 1326–1334, Nov. 2001.

[8] C. Disselhorst-Klug, J. Silny, and G. Rau, “Improvement of spatial resolution in surface-EMG: a theoretical and experimental comparison of different spatial filters,” *IEEE Trans. Biomed. Eng.*, vol. 44, no. 7, pp. 567–574, Jul. 1997.

[9] W. G. Besio, K. Koka, R. Aakula, and W. Dai, “Tri-polar concentric ring electrode development for Laplacian electroencephalography,” *IEEE Trans. Biomed. Eng.*, vol. 53, no. 5, pp. 926–933, May 2006.

[10] W. G. Besio, R. Aakula, K. Koka, and W. Dai, “Development of a Tri-polar Concentric Ring Electrode for Acquiring Accurate Laplacian Body Surface Potentials,” *Ann. Biomed. Eng.*, vol. 34, no. 3, pp. 426–435, Feb. 2006.

[11] K. Koka and W. G. Besio, “Improvement of spatial selectivity and decrease of mutual information of tri-polar concentric ring electrodes,” *J. Neurosci. Methods*, vol. 165, no. 2, pp. 216–222, Sep. 2007.

[12] W. G. Besio, H. Cao, and P. Zhou, “Application of Tripolar Concentric Electrodes and Prefeature Selection Algorithm for Brain-Computer Interface,” *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 16, no. 2, pp. 191–194, Apr. 2008.

[13] Y. Boudria, A. Feltane, and W. Besio, “Significant improvement in one-dimensional cursor control using Laplacian electroencephalography over electroencephalography,” *J. Neural Eng.*, vol. 11, no. 3, p. 35014, 2014.

[14] O. Makeyev *et al.*, “Toward a Noninvasive Automatic Seizure Control System in Rats With Transcranial Focal Stimulations via Tripolar Concentric Ring Electrodes,” *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 20, no. 4, pp. 422–431, Jul. 2012.

[15] A. Feltane, G. F. Boudreaux-Bartels, and W. G. Besio, “Automatic Seizure Detection in Rats Using Laplacian EEG and Verification with Human Seizure Signals,” *Ann. Biomed. Eng.*, vol. 41, no. 3, pp. 645–654, Oct. 2012.

[16] W. G. Besio *et al.*, “High-Frequency Oscillations Recorded on the Scalp of Patients With Epilepsy Using Tripolar Concentric Ring Electrodes,” *IEEE J. Transl. Eng. Health Med.*, vol. 2, pp. 1–11, 2014.

[17] O. Makeyev, Q. Ding, and W. G. Besio, “Improving the accuracy of Laplacian estimation with novel multipolar concentric ring electrodes,” *Measurement*, vol. 80, pp. 44–52, Feb. 2016.

[18] O. Makeyev and W. G. Besio, “Improving the Accuracy of Laplacian Estimation with Novel Variable Inter-Ring Distances Concentric Ring Electrodes,” *Sensors*, vol. 16, no. 6, p. 858, Jun. 2016.

[19] W. G. Besio and M. Fasiuddin, “Quantizing the depth of bioelectrical sources for non-invasive 3D imaging,” *J Bioelectromagn*, vol. 7, pp. 90–3, 2005.

[20] D. C. Montgomery, *Design and analysis of experiments*. John Wiley & Sons, 2008.