Estimation of the Focality of Coils and Quality of Stimulation of Biological Tissues During Transcranial Magnetic Stimulation

Ivan C. Carmona1, Oluwaponmile F. Afuwape2, David C. Jiles2,3, Ravi L. Hadimani1,4

1Dept. of Mechanical and Nuclear Engineering, Virginia Commonwealth University, Richmond, VA, USA, 23284.
2Dept. of Electrical & Computer Engineering, Iowa State University, Ames, IA, USA, 50011.
3Dept. of Materials Science & Engineering, Iowa State University, Ames, IA, U USA, 50011.
4Dept. of Biomedical Engineering, Virginia Commonwealth University, Richmond, VA, USA, 23284.

Transcranial Magnetic Stimulation (TMS) is a well-established neurostimulation technique that regulates the synaptic activity of neurons to treat several neurological conditions and psychiatric disorders. During TMS, electric fields (E-fields) are induced within the brain through the application of time-varying magnetic fields, using coils located outside the head. Different definitions in the literature calculate the focality of the E-field estimating the stimulated area during TMS. Most of them differ in measurement methodologies, showing lack of homogeneity and diverse criteria toward a unique conception, without evaluating possible scenarios of under-stimulation of the target and over-stimulation of adjacent biological tissues. Another common fact in the field is the use of “focality” definitions without reference to a target area or focal distance, parameters intrinsically related and required for comparison between coils. Furthermore, to evaluate the degree and quality of stimulation, a criterion indicating how well the stimulated area covers the target area is required. This work proposes a generalized function and methodology for the focality quantification in TMS coils, considering target area, focal distance, maximum magnitude of the E-field and stimulation threshold. New definitions such as “specific focality (sf)” and “focality form factor (df)” are introduced to describe the suitability of coils for specific stimulation applications. The proposed definitions also offer a general framework to compare coils using homogeneous methodology, parameters and nomenclature, with potential impact on the standardization of measurement methods in the industry of TMS devices. Using finite element simulation tool, ANSYS Maxwell 3D, we calculated the specific focality over an MRI-based realistic head model of an adult healthy human subject. The proposed definition assigned dimensionless values to three coils under study, compared to results in surface units of pre-existing definitions. The coils studied are: a figure-of-eight (F8) coil, a quadruple butterfly coil (QBC) and a quintuple AISI 1010 carbon steel core coil (QCC). The results confirm the suitability of the method to evaluate contexts of specific target area and focal distance, and identify scenarios of focal stimulation, under-stimulation or over-stimulation with respect to the target size.

Index Terms— TMS coil focality, focality measurement, TMS coils, magnetic stimulation, neuromodulation.

I. INTRODUCTION

Transcranial Magnetic Stimulation (TMS) is a non-invasive neurostimulation technique based on the application of time-varying magnetic fields from outside the cranial cavity. TMS coils induce eddy current and an associated electric field (E-field) in different partially conductive layers of biological tissue, including the skull, scalp and cerebrospinal fluid (CSF), until reaching the target area in the brain cortex.

One of the main concerns about the cortical stimulation during TMS sessions is the capability of the coil to be focal. This depends on several parameters, but mainly on its physical characteristics as an electromagnetic transducer. This paper proposes a methodology for the focality assessment, considering specific coil parameters, as well as a detailed framework for comparison between different TMS coils.

II. EXISTING FOCALITY DEFINITIONS IN THE LITERATURE

The scientific literature contains diverse definitions of what focality in a TMS context is [1]–[10]. Although significantly different from each other, such definitions are often used in the design of coils intended to be focal for the E-field [5], [7], [10], [11]. Thielencers & Kammer at [1], citing Roth et al [2], claim: “The focality is normally defined as the cortical area in which the electric field strength exceeds a certain value relative to the maximum”. Other authors such as Deng [4] have provided the alternative definitions of “half-value area”, “A½” (average area of the cortex where the electric field exceeds half of its maximum strength), and “electric field tangential spread”, “S₀” –or “half-value spread” – renamed by Koponen as effective surface area [6], and defined as follows.

$$S_{\frac{1}{2}} = \frac{V_{N}}{d_{N}} \tag{1}$$

In (1), the numerator is the half-value volume, “V_N” (volume of a brain region with an E-field “as strong as or stronger than half of the maximum electric field” [4]). In the denominator, “d_N” represents the “half-value depth”, radial distance from the cortical surface to the farthest point within V_N.

March et al. state in [8] that the tangential spread calculation (1), being a mere geometric ratio between volume and depth, cannot be the only indicator for a good electric field profile, but it also must consider the maximum E-field produced by the coil, especially for proper coil design, analysis and comparison.

Koponen et al. [6] introduced a new definition in the TMS context using a different threshold for the E-field (E), indicated as “the area where the energy density of the stimulation exceeds 50 % of the maximum” (E/Emax ≥ 1/2 ≈ 70 %, using the maximum value of the E-field, “Emax”, as the reference).

Despite being very useful, the above definitions show a lack of homogeneity in the area regarding the concept of focality, and a variety of parameters involved. Yet, they all present ideas for the calculation of the focality around the magnitude of the E-field in one specific area or volume. Nonetheless, the biomedical field still requires a figure of merit that considers
the influence of the focal distance and the specific shape of the target region in the focality calculation, in order to quantify how well the stimulation energy fits the intended geometry. This figure of merit should be descriptive by itself of the suitability of a coil to perform focal stimulation of biological tissues, under well-defined criteria.

Different clinical settings have their own values for the stimulating current flowing through the TMS coils, usually referred to as TMS intensity. This produces diverse magnetic flux densities and, therefore, E-field magnitudes and distributions over the brain surface used for each treatment. In very superficial targets over the cortex – as in most of the existing TMS applications – the induced E-field is a direct consequence of the magnetic flux lines that effectively can reach that specific area. In that particular case, the assessment of the focality is still a relatively easy task.

On the other hand, in deep TMS applications – due to the field spreading – the magnetic flux density will be too weak to induce an E-field of the required magnitude in deeper target regions by itself. It is because of the propagation of the induced charges, from the nucleation points over the surface, deep into the conductive cortical tissue, that the resulting path of highest current density reaches a deep target to produce a localized E-field [12]. In this scenario, the spreading of the induced charges determines the spreading of the E-field through the conductive tissue, which many times also permeate non-targeted areas. The propagation and E-field values at deeper regions are also influenced by the inhomogeneity and complex geometry of the brain. All these factors make it significantly difficult to evaluate the focality and quality of stimulation inside and over the cortex. In consequence, the focality definition for coils used in the stimulation of biological tissues should consider the heterogeneous character of the conducting volume, and how well the E-field covers both the target and non-target regions.

Other findings in the literature include works reporting “focality” without describing a “focal point”, a “focal distance” or a “target”. Instead, these works use definitions that represent the coverage of the E-field above a defined threshold, expressed in surface units over a region. This certainly reflects the size of the stimulated area, but not how well it overlaps the target area.

Fig. 1 – Scenarios of a) under-stimulation; b) focal stimulation and c) overstimulation. Target areas in blue, stimulated areas in red and focally stimulated areas (intersection) in purple.

As a result, we have identified a need in the biomedical and neurostimulation fields for a criterion for the focality that indicates the relation between the stimulated and the targeted regions, in order to determine scenarios of focal stimulation, under-stimulation and overstimulation (see Fig. 1).

Finally, a lack of common reference for measurement and comparison between TMS coils makes it difficult to assess – both in research and clinical settings – their suitability for one particular stimulation environment or set of parameters, using a unique framework.

III. METHODOLOGY

A. Definitions

In order to quantify the suitability of a coil to stimulate a target region focally, we have defined a weight function that satisfies the following requirements: a) Need to quantify the focality in a continuous normalized scale from zero (0 = non-focal) to one (1 = fully focal), alternatively representable in percentage terms. b) Need to grow towards unity (y = 1) from each side of the curve, with a soft peak, being continuous and fully differentiable in its entire domain. c) The rolloff factor from the peak to each of the sides should be high enough to benefit only scenarios of high overlap between the stimulated area (A_s) and the target area (A_t), and rapidly decrease in cases of low overlap or overstimulation of non-targeted areas.

\[
AES\text{-}erfc_{d_n} = \text{erfc}(2.5 \cdot d_n) \times \text{erfc}(-2.5 \cdot d_n) \quad (2)
\]

Equation (2) shows the proposed function with the previously described characteristics, which we have named “Adjusted Even Symmetry Error Function Complement” or AES-erfc (Fig. 2a). Notice that the x-axis in Fig. 2a contains the values of a normalized dimension (d_n) related to the level of overlap between the targeted area (A_s) and stimulated area (A_t), defined as “focality form factor” (Eq. 3).

\[
d_n = \frac{A_s - A_t}{A_t} \Leftarrow (A_s > 0) \& (A_t \geq 0) \& (\{A_s \cap A_t\} = \{A_t \cap A_s\}) \quad (3)
\]

The y-axis in Fig. 2a shows the normalized weight assigned to such levels of overlap, termed “specific focality” (sf).

Since the AES-erfc is a symmetric function, it becomes zero by the right side at infinity. However, by the left side it is restricted to a minimum value of 8.1374x10^{-4}, where it should be zero when d_n = -1 (no area stimulated). This means an error of 0.0814 % in the AES-erfc at this point (Fig. 2b).

Though the error is minimal, in order to keep the accuracy we have calculated a correction term that makes the specific focality – and its error – to be zero at d_n = -1 (Fig. 2b).

The correction term is given by Eq. 4 (see Fig. 2c), where “U” is the Heaviside function introduced to make the expression valid only up to d_n = 0.

\[
ct(d_n) = [\text{erfc}(-2.5) \times \text{erfc}(2.5)] \cdot d_n \cdot U(-d_n) \quad (4)
\]

Now, the specific focality is given by the new “Corrected-Adjusted Even Symmetry Error Function Complement” or CAES-erfc, defined as:

\[
sf = \text{erfc}(2.5 \cdot d_n) \times \text{erfc}(-2.5 \cdot d_n) + ct(d_n) \quad (5)
\]

AES-erfc and CAES-erfc can be used discretionally. CAES-erfc allows accurate results in focality quantification for...
comparisons of coils, whereas AES-erfc is better for rapid estimations where a minor error is acceptable.

Based on the range of \( d_s \) using CAES-erfc, Fig. 2a makes it possible to identify scenarios of overstimulation (\( d_s > 0 \)), focal stimulation (\( d_s = 0 \)), under-stimulation (\(-1 < d_s < 0 \)) or no stimulation (\( d_s = \pm 1 \)). Moreover, the user may define a flexible criterion for what “full” or “high” focality would be for a particular application. This criterion may be based on either a specific focality threshold (\( f_{ts} \)) or a focality form factor threshold (\( d_{ts} \)).

Eq. (2) to (5) should be used only when one single area segment exists both in the stimulated area and in the target area, and one of them perfectly overlaps or contains the other one inside, for a non-null target (Fig.1). However, the lack of homogeneity in the brain volume often results in multiple segments of stimulated area covering target and non-targeted area segments. This leads to more complex scenarios of partially focal stimulation of target segments, with potential overstimulation of non-target segments, explained next (Fig. 3).

Since combined scenarios of partial focality in target segments with overstimulation of adjacent areas are common, the focality form factor needs to be redefined in two parts.

a) The first part (6) calculates a defined focal stimulation factor (\( \psi \)) as one minus the ratio between the total area of \( N \) focially stimulated segments (\( \Sigma A_{ft(n)} \)) and the total target area (\( \Sigma A_{t(n)} \)).

\[
\psi = 1 - \frac{\sum_{n=1}^{N} A_{ft(n)}}{\sum_{n=1}^{N} A_{t(n)}}, \quad \text{with} \quad \{ A_{ft(1,2,..N)} \} = \{ A_{(1,2,..,t)} \} \cap \{ A_{(1,2,..,m)} \} \tag{6}
\]

b) The second part, called overstimulation factor of the adjacent areas (\( \chi \)), is calculated as the ratio of the sum of all the existing overstimulated area segments outside the target (\( A_{oa} \)) to the total area of the target segments (\( \Sigma A_{t(n)} \)) in (7).

\[
\chi = \frac{\sum_{n=1}^{N} A_{oa(n)}}{\sum_{n=1}^{N} A_{t(n)}} \tag{7}
\]

Now, the focality form factor can be redefined as a complex value (\( d_{nc} \)) that considers both the focal behavior in the target and the overstimulation in the surroundings. These behaviors are simultaneously expressed in the orthogonal real and imaginary axes of the complex plane, to create a complex focality diagram (Fig. 4), according to Eq. (8).

\[
d_{nc} = \psi + i\chi \tag{8}
\]

Notice from Eq. (6) to (8) that, when the overstimulated areas are null and there is only one segment both stimulated and target area, Eq. (3) and (8) are of identical modulus and opposite signs. This sign change was intentionally inserted in (6) to restrict the complex focality diagrams to the first quadrant of the complex plane. The complex focality form factor (\( d_{nc} \)) indicates at all time the specific scenario of focal stimulation of the target, and adjacent overstimulation for each coil configuration (Fig. 4).

In the particular case in which the stimulated area is of smaller or equal size, and completely inside the target (Fig. 1a and 1b), the focality form factor (\( d_{nc} \)) is negative. Then, its equivalent complex focality form factor (\( d_{nc} \)) will be positive, purely real and of the same modulus as \( d_{nc} \). Contrarily, when the stimulated area is bigger than the target (Fig. 1c), and this last one is completely inside, the focality form factor (\( d_{nc} \)) is positive (including the zero). In that case, its equivalent complex focality form factor (\( d_{nc} \)) will be a positive purely imaginary quantity of the same modulus. These conversions are shown in (9) and (10).

\[
\begin{align*}
d_{nc} &= -d_{ns} & (9) \\
d_{nc} &= jd_{ns} & (10)
\end{align*}
\]

Eq. (9) and (10) are used to obtain the complex focality form factor and the complex focality diagram (Fig. 4) only for cases in Fig. 1. However, for all other cases (e.g. those in Fig. 3), the complex focality form factor will result in non-null real and imaginary parts. Therefore, Eq. (6) to (8) represent the general equations to be used in any case to obtain the complex focality form factor and diagram.

Now, we redefine the calculation of the specific focality as a function of the modulus of the complex focality form factor (\( d_{nc} \)). Then, for all cases, the focality of the coil can be assessed using Eq. (11), obtained replacing \( d_{nc} \) by \( |d_{nc}| \) in (2). The domain of (11) (possible values for |\( d_{nc} \)|) will be from zero to infinity, while its range will be all possible values of AES-erfc to the right side of the peak of full focality. Left side of AES-erfc is not part of the domain when \( |d_{nc}| \) is used as an argument in (2).

\[
s_f = \text{erfc}(2.5 \cdot |d_{nc}|) \times \text{erfc}(−2.5 \cdot |d_{nc}|) \tag{11}
\]

IV. RESULTS

A. Surface Specific Focality (\( s_f \)) in Thin Targets

Intended for very thin targets of thicknesses that cannot be measured, computed or estimated, \( s_f \) was calculated as follows.

a) Define the planes with the target areas to be stimulated.

b) Plot the modulus of E-field (|E|) for each plane of interest.

c) Define an E-field stimulation threshold.

d) Using a color map, identify the edges of the segments of the stimulated area with E-field above the threshold.
e) For stimulated segments of regular geometries (e.g., circle, square, etc.), calculate the surface area ($A_s$) directly. If irregular, simplify it to the closest regular shape(s) possible.

f) Find the complex focality form factor with Eq. (6) to (8), the specific focality (11), and the complex focality diagram.

### B. Specific Focality in a Target Volume ($sf_v$)

The volumetric specific focality ($sf_v$) of the E-field was obtained from recurrent calculation of the surface specific focality ($sf_s$) over consecutive secant planes. The target was divided into multiple trapezoidal sections of different cross-sectional areas and variable heights to cover the entire volume.

\[
sf_{vF} = \frac{1}{V} \sum_{n=1}^{N} \left[ \frac{A_{sn} + A_{sn+1}}{2} \cdot |z_{n+1} - z_n| \right] \quad (12)
\]

Eq. (12) calculates the volumetric $sf$ as the summation of the products between: a) the average surface specific focality of the two planes that define a trapezoidal section; b) the average volume of the section, normalized with respect to the total volume of the target. Similar to the surface specific focality, the volumetric specific focality provides dimensionless values.

### C. Nomenclature

Equation (13) shows the proposed nomenclature for its general use in results of the specific focality of the E-field for TMS coils.

\[
z \Psi \frac{A_t}{th \cdot X_E \cdot A_s} \quad (13)
\]

The nomenclature in (13) allows to express the specific focality in a unique symbol with four parameters. a) The focal distance ($z$) represents the separation between the lower point of the coil and the target plane. In volumes, this distance is considered up to the mid-depth of the target volume. b) The stimulation threshold ($th$) is the minimum required E-field in points considered as “stimulated”, shown in terms of $E_{max}$ to allow comparison against safety criteria. c) The target area ($A_t$) is the area intended to be stimulated. d) The stimulated area ($A_s$) is the resulting area of the stimulated surface. When reporting volumetric specific focality, $A_t$ and $A_s$ should be replaced by their volumetric equivalents $V_t$ and $V_s$. Sub-index X should be replaced for “$V$” for volumetric and “S” for surface $sf$.

### D. Simulation Results

For validation of the methodology, we performed finite element simulations on ANSYS Maxwell 3D Software with three focal TMS-coils over a realistic head model. Our model, obtained from magnetic resonance imaging (MRI) of a healthy adult subject, includes: scalp, skull, cerebrospinal fluid (CSF), gray matter and white matter. Though the electromagnetic properties of these layers vary in the literature due to uncertainties and physiological reasons between subjects [13]–[15], we have used the values found in Table I [13]. As the induced E-fields do not depend on permittivity values in tissues at TMS frequencies [16], $\varepsilon_r$ in Table I are merely informative.

The stimulation target is a volume in the First Dorsal Interosseous (FDI) region of the primary motor cortex (M1), in the left lobe of the brain. When stimulated, this region produces an involuntary thumb twitch in the subject. To define the exact volume of stimulation we obtained the intersection between the mentioned region and a cylinder of outer diameter (OD) of 13 mm and 5 mm of depth, shown in purple in Fig. 5a.

Fig. 5 - Simulation setup. a) Target in the FDI region defined by the purple cylinder b) Figure-of-eight (Fo8) coil; c) Quadruple butterfly coil (QBC); d) Quintuple AISI 1010 Carbon Steel Core Coil (QCC).

As shown in Fig. 5 b to d and Table II, the coils simulated were: 5b) Figure-of-eight (Fo8) coil; 5c) Quadruple Butterfly Coil (QBC) [5], [17], [18]; 5d) Quintuple AISI 1010 Carbon Steel Core Coil (QCC) [12]. In Table II: OD = outer diameter, ID = inner diameter, $\Phi_{1/2}$ = opening angle between coils, NT = number of turns (# of layers x turns), Xsect = dimensions of the cross-sectional area (width x height), $H$ = height of the coil.

<table>
<thead>
<tr>
<th>Coil</th>
<th>Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>QBC</td>
<td>OD = 70 mm, ID = 28 mm, $\Phi_{1/2}$ = 45°, NT = 1x9, Xsect = 5x1 mm</td>
</tr>
<tr>
<td>Fo8</td>
<td>ID = 52 mm, OD = 88 mm, H = 7 mm, NT = 2x9, Xsect = 7x1 mm</td>
</tr>
<tr>
<td>QCC</td>
<td>NT = 2x25, Xsect = elliptic: semi-major axis = 10.6 mm, semi-minor axis = 2.8 mm, H = 25.4 mm</td>
</tr>
</tbody>
</table>

The stimulation current was a single bipolar pulse of 5 kA (peak), with sine waveform at 2.5 kHz. The coils were placed over the stimulation point, tangentially to the scalp surface, at 45° from the horizontal plane in a front-view of the head.

Using a transient solver, we defined 20 time-steps for a period and used adaptive meshing of variable size tetrahedra. Restricting the elements to sizes $\leq 3$ mm in the gray matter and $\leq 7$ mm in the surroundings, we refined the target to ensure sizes $\leq 0.3$ mm and 15 tetrahedra/mm² for proper gradient resolution. We have post-processed the resulting E-field with smoothing algorithms based on spatial average. This allowed us to obtain more continuous transitions based on the gradients of the original field. Along with the refined mesh in the target, this minimizes the appearance of outliers that result from the integration of the vector field.

<table>
<thead>
<tr>
<th>Coil</th>
<th>$\frac{th = E_{max}2/A}$ ($\sigma$ mm²)</th>
<th>$\frac{Conclusion from sf_v using th = E_{max2}/A}$ ($\sigma$ mm²)</th>
</tr>
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<td>Fo8</td>
<td>0.9556 (4.437 %)</td>
<td>165 $\times 10^{-2}$ (82.5 %)</td>
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<tr>
<td>QBC</td>
<td>0.9173 (97.36 %)</td>
<td>132 $\times 10^{-2}$ (95.5 %)</td>
</tr>
<tr>
<td>QCC</td>
<td>0.000096 (0.096 %)</td>
<td>3 $\times 10^{-2}$ (0.16 %)</td>
</tr>
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TABLE III

RESULTS OF THE SURFACE $sf_v$ VS. EXISTING DEFINITIONS ($Z = 5$ mm)

<table>
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<tr>
<th>Coil</th>
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</table>
For the quantification of both the surface and volumetric specific focalities, we defined eleven secant planes and obtained ten trapezoidal segments of the target volume. Then, the surface specific focality was calculated by plane defining a stimulation threshold as a fraction of $E_{max}$. Ultimately, the volumetric specific focality was computed over the target volume for each coil, with a discretized calculation based on (12).

Table III compares the existing definitions of half-value area ($A_{HVA}$) and half-energy density area ($A_{EVA}$) against the surface specific focality $(sf_s)$ at $z = -5$ mm. We have used the same thresholds $(th)$ of such definitions as criteria to find the edges of the stimulated areas in $sf_s$. Table IV does the same comparing the existing half-value area ($A_{HVA}$) and tangential fields spread ($S_{thr}$) with the results of volumetric specific focality ($sf_v$).

In addition, the proposed nomenclature makes it possible to report focality values along with their parameters of focal distance, stimulation threshold, target area and stimulated area (or their volumetric equivalents), for both evaluation and design purposes. In design tasks, the manufacturer or designer should particularly report unitary—or almost unitary—specific focalities, with a list of all the possible/tested conditions or applications for which the coils have been designed.

Ultimately, the proposed nomenclature has the potential to be used in research, industrial and clinical settings. This provides researchers and manufacturers with the possibility to create standards around the specific focality, fixing parameters for testing and measurement in different TMS applications.

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### REFERENCES


