Design of a Multi-Locus Transcranial Magnetic Stimulation Coil With a Single Driver

Shuang Liu, Akihiro Kuwahata, and Masaki Sekino

Abstract – Transcranial magnetic stimulation (TMS) is used extensively in research and clinical applications pertaining to psychiatric and neurological disorders. To satisfy the requirements of clinical treatment and improve understanding of the synergies among different brain regions, researchers are investigating multi-locus TMS. However, multi-locus TMS based on multiple drive circuits is unable to stimulate separate brain areas simultaneously when magnetic fields interfere with each other or size conflicts occur. In this study, we propose a design for a multi-locus TMS coil with a single-current driving device. The key concept underlying this method involves solving the stream function directly from the target electric field using Tikhonov regularization and obtaining the corresponding coil shape represented by the contour line drawing of the stream function. Our design results in novel multi-locus stimulation coils using a single driver that can realize multi-locus–induced electric fields inside a brain model.

1. Introduction

Transcranial magnetic stimulation (TMS) is a noninvasive biological stimulation technology that is used extensively in research and clinical applications involving psychiatric and neurological disorder [1]. The principle of TMS is based on Faraday's law; specifically, a strong pulse magnetic field (1 T in 300 μs) generates an electric field strong enough to depolarize nerve cells. Conventional TMS coils were designed mainly to investigate the function of a certain brain region without affecting other areas of the brain; in other words, the focality of the electric field is the most important parameter in such coils.

Recently, based on the cognition of connectivity between brain regions, TMS has evolved from a single-locus stimulation application to the use of multiple TMS coils for investigating multiple brain regions. For instance, in studies of the action preparation potential of the dominant hand and the nondominant hand, to eliminate the data bias caused by separate unilateral experiments, double-coil stimulation of the primary motor cortex (M1) on both sides (1 ms separation) in one experimental trial can be performed under the same stimulation conditions [2, 3]. The 1 ms interval between two stimulations is essential because simultaneous stimulation will cause a reduction of the motor-evoked potential (MEP) signal due to the magnetic field interference between the coils or cortical interactions through the corpus callosum. However, because no coil can stimulate two M1 regions under exactly the same conditions, the influence of magnetic field interference on MEP reduction cannot be ruled out. In addition, when multiple separate coils are utilized to change the direction of the induced electric field or the stimulation site, the size and position of the coils may cause conflicts between different coils.

At the same time, research on transcranial direct current stimulation has shown that multiple stimulation positions can improve the inhibitory effect of chronic pain [4, 5]. Like direct current stimulation, TMS also generates an electric current in the brain; thus, these results reveal the possibility of multi-locus TMS improving the therapeutic effect in the future.

Because of these research needs and clinical therapeutic requirements, numerical studies have verified the feasibility of multi-focus TMS coils with multi-drivers [6, 7]. Consequently, in 2018, the first multi-locus TMS coils with multi-drivers were implemented by combining multiple known basic coils (as in a figure eight) and circle coils [8]. However, because different large-current (3 kA) TMS drivers need to be controlled separately, the currently implemented multi-focus coil with multi-driver can move the focus position through the current changes of only two drivers. The multi-locus stimulation coil constructed in this way can change its focus only within a limited focus range of 30 mm. Hence, it cannot achieve simultaneous stimulation of the left and right M1. There is no coil that can stimulate multiple brain regions simultaneously.

To overcome these drawbacks, we propose a new design for a multi-locus TMS coil using a single driver. Stimulation by a single coil and a single drive circuit can avoid the interference of magnetic field and size. Furthermore, by designing the coil inversely from the target-induced electric field, multi-point stimulation of the brain area can be ensured. Our design involves solving the stream function directly from the target-induced electrical field.

2. Methods

The proposed method for designing a multi-locus TMS coil can be divided into three steps. First, the distribution of the desired induced electric fields ($\vec{E}$) in the region of interest is determined. Next, the current density vector ($\vec{J}$) on the coil is expressed using the scalar potential stream function Ψ, and the ill-posed linear equation $E = A\ \Psi$ is solved by Tikhonov

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regularization. Finally, the contour line of the stream function, namely, the coil winding path that corresponds to the target electric field distribution, is represented.

The vector potential of the magnetic field in the induced region can be represented as

$$\vec{A}(x,y,z,t)=\frac{\mu_0}{4\pi}\iint\frac{\vec{J}(x',y',t)}{|\vec{r}'-\vec{r}|}dx'dy' \tag{1}$$

where $\vec{A}(x,y,z,t)$ is the vector potential in the target space (x, y, z) and $\vec{J}(x',y')$ is the current density with unit A/m^2 on the TMS coil plane coordinates (x', y'). Position vector $\vec{r}$ is defined in the target space, and $\vec{r}'$ is defined on the coil plane with a constant z value. The electrical field $\vec{E}$ with unit V/m induced by the TMS coil inside the brain can be represented by

$$\vec{E}=-\nabla\varphi-\frac{\partial\vec{A}}{\partial t} \tag{2}$$

In actual TMS, the first electrostatic potential cannot be ignored because of the varied conductivities of different brain tissues. However, to investigate the properties of the coil itself, we assume that the coil is discharged into the air. Therefore, the first term in (2) can be regarded as zero ($\varphi=0$). After producing the coil geometries, we consider this electrostatic term to evaluate the resulting stimulation in the brain models. The current density $\vec{J}(x',y',t)$ can be represented as $\vec{J}(x',y')*sin(\omega_0 t)$, then the induced electrical field is expressed as shown in (3), as the distribution of the induced eddy current is determined by the coil winding pattern only:

$$\vec{E}(x,y,z)=-\frac{\mu_0}{4\pi}\omega_0\cos(\omega_0 t)\iint\frac{\vec{J}(x',y')}{|\vec{r}'-\vec{r}|}dx'dy' \tag{3}$$

Under this quasi-static condition, $\frac{\mu_0}{4\pi}\omega_0\cos(\omega_0 t)$ can be expressed as a constant C. We set the frequency ω_0 to 3.3 kHz, which matches the pulse length of about 300 µs used for the general case. The current density vector $\vec{J}$ on the coil plane is expressed by a scalar stream function [9] as follows:

$$\vec{J}(x',y')=\left(\frac{\partial\Psi}{\partial y'},-\frac{\partial\Psi}{\partial x'}\right) \tag{4}$$

By substituting (4) into (3), we derive the relationship between the induced electrical field and stream function Ψ as

$$\begin{cases} E_x(x,y,z)=-C\iint\frac{\partial\Psi(x',y')}{\partial y'}\frac{1}{|\vec{r}'-\vec{r}|}dx'dy' \\ E_y(x,y,z)=C\iint\frac{\partial\Psi(x',y')}{\partial x'}\frac{1}{|\vec{r}'-\vec{r}|}dx'dy' \end{cases} \tag{5}$$

where $E(x, y, z)$ is the eddy current field at the target space and Ψ (x', y') is the stream function on the TMS coil surface. After obtaining this relationship, we establish a discrete numerical method and inversely solve the stream function through the induced electric field.

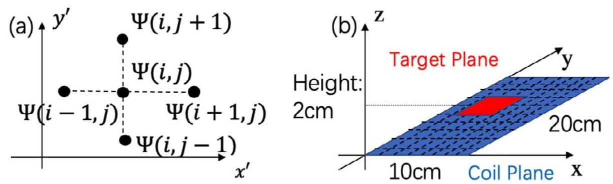

Figure 1. Finite-difference grid. (a) Relationship between the index of the matrix and the Cartesian coordinates. (b) Geometric setup for coil design.

2.1 Numerical Implementation

Using the derivation based on the electromagnetic theory shown in (5), we established the relationship between the stream function and the induced electric field.

The discretization of the differences is expressed by

$$\frac{\partial\Psi(x',y')}{\partial y'}=\frac{\Psi(i,j+1)-\Psi(i,j)}{\Delta y'} \tag{6}$$

where $\Delta y'$ is the grid length in the y'-direction of the finite-difference grid and $\Psi(i, j)$ represents the Ψ matrix value at row index i and column index j. The setting of the Ψ matrix is shown in Figure 1a.

We constructed a finite-difference grid on a coil plane of dimensions 20 cm × 10 cm using 100 × 50 points. The target electric field was set 2 cm away from the plane in an out-of-plane direction using 25 × 25 points, considering the 2 cm penetration thickness of the skull and cerebrospinal fluid. Using this grid setting and (6), the discretization form of (5) can be represented as follows:

$$E_x(x,y,2)=-C\sum_{j=0}^{N_y}\sum_{i=0}^{N_x}\frac{\Psi(i,j+1)-\Psi(i,j)}{\sqrt{(x-i\Delta x)^2+(y-j\Delta y)^2+(2-0)^2}}\Delta x' \tag{7}$$

To design the actual coil based on this discretization, namely, a linear equation $E=A\Psi$, the electric field strengths of the desired stimulus location and other locations can be set to nonzero and zero, respectively. For the setting of the target electric field, a natural idea is to directly set the uniform distribution, but this will cause the flow function to require more high-order terms to fit the uniform distribution. Therefore, we set the distribution of the target electric field to a Gaussian distribution, which will produce a smoother winding method.

This ill-posed equation can then be solved directly from the target electric field using Tikhonov regularization as follows:

$$\Psi=\underset{\Psi}{\operatorname{argmin}}\|A\Psi-E\|_2^2+\lambda\|\Psi\|_2^2, \tag{8}$$

where $||_2$ is the L2 norm and the hyperparameter λ can

Table 1. Summary of coil specifications used in this study and simulation results

N	E_{max} at 1 kA (V/m)	Number of coil turns	Inductance (μH)	Current for $E > 100$ V/m (kA)
Figure eight	57.95	10	10.3	1.73
1	66.26	9	8.30	1.5
2(a)	49.12	9	10.12	2.03
2(b)	24.14	11	9.01	4.14
3(c)	23.75	11	9.31	4.21
3(d)	27.07	10	10.60	3.69
Desired			6–12	<5 kA

be selected using the L-curve [10]. The physical meaning of the L2 norm of the stream function is to minimize the magnetic field energy of the coil. This will help to develop a more efficient coil under energy conversion; we need to ensure that a strong electric field can be generated at each stimulation focal point under limited energy supply. Finally, the corresponding coil shape can be obtained by drawing the contour lines of the stream function Ψ [9]. The number of contour lines equals the number of coil turns. The number of coil turns determines the inductance value of the coil, and the value of the inductance needs to be within a certain desired range for reasonable pulse width. In the design process, we first enumerate some candidates for the number of turns and design, such as 7–13 turns, and then calculate the inductance through the magnetic field energy calculation and exclude the candidates for the turns within a reasonable range. This numerical implementation program is written in MATLAB version 2020b (MathWorks, Natick, MA).

To verify that our coils can be derived using a single-pulse generator, we ensured that the inductance of the coil matched the relevant parameters of the driving coil by changing the number of coil turns. To match the pulse width of the discharged electric current in the compact Magstim magnetic stimulator unit (capacitance = 226 μF), the inductance of the TMS coil must range from 6 μH to 12 μH. However, considering the difference between the actual manufactured coil and the theory, we set the inductance of the coil consistent with the conventional figure-eight coil, which is about 10 μH. We calculated the inductance of the multi-locus TMS coil using the magnetic field energy method. In addition, the threshold electric field intensity at which nerve cells can fire is 100 V/m, and the coil must be designed such that the maximum current intensity of the drive circuit does not exceed 5 kA.

3. Results

We verified the single-, double-, and triple-locus target electrical field configurations designed using the proposed method. A summary of the specifications of these coils appears in Table 1. The serial numbers in parentheses in the first column correspond to the serial numbers in Figure 2. For the single-locus TMS coil, the

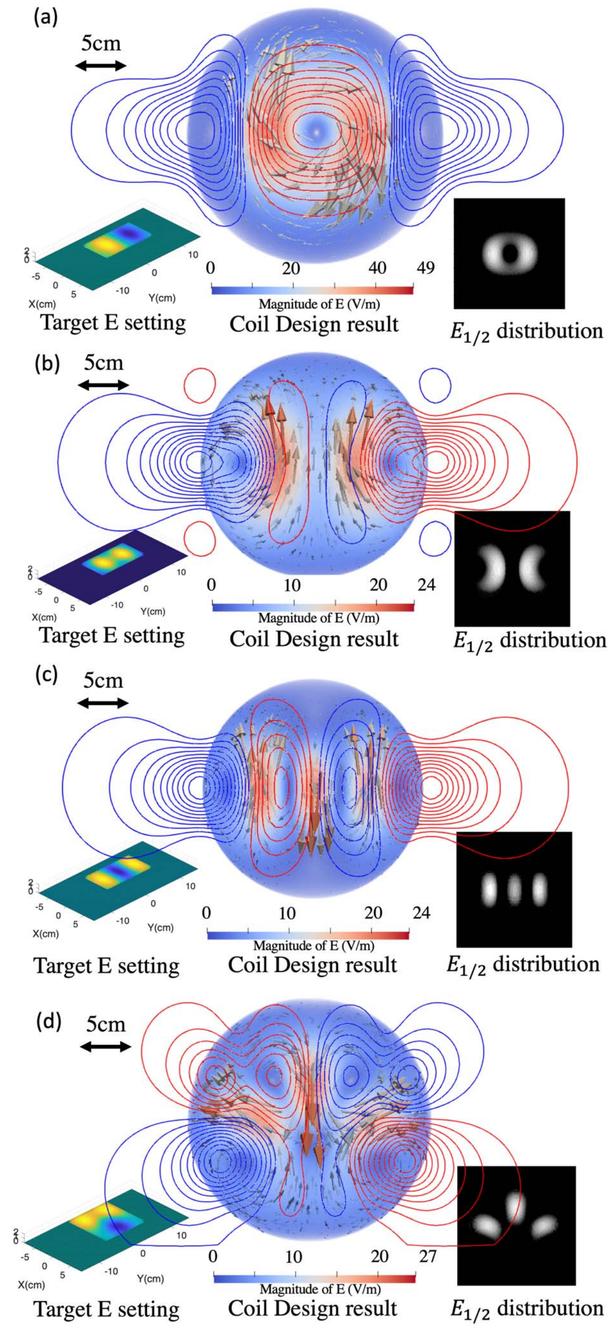

Figure 2. Diagrams of the multi-locus TMS coils and simulation results. The sub-figures to the left show the target eddy current settings. The color maps represent the magnitudes of the E_x components, and yellow indicates that the direction along the x-axis is positive. The central sub-figures represent the winding paths of the coils and the electric field distributions in the hemispherical brain models at a current of 1 kA. The red and blue colors represent the currents in the coils in the counterclockwise and clockwise directions, respectively. The sub-figures to the right show the half-value areas of the maximum eddy current electric field intensities $E_{1/2}$. The area of the white block reflects the focality of the coil. We designed (a) two loci with opposite electric field directions, (b) two loci with the same electric field direction, (c) three loci with the negative direction at the center and positive directions at the edges, and (d) three loci using a triangular arrangement.

efficiency improvement amounted to 39.40% over the efficiency of the conventional figure-eight coil, indicating that our method is suitable for designing TMS coils.

The double-locus TMS coil can stimulate two positions of the brain; hypothetically, it should stimulate targets on both the left and the right side of the M1 cortex [2]. First, because of the divergence-free nature of the electrical field ($\nabla \cdot E = 0$), it is natural to set opposite directions for the electric fields at the two focal points. The distance between the two focal points was set to 6 cm based on the typical structure of the brain. Solving the stream function using (8) revealed that the optimal value of the hyper-parameter λ given by the L-curve is 0.4. As the L-curve marks a compromise between the estimation error and the smoothness of the stream function Ψ, a larger λ can lead to a smoother stream function. We set λ to 1 for the fabrication of the TMS coils. The result of implementing this double-locus TMS coil design is shown in Figure 2a. In addition, because the response of the TMS is related to the direction of the electric field, we designed two focal areas with the same electric field direction, as shown in Figure 2b. Comparing Figures 2a and 2b shows that the maximum electrical field strength (49.12 V/m) in Figure 2a is significantly larger than that in Figure 2b (24.14 V/m). Thus, if the influence of the electric field direction is not considered, the TMS coil in Figure 2a exhibits higher stimulation efficiency.

To our knowledge, this method is the first to enable the implementation of triple-locus TMS coils. The focus positions in this case were set in the following two ways: the linear arrangement seen in Figure 2c and the triangular arrangement displayed in Figure 2d. Considering the evaluation of the double-locus TMS coil (Figures 2a and 2b), we verified that the coil generating the target electric field using opposite electric field directions is more suitable for a single-drive circuit. In the linear arrangement, we set the electric field direction in the center the same as the electric field directions on the outer sides. In contrast, for a triangular arrangement, the electric field direction of the central vertex was set opposite to the electric field directions on the outer sides.

For all the designed TMS coils, the inductance, electric current, and electric field strength satisfied the specifications of a commercial TMS pulse generator (i.e., Magstim), indicating that the designed TMS coils can be applied to clinical treatments and brain science research.

4. Discussion

Our novel method can facilitate stimulation of arbitrary multiple regions in the brain with the multi-locus TMS coil. This design will enable new clinical treatments for brain disorders. Moreover, our method does not rely on the operator's experience, and it is possible to implement the coil-based TMS rapidly using the inverse problem method after setting the target stimulation positions. The most important parameters in the design process are the target electric field distribution and the hyperparameter λ in (8). Regarding the setting for λ, because the TMS coil does not need to precisely match the target electric field, the value of λ needs to be slightly larger than the optimal value given by the L-curve, unlike the general inverse problem-solving procedure. We also found that setting the opposite electric field distribution in double-locus coils can produce a more efficient coil.

Our future work will focus on the following aspects. First, the actual coil will be implemented with three-dimensional printing technology, and we will evaluate the resulting coil by measuring the magnetic field and inductance. Moreover, to ensure the safety of the coil for human use, we will explore the temperature increase of the coil during treatment. Second, because multi-locus coils exhibit higher energy dispersion than their single-locus counterparts, we plan to further optimize the coil efficiency. One possible method is to change the coil plane to a curved surface that fits the skull; as the coil will be placed closer to the skull, it will undergo less magnetic field attenuation. Another possible method involves the addition of an iron plate above the coil [11]. Finally, we plan to further improve our method of solving the stream function. At present, the constraint conditions of a single driver are realized by manually adjusting the number of coil turns after obtaining the stream function. The improvement will involve introducing the constraint conditions associated with nerve excitation ($E > 100$ V/m), inductance ($L \in [6, 12]$ μH), and current ($I < 5$ kA) in the solution process. These conditions will be imported through convex optimization.

5. Conclusion

We proposed a novel method for designing a multi-locus TMS coil to realize simultaneous stimulations of multiple regions of the brain. We numerically demonstrated double- and triple-locus stimulations that can investigate multi-functional brain connectivity. Furthermore, we evaluated the directions of the electric fields to selectively stimulate brain nerves. The inductances and electric currents of our designed coils matched the required specifications for a conventional device intended for clinical treatment of brain disorders. We plan to demonstrate the feasibility of our design using a multi-locus TMS coil to treat actual brain disorders.

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