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Transcranial Magnetic Stimulation: Design of a Stimulator and a Focused Coil for the Application of Small Animals

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Abstract

Transcranial magnetic stimulation (TMS) is a non-invasive, safe, effective, and food and drug administration approved treatment for major depressive disorder. TMS relies on time-varying magnetic fields to induce an electric field in the brain, resulting in depolarization or hyperpolarization of the neurons. Recently, there has been extensive research to improve the magnetic coil design, effectiveness of TMS treatment, and improvement in the computer modeling of human brains, yet little development is reported on the TMS pulse generators and coil design for small animals. TMS pulse generators, or stimulators, are the circuits which provides pulse current to drive the inductive coils (TMS coils), used to generate time-varying magnetic fields. Commercial TMS stimulators are expensive and have limitations of using standard and non-customizable coils. These stimulators do not support small inductive loads, which require high-current capabilities. Furthermore, the commercial animal coil stimulates the entire body of a mouse, as they are designed for large animals. In this paper, the authors present the design of a small sized TMS stimulator and a focused coil for the application on small animals such as mice. The proposed TMS stimulator will have the potential of handling small inductive loads enabling stimulation of specific regions within the mouse brain.

Keywords

Small animal transcranial magnetic stimulation (TMS) coil, TMS, TMS stimulator

Disciplines

Biomedical | Electrical and Computer Engineering | Electromagnetics and Photonics | Mental Disorders | Psychiatry and Psychology

Comments

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Stimulation: Design of a stimulator and a focused coil for the application of small animals

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Transcranial Magnetic Stimulation (TMS) is a non-invasive, safe, effective and Food and Drug Administration (FDA) approved treatment for Major Depressive Disorder (MDD). TMS relies on time-varying magnetic fields to induce an electric field in the brain, resulting in depolarization or hyperpolarization of the neurons. Recently, there has been extensive research to improve the magnetic coil design, effectiveness of TMS treatment and improvement in the computer modelling of human brains, yet little development is reported on the TMS pulse generators and coil design for small animals. TMS pulse generators, or stimulators, are the circuits which provides pulse current to drive the inductive coils (TMS coils), used to generate time varying magnetic fields. Commercial TMS stimulators are expensive and have limitations of using standard and non-customizable coils. These stimulators do not support small inductive loads with high current capabilities. Furthermore, the commercial animal coil stimulates the entire body of a mouse, as they are designed for large animals. In this article, the authors present the design of a small sized TMS stimulator and a focused coil for the application on small animals such as mice. The proposed TMS stimulator will have the potential of handling small inductive loads enabling stimulation of specific regions within the mouse brain.

***Index Terms*—TMS, Transcranial Magnetic Stimulation, small animal TMS coil, TMS stimulator**

I. Introduction

Transcranial Magnetic Stimulation (TMS) is a non-invasive and outpatient treatment for Major Depressive Disorder (MDD) [1]. It has also proven to produce beneficial effects for other neurological and psychiatric disorders including: Parkinson's Disease (PD), Obsessive Compulsive Disorder (OCD), Anxiety, Post-Traumatic Stress Disorder (PTSD) and Schizophrenia [2]–[6]. TMS is based on the principal of Faraday's law of induction, in which time-varying magnetic fields are used to induce an electric field in the brain. TMS electrically stimulates the neurons in the human cortex, modifying the localized neuronal activity, when given repeatedly over a period of 6-8 weeks in 30-40 sessions of 30-40 minutes, in the form of trains of pulses.

Recently, researchers have shown interest in investigating the effect of TMS in neurological disorders which have not been explored, by utilizing animal trials [7]. This is because, animal trials are required to test the efficacy and safety of the treatments before using the new treatment on human subjects. Furthermore, animal trials can reduce research cost and speed up the development of new TMS treatment procedures. Substantial research has been published related to the improvement of coil design, using head models and clinical trials for humans [8], [9]. However, few studies are available on coil designs and even less on TMS stimulators for the use on small animals such as rodents and mice [10]. Current commercial TMS stimulators are very expensive and they have limited usage due to the coil's unique geometry and size. Perhaps an important limitation is that, commercial coils are large enough to stimulate the entire body of the small animal, so high focality studies are impossible.

Hence, in this article a small sized TMS stimulator along with a focused coil design for the application of small animals (mice and rodents) has been proposed. This new design was created to focally stimulate the portion of the rodent brain instead of stimulating their whole body, as with a standard, human sized, stimulating coil case. This novel design provide the practitioner or researchers an opportunity to choose TMS coils suited to their requirements, since commercial TMS stimulators do not support small inductive loads [11]. Mice brains are relatively small in size when compared with the human brains, consisting approximately 2 cm^2 of surface area, whereas human brains have about 100 times more [12]. The distance between the coil and the brain of mouse is very small. Therefore, to stimulate the brain, the required magnetic field will have to be only about 0.1 Tesla at a signal frequency of 2.5 kHz [10]. This means the circuit designed must be capable of handling current up to 1000 A. In addition, the proposed circuit provides additional advantage by providing compatibility for custom-made TMS coil to this stimulator, which can be changed to match the required specification of TMS stimulation. This small sized, light weight, custom-coil-compatible and low cost TMS stimulator can be easy fabricated in research labs that will advance and speed up the TMS research and address the scientific gaps in neuromodulation [7].

In this article we present the computer modelling of the focused coil, followed by the design consideration for the TMS stimulator and measurement of the magnetic field (H-Field) of the focused coil.

II. Computer Modelling

Sim4life, [13] a finite element tool was used for the computer modelling of the coil and a MRI derived heterogeneous small male rat model, weighing 198 grams was used [14] for the analysis of the results. The tissue properties for the small rat model were used from IT'IS (Information Technologies in Society) foundation material database [15] at the operational frequency of 2.5 kHz. Fig. 1 illustrates a small male rat model along with a focused coil. This coil has 40 turns in the shape of a cone, with the smallest radius of 0.9 cm. A Mn-Zn Ferrite material in the shape of a cylinder with relative permeability of 1000 has been positioned inside the coil to further improve the focality and increase the magnetic flux density towards the animal brain. The coil configuration has been angled to provide maximum magnetic field on the brain of a rat model.

Figure 1. Focused coil along with a ferrimagnetic material, positioned on a small male rat model.

Fig. 2 and Fig. 3 present the H-Field and surface E-Field (electric field) profiles on the mouse model respectively. These images have a linear scale with the highest value represented by the lightest color. With the 1000 A of current and a ferrimagnetic material with relative permeability of l000, the maximum H-Field is 0.5 MA/m (0.6 Tesla) and the surface E-Field on the cerebral hemisphere is 93 V/m, which is close to the threshold value to stimulate humans (100 V/m) [16].

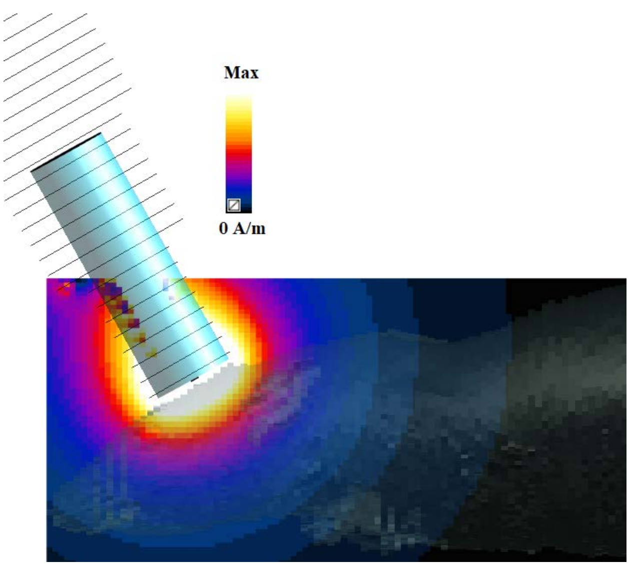

Figure 2. Shows the H-Field profile on a mouse model, maximum H-Field value is 0.5 MA/m.

The results from the computer modelling state that 1000 A of current with this focused coil is sufficient for the stimulation of mouse. Due to the coil's position, only the left half of the cerebral hemisphere will be stimulated. The ferrimagnetic material was used to enhance the H-Field near the mouse brain. Without the ferrimagnetic material, the H-Field value was centered within the coil, making it unusable for mouse stimulation. Use of ferrimagnetic material was a simple solution to improve the E-field in the brain, while keeping the focality of the coil. Since the H-field is maximum at the edge of the coil, positioning the corner of the coil at the center of the cerebral hemisphere, stimulates only the left half of the mouse brain.

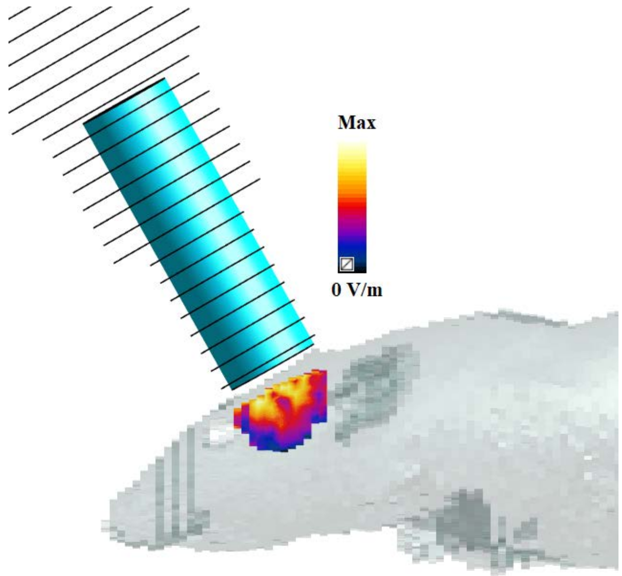

Figure 3. Illustrate the surface E-Field on the cerebral hemisphere of a rat model, maximum E-field value is 93 V/m.

III. System Design and Results

Fig. 4 shows the circuit diagram of the proposed TMS stimulator, which has been divided into three main sections: Alternating Current (AC) to Direct Current (DC) converter, voltage step down and load with a feedback.

In the AC to DC section, 120 VAC signal is converted to DC voltage with the help of two diodes and a capacitor (C1, D1 and D2).

The converted DC voltage is applied across two resistors (Potentiometer (Pot) and R6). One of the resistors is a variable potentiometer resistor (Pot) which gives the control over the level of voltage developed across the discharge capacitor (C3). By using the variable resistor, the voltage can be stepped down to required value.

In the third stage, C3 is connected to the inductive load (L1), which has the feedback path connected to the resistors for the dissipation of the return power. Diodes (D3-D5) are used to make sure that the current travels only in one direction, during the discharge cycle. Transistor (Q2) has been used for the switching, while the microcontroller feeds the control signal to the switching system. Current sense resistor (R5) is used to measure the current across the transistor.

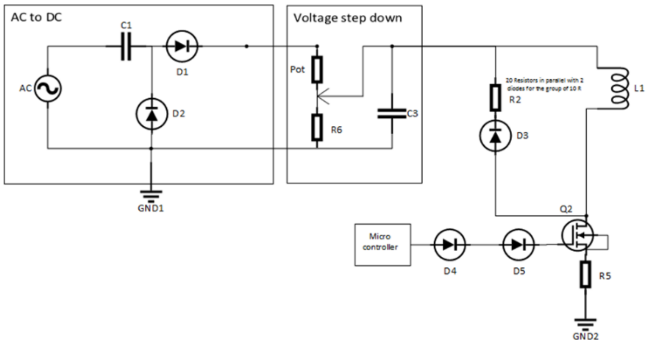

Figure 4. Schematic of a TMS stimulator circuit.

Fig. 5 shows the experimental setup of a TMS stimulator. The black circular component in Fig. 5 is a charge storage capacitor (C3), while the white rectangular component is a switching transistor (Q2). The yellow perforated PCB board on the right side of Fig 5. has a potentiometer (Pot) and 20 resistors (R2), along with a current sense resistors (R5). The signal was applied to the circuit using an Arduino microcontroller, which is mounted on the wall of a stimulator (Fig. 5). The power rating for each component used, was calculated above the required power rating for better durability. Several ground bars are used for stable connections to ground, positive supply and for the connection between the coil and the capacitors. The H-Field was measured using a Gaussmeter (Lake shore 475 DSP Gaussmeter) with and without a ferrimagnetic material.

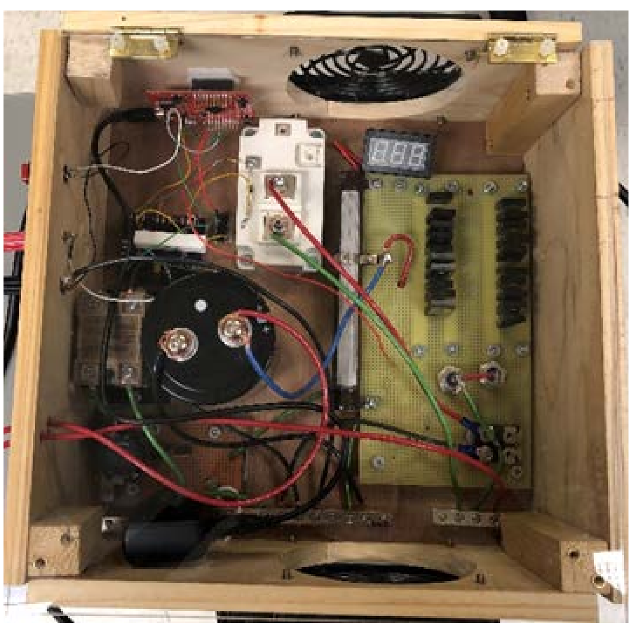

Figure 5. The fabricated TMS stimulator circuit for small animals.

Similar coil to the one used in the computer modelling, was fabricated with equal number of turns and geometry, for the accurate comparison of the results. Fig. 6 shows the coil positioned on a plastic mouse model, which represents the size of an actual mouse. As illustrated this coil is small enough to stimulate a portion of a mouse brain.

Figure 6. TMS coil is positioned on a plastic mouse model.

A. Power Rating Design Consideration for AC-DC Converter

Capacitor C1 would be charged and discharged every half cycle of the 60 Hz sinusoidal signal, provided from a 120V ac power outlet. Assuming 10 A of peak current flow through the AC to DC converter circuit, the capacitor C1 can be calculated and chosen using equation 1.

$$C1 = \frac{I\,t}{V} \tag{1}$$

In equation 1, ‘I’ represents the average current flowing through the capacitor in one half cycle of the sinusoidal signal, ‘t’ is the half cycle of a sinusoidal period, and ‘V’ is the average voltage experienced by the capacitor C1. Thus, the minimum value of C1 can be calculated as ~700 µF, although the authors have used 1200 µF capacitor (Table 1), with a voltage rating of 250 V.

Ignoring any voltage loss across the diodes D1 and D2, the variable resistor and resistors R6 would experience 240 V across them. Hence these resistors need to handle a minimum of 28.8 W, whereas resistors with 100 W of power rating has been used in the circuit.

B. Power Rating Design Consideration for Voltage Step Down Stage

Capacitor C3 needs to able to supply the required amount of charge during each discharge cycle, while maintaining a stable collector to emitter voltage across the IGBT (Insulated-Gate Bipolar Transistor) transistor. The discharge cycle represents the duration of time, in which a high current flow exists through the magnetic field generating coil. Equation 2 describes the calculation of minimum capacitance for C3.

$$C3 = \frac{I\,t}{V_{initial} - V_{final}} \tag{2}$$

In equation 2, ‘I’ and ‘t’ represents the average current and time, similar to an equation 1, while $V_{initial}$ and V_{final} represents the initial capacitor voltage before the discharge cycle and final capacitor voltage after the discharge cycle, respectively. C3 was calculated to be 10 mF, for flowing 1000 A of current in the coil for a duration of 400 µs (= t).

C. *Final Power Rating Design Consideration*

The parallel resistors (R2) are used to dissipate the energy after the discharge cycle, in order to avoid any return power to the transistor or control circuits, which were connected to the gate of transistor. There are 20 resistors connected in parallel to reduce the cost of the resistors, as the resistors cost increases with the rated wattage.

The voltage developed across the transistor (Q2) is due to supply voltage and also from the voltage developed across a load coil, when current flows through it. During the fall time of the pulse, the voltage polarity across the inductor is reversed, resulting in a net voltage appearing across the collector-emitter nodes of the transistor, as the summation of inductor voltage (V_{ind}) and supply voltage. The inductor voltage is given by equation 3.

$$V_{ind} = L\frac{dI}{dt} \qquad (3)$$

Voltage developed across the coil, during the rising time of the current pulse, would be 220 V, considering a rise time of the pulse = 100 µs, ‘I’ = 1000 A and L = 22 µH, as given by equation 3. During the fall time of the current pulse, due to the reversed polarity as mentioned above, net 420 V will develop across the transistor. The authors have chosen to use a transistor with the voltage rating of 1200 V and current rating of 800 A (pulsed current over 1 ms) for the safe and stable operation range of the transistor.

Table 1. Description and ratings of the components used in the circuit.

Name	**Labels in Fig. 1**	**Values and power ratings**
Capacitor	C1	1200 µF, 250 V
Diodes	D1 and D2	15ETH03PBF-ND, 300 V, 15 A
Potentiometer/Variable resistor	Pot	1kohm, 100 watts
Resistor	R6	1kohm, 100 watts
Discharge capacitor	C3	10000 µF, 200 V
Feedback resistors	R2	0.2ohm, 100 watts
Feedback diode	D3	VS-1N1186GI, 200V, 35 V
Inductor	L1	22 µH
Insulated-Gate Bipolar Transistor (IGBT)	Q2	FZ400R12KE4, 1200 V, 800 A
Diodes	D4 and D5	1N4004DICT-ND, 400 V, 1 A
Current sense resistor	R5	0.0005ohm,100 watts

D. *Magnetic field measurements*

The TMS stimulator is designed as a monophasic pulse current source and tested for reliable operation, producing one pulse every 15 seconds which allows to dissipate the heat generated inside the transistor junctions. The temperature of the coil during the test remained at the room temperature. All the components were able to handle the 1000 A making it a reliable circuit. The Ni-Zn Ferrite material (C2050) in the shape of rectangular bar is used for the test having relative permeability of 100 [17]. Without the ferrimagnetic material, the computer modelling showed the surfaced E-Field on brain of 10 V/m which agrees with the experimental value of H-Field of 90 KA/m, when the probe sensor is at center of the coil. Since, this coil is very small, we have measured two values of the H-Field, one at the center and one at the side of the coil at 1 mm distance away from the coil (Table 2). The H-Field values has increased with the ferrite, as expected and it can be further improved with the help of ferrite of higher permeability. Furthermore, the rise time of a pulse was close to 100 µs with the ferrite, with 1000 A flowing through the coils.

Table 2. Magnetic Field measurement results with and without the ferrite at the center and at the corner of the coil.

	Center (kA/m)	Corner (kA/m)
Coil alone	80	67
Coil with NiZn ferrite	138	148

IV. Discussion and Conclusion

This article proposes a focused coil and a TMS stimulator for applications on small animals such as rodents and mice. It is designed with the aim to stimulate part of a small animal brain instead of stimulating their whole brain, as is the case with the commercial animal coils that are designed for large animals. The design of the stimulator was unique, since it can handle small coils unlike commercial stimulators which has restriction on the minimum value of inductors that can be supported. The results of the experiments are validated by finite element analysis using rat brain model.

Our small animal TMS stimulator and the focused coil are suitable for the pre-clinical studies using small animals. This circuit has several advantages such as low cost, light weight (2 kg), which allows it to be moved around easily, and easy to fabricate in the electrical lab. It can also support different custom shapes of the coils which makes it very useful for fast prototyping and testing.

The new design of the stimulator is flexible for the addition of extra set of transistor and discharge capacitor in the future to increase the current in the coil, thus increasing the magnetic field. Although, this design is limited for single pulse stimulation, it can be used for the application of r-TMS by changing its component to support higher power ratings and with better thermal dissipation capabilities. It can be further improved by adding a simple user interface, which communicate with the microcontroller, thereby allowing the user to control the waveform shape of the pulse, as desired. This functionality can be implemented by performing small modifications in the micro-controller’s code.

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