flexTMS—A Novel Repetitive Transcranial Magnetic Stimulation Device With Freely Programmable Stimulus Currents

Norbert Gattinger, Georg Moessnang, and Bernhard Gleich*

Abstract—**Transcranial magnetic stimulation (TMS) is able to noninvasively excite neuronal populations due to brief magnetic field pulses. The efficiency and the characteristics of stimulation pulse shapes influence the physiological effect of TMS. However, commercial devices allow only a minimum of control of different pulse shapes. Basically, just sinusoidal and monophasic pulse shapes with fixed pulse widths are available. Only few research groups work on TMS devices with controllable pulse parameters such as pulse shape or pulse width. We describe a novel TMS device with a full-bridge circuit topology incorporating four insulated-gate bipolar transistor (IGBT) modules and one energy storage capacitor to generate arbitrary waveforms. This flexible TMS (*flexTMS*) device can generate magnetic pulses which can be adjusted with respect to pulse width, polarity, and intensity. Furthermore, the equipment allows us to set paired pulses with a variable interstimulus interval (ISI) from 0 to 20 ms with a step size of 10 μs. All user-defined pulses can be applied continually with repetition rates up to 30 pulses per second (pps) or, respectively, up to 100 pps in theta burst mode. Offering this variety of flexibility, *flexTMS* will allow the enhancement of existing TMS paradigms and novel research applications.**

Index Terms—**Biomedical engineering, insulated-gate bipolar transistor (IGBT), power electronics, stimulation device, transcranial magnetic stimulation (TMS).**

I. Introduction

TRANSCRANIAL magnetic stimulation (TMS) allows us to noninvasively and focally stimulate the brain of awake subjects without delivering significant pain [1], [2]. Strong magnetic fields are thereby generated by brief high-amplitude current pulses which are delivered to a coil that is placed over the examination area on the head. The stimulation focus can be controlled by the geometric design of this coil. These brief time-varying magnetic fields induce electric fields that are able to modulate neural activity. Nowadays, TMS is widely used in research and has become a well-established diagnostic tool for conduction studies of central motor pathways in neurology and neurosurgery [3]–[6].

In principle, the power circuit of a TMS device consists of a capacitor which acts as an energy storage, a power switch, and an application coil. All these components have to withstand both high voltage and high current. The stimulus strength is chosen by charging the pulse capacitor to a defined voltage level. After closing the power switch, the current through the coil rises sinusoidally, due to the *RLC* circuit topology consisting of pulse capacitor *C*, coil inductance *L,* and parasitic ohmic losses *R*. Based on the shape of the flowing coil current, two different classes of stimulus waveforms can be distinguished: biphasic (or polyphasic) and monophasic ones [7]. To generate a monophasic waveform, the self-induction of the coil has to be damped after a quarter of the *RLC* oscillation period. This can be achieved by using a shunting diode and a power resistor in parallel to the application coil [8]. As a result, the initial rise phase of the coil current is sinusoidal until it reaches its maximum and then falls smoothly back to zero. As all pulse energy is lost due to damping, the energy storage capacitor has to be completely recharged for every single pulse. In contrast, if additional damping circuitries are omitted, energy can oscillate freely between the application coil and the pulse capacitor. Therefore, biphasic pulses are generated when the power switch is not opened until one oscillation cycle is completed. The major part of the pulse energy flows back to the high-voltage capacitor and, hence, can be reused for the following stimulus. Compared to monophasic waveforms, less energy has to be recharged, which is why most repetitive transcranial magnetic stimulation devices (rTMS) use biphasic waveforms (The Magstim Company, MagVenture, Neuronetics). In contrast to electrical stimulation, the pulse duration of commercially available TMS devices cannot be adjusted, as this requires a change of the resonant frequency. Therefore, being able to adjust the pulse width might open the possibility of preferentially stimulating a specific neuronal population in a spatially overlapping cortical network [3], [9].

Peterchev *et al.* introduced a novel monophasic magnetic stimulator design that allows us to control the pulse width of a monophasic stimulation pulse *(cTMS)* [10], [11]. They lately presented an advanced device which is able to apply both monophasic and biphasic pulses [12], [13]. Their major aspect was to induce almost rectangular electric fields which can be adjusted with respect to strength and duration. Therefore, the *cTMS* device applies triangular coil currents of different length and slope. We, however, introduce a new stimulation device based on sinusoidal current pulses that can be arbitrarily

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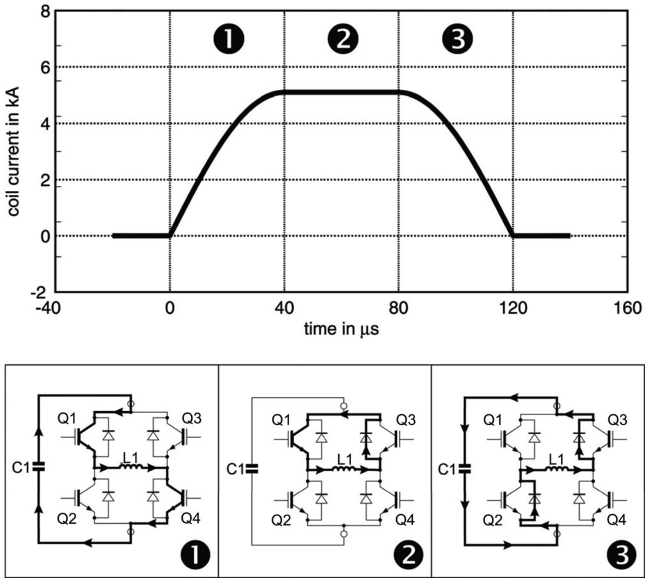

Fig. 1. Current paths of the IGBT full bridge during a monophasic trapezoidal pulse shape.

altered. Our aim was to build one single stimulation device which can produce both established (sinusoidal) waveforms and new, almost freely programmable, pulse shapes.

II. Device Design

A. Circuit Topology

The functionality of the circuit is explained using the example of a monophasic trapezoidal pulse shape as shown in Fig. 1.

FlexTMS waveforms are always piecewise defined pulses consisting of at least two of the three segments:

1) a positive slope (segment up);
2) no slope (hold phase);
3) a negative slope (segment down).

The maximum duration of the segments up and down is given by the time period of the fundamental oscillation frequency of the device (*T*/4) and is, in our case, 40 μs. The minimum segment length is defined by the switching capability of the high-power switches and is 10 μs for this device. The duration of the hold segment is independent of the fundamental oscillation frequency and can even be 1000 μs or more. The fundamental oscillation period of the device is given by the inductance of the application coil L_1, the capacitance of the pulse capacitor C_1, and the parasitic ohmic losses *R*. The pulse capacitor C_1 is charged to a certain voltage. In our case, the 100% maximum stimulator output (MSO) is equivalent to 2200 V. When IGBT Q_1 and Q_4 are turned ON, the current will flow in the positive direction through the coil (see Fig. 1, inset 1), which leads to a positive slope of the current. In this example, a hold phase follows the current rising phase. During hold phase, IGBT Q_4 is turned OFF and the current circulates as illustrated in Fig. 1, inset 2. The current will be damped due to ohmic losses at the IGBT's on-resistance and other parasitic resistors. The shorter the hold phase, the more negligible the damping during this phase. To achieve a descending current, IGBT Q_1 has to be turned OFF, which makes the current flow back to the pulse capacitor C_1 as indicated in Fig. 1, inset 3. To start a negative current pulse, Q_2 and Q_3 have to be turned ON instead of Q_1 and Q_4.

In this circuit topology, only segments with the length of $T/4$ can reach 100% MSO. Shorter segments will force the appropriate IGBT to be switched OFF before the current reaches its maximum. This allows the user, for example, to create a set of two pulses: one below a given threshold [e.g., at 60% resting motor threshold (RMT)] and a second one above a given threshold (e.g., at 130% RMT). The duration between the two pulses is then called interstimulus interval (ISI) and can be freely chosen between 0 and 20 ms in steps of 10 μs. Some examples for different pulse shapes are shown in Fig. 3.

B. Circuit Implementation

The basic power circuit of our device is shown in Fig. 2 and the corresponding data are given in Table I. All system components, except for the application coil, were installed in a grounded aluminum enclosure. To keep the schematic simple, the embedded PC, by which the stimulation device is adjusted, as well as the control electronics is not shown in Fig. 2. The main communication between embedded PC and control circuits takes place via CAN and RS-232 connection, which were both galvanically isolated. The IGBT drivers as well as the full-bridge controller were custom-made, whereas parts of the power supply and the charging circuitry were taken from a PowerMAG stimulator (MAG & More GmbH, Munich, Germany).

1) Power Supply and Energy Storage: The energy storage (pulse capacitor) C_1 is charged by the standard power supply of a PowerMAG stimulation device (MAG & More GmbH, Munich, Germany), which is connected to the power mains (230 VAC ± 10%/50 Hz). The default configuration of the device incorporates C_1 as 66 μF. The voltage of the capacitor can be adjusted in the range of 0–2200 V in steps of 22 V, thus leading to a stimulation intensity accuracy of 1%. One main advantage of the device is that C_1 can be a polarized capacitor. The two capacitors C_2 and C_3 are used for balancing.

2) Power Switches: All four switches (Q_1/D_1–Q_4/D_4) are implemented with IGBT modules that are rated to a maximum voltage of 3300 V and a continuous load of 1000 A. As at 100% MSO the peak current flow is up to 5 kA, the specified peak value is exceeded. The usage of IGBTs under exceeded current rating conditions in TMS devices is possible because of the expedient duty cycle [11]–[13]. In an overheating study, we connected a standard figure-8 coil (P/N 510519, MAG & More GmbH, Munich, Germany) to our device and did repetitive stimulation (20 pps, 60% MSO, biphasic pulse with $T = 160$ μs) until the temperature limit of 40 °C of the stimulation coil was reached. At first, both the coil and the *flexTMS* device were tempered to 22 °C. After 6 min of repetitive stimulation, the coil temperature limit was achieved, whereas the temperature of the IGBTs only slightly increased (+4 °C). Thus, one can assume that neither the heating of the IGBTs nor the power load is critical, which is why no further heatsinks are needed.

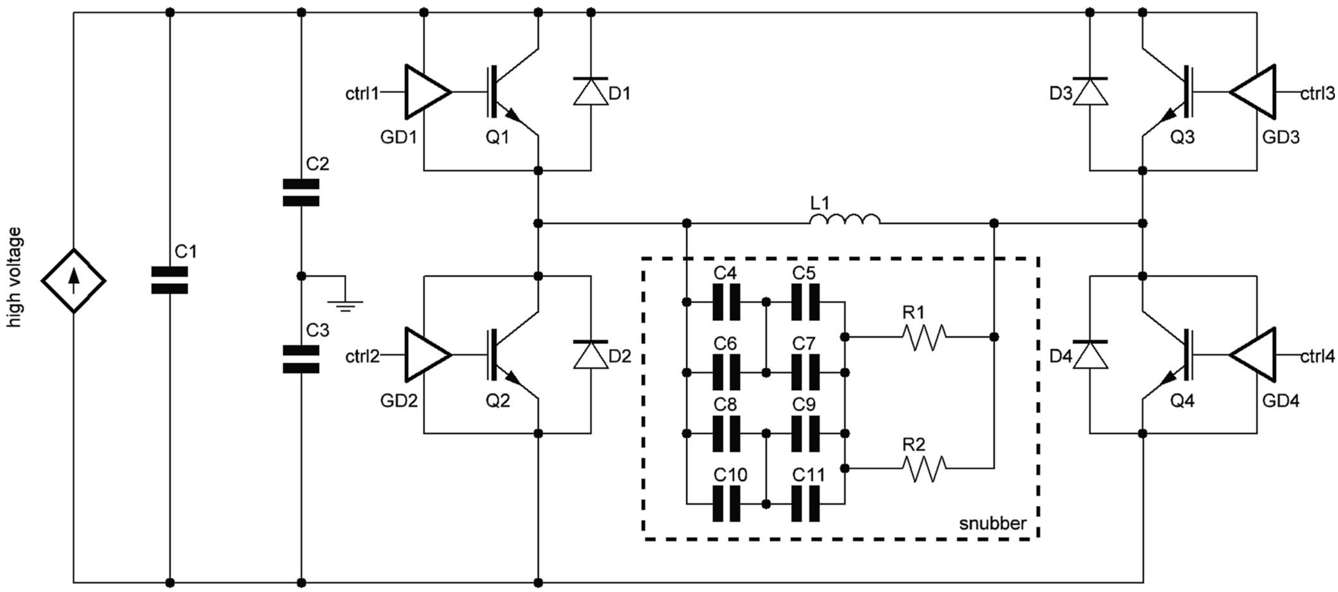

Fig. 2. Simplified schematic of the *flex*TMS power circuitry.

TABLE I
MAIN POWER TRAIN COMPONENTS

Component	Assignment	Rating	Part #	Manufacturer
C_1	Energy storage	3 x 22 μF $\pm$ 10 %	KMKP 1400-22IB	Vishay Roederstein
C_2, C_3	Symmetry capacitors	0.47 μF, 1600 VDC	RBPS	Aerovox
$C_4 - C_7$	Snubber	270 nF, 2500 VDC	MNKP386	Vishay Dale
$C_8 - C_{11}$	Snubber	100 nF, 2500 VDC	MNKP386	Vishay Dale
R_1, R_2	Snubber	1.5 Ω	HS100	Arcol
$Q_1 - Q_4$	IGBT	3300 VDC, 1000 A	FZ1000R33HE3	Infineon
$D_1 - D_4$	Free–wheeling diode	3300 VDC	FZ1000R33HE3 (included)	Infineon
$GD_1 - GD_4$	IGBT gate driver	3300 VDC	–	custom made
ctrl1-ctrl4	Full bridge controller	–	–	custom made

3) Snubbers: The IGBT switches Q_1–Q_4 have a maximum collector–emitter voltage rating of 3.3 kV. The 1.1 kV safety margin accommodates for transient voltage spikes which occur during switching the IGBTs ON and OFF. Instead of using big snubbers on each of the four IGBTs, it is sufficient to use one in parallel to the stimulation coil L_1. The snubber consists of C_4–C_{11}, R_1, and R_2 and serves the purposes of taking over a portion of the IGBT current during turn-off and suppressing high-amplitude ringing of the IGBT collector–emitter voltage as discussed in [13]. The two balancing capacitors C_2 and C_3 work as an additional snubber. The sizes of C_2–C_{11} as well as R_1 and R_2 were optimized to limit the collector–emitter voltage to 3.2 kV and to restrict the peak power dissipation of R_1 and R_2 to 100 W each.

4) IGBT Driver: The advantages of IGBT technology can only be exploited with optimal and application-orientated driving capability. The complex demands made on IGBT drivers, especially for rTMS devices, which are usually in the high-power and high-voltage regime, call for a custom-made IGBT driver circuit, which links stimulator control and power semiconductor. Our custom-made driver was designed for general use in the field of magnetic stimulation devices and can be easily adapted to different applications. It was also implemented in a multisine stimulator described in [14]. Since IGBT's current loads exceed manufacturers' ratings, the overcurrent protections of commercial drivers do not fit the changed needs. For that reason, IGBT losses have to be minimized and an appropriate overcurrent handling has to be implemented. At the given realization, 90% of IGBTs' gate-on-resistance (+18 V) is achieved within 1.2 μs. Together with the snubber circuitry, the gate-off-timing influences the peak transient voltage spikes occurring while switching the IGBT OFF. Thus, the gate-off-timing was chosen to be 8 μs. The maximum IGBT switching frequency for the implemented gate timings is 100 kHz, which enables complex pulse shapes and allows a minimum segment length of 10 μs.

5) Full-Bridge Controller: The full-bridge controller will turn the four IGBTs of the bridge ON and OFF by control fibers. To prevent the pulse capacitor C_1 from short circuit, the full-bridge controller makes sure that two IGBTs of a bridge string are never switched ON at the same time. This is achieved by implementing a look-up table in a fast 8-bit parallel EEPROM (AT28C64B-15, Atmel Inc., San Jose, CA), which is controlled by an 8-bit microcontroller (PIC18F4480, Microchip Technologies Inc., Chandler, CA) running at 32 MHz. The full-bridge controller was designed to control up to eight single IGBT switches with a timing accuracy of 1 μs. It has an optical isolated 1 MBaud CAN–bus interface to communicate with the IGBT driver boards and other control systems inside the stimulator (polling for current values, temperature, voltages, etc.). An RS-232 interface is used for communicating with the embedded PC at 115 200 Baud.

6) Coil: In principle, the *flexTMS* can operate with any kind of stimulation coil, provided that the coil inductance is in the range of 9 μH $\leq L_1 \leq$ 16 μH and that the coil can sustain the maximum voltage and energy delivered by the *flexTMS* device. The use of other coil inductivities is conceivable, but has to be tested concerning their maximum current flow and their resulting transient voltages. The use of coils with inductances lower than 9 μH, which can be needful for certain animal studies, would perhaps limit the maximum output power of the stimulation device. The *flexTMS* circuit design makes the maximum pulse width in most parts independent from the coil inductance L_1, although L_1 in conjunction with the pulse capacitor C_1 determines the resonant oscillation period and, therefore, the current rise rate $\mathrm{d}I/\mathrm{d}t$ as well as the maximum current flow.

7) Embedded PC: The stimulator is controlled by different electronic circuits. The *flexTMS* device uses the PowerMAG (MAG & More GmbH, Munich, Germany) stimulation platform with modified firmware and an additionally embedded PC (i-PAN7, Keith & Koep GmbH, Wuppertal, Germany) running with Windows CE 6.0 (Microsoft, Redmond, WA). Pulses can be created on a normal PC (see Section IV) and are transferred via USB flash drive onto the stimulation device. The display of the embedded PC shows the coil current, the induced electric field, and the gradient of the induced electric field. Some numerical properties, like the integral of the current waveform over time, are shown in the display as well.

III. Examples of Coil Currents

We recorded the coil current and electric field for various pulse shapes with a figure-8 air core coil (P/N 510519, MAG & More GmbH, Munich, Germany). The coil current and the electric field were measured with a Rogowski current probe (CWT60B, Power Electronics Measurements Ltd., Nottingham, U.K.) and a search coil, respectively. The search coil was made of a five-turn circular winding with an outer diameter of approximately 2 cm and an inner diameter of approximately 0.5 cm, which was positioned parallel to the TMS coil plane with a distance of roughly 1 mm at the focus of the figure-8 coil. The search coil output voltage is proportional to the electric field; however, the exact calibration of the search coil output is irrelevant as long as the position remains the same for every investigated pulse shape. In Fig. 3, 12 *flexTMS* example pulses are compared. Each inset shows the coil current waveform and the induced voltage of the search coil. All pulse shapes are measured at 100% MSO and are comparable to 100% MSO of the PowerMAG stimulator (MAG & More GmbH, Munich, Germany) as described in [15].

IV. Software and Workflow

Assuming that a desired pulse shape is not stored in the *flexMAG*, the waveform can be individually designed by using our custom-made software *PulseDesigner*. Every pulse may consist of three basic segments: segment up, segment hold, and segment down. Systemic damping, which occurs due to ohmic losses, is taken into account by the software. The duration of each segment can be defined by direct numeric input and by sliding the segment's contour with the mouse. Each segment has a minimum duration of 10 μs to let the IGBTs switch ON and OFF appropriately and can further be adjusted in steps of 1 μs. The switch-off delay, caused by the discharge resistor of IGBT's gate, is taken into account and is compensated in the switching scheme. As the pulse shape is formed by an oscillating circuit, the ascending and descending segments are parts of the inherent resonant sine wave (up to 100 segments per pulse are possible). Pulse shapes are stored in a descriptive file format or can be translated into a switching scheme for a transmission to the *flexTMS* stimulator.

The stimulation intensity can be adjusted with the knobs on the front of the device or can be directly programmed into the pulse file. Thus, the user is free to add a stimulation intensity to a pulse by running *PulseIntensity*. Furthermore, even whole sets of pulses with different intensities can be created with this tool. The programmed pulse intensity is automatically adjusted when the pulse is selected onto the device.

A further option is the reorganization of pulse sets in a random manner with *Randomizer*. For good scientific practice, it is crucial to randomize as much parameters as possible (e.g., intensity, order of pulse shapes, and polarity) while performing the experiments. The user can decide how many repetitions of the selected pulses should be applied and the software creates a random set of these pulses.

After the pulses or even sets of pulses were created and optionally randomized, they have to be transferred to the device itself. Currently, this is done via a USB flash drive to avoid problems concerning the European standard for medical electrical equipment (EN60601-1), which may occur when medical devices and nonmedical devices are plugged together. Once transferred to the stimulation device, the pulses stay there as long as they are not deleted or overwritten. The actual stimulation pulse can be selected via mouse, keyboard, or touch display. The chosen pulse will be applied to the subject after pressing the stimulation push button. One has to keep in mind that always both parameters together—the relative peak current level set with *PulseDesigner* and the chosen MSO level of the device—lead to the actual peak current level of the stimulation coil. Thus, one can have exactly the same peak current flow in the coil with different pulse dynamics. For example, a pulse restricted to 50% peak current flow and applied with 100% MSO would reach the same current value as a pulse set to 100% with *PulseDesigner* and applied with 50% MSO, but indeed they will clearly differ in their dynamics. Screenshots and more information about the software will be published on our website *http://www.imetum.tum.de*.

V. Experimental Results

As an experimental proof of principle, we compared three biphasic testing pulses with a biphasic sinusoidal pulse shape [see Fig. 3(a)], which is exactly the same pulse duration and

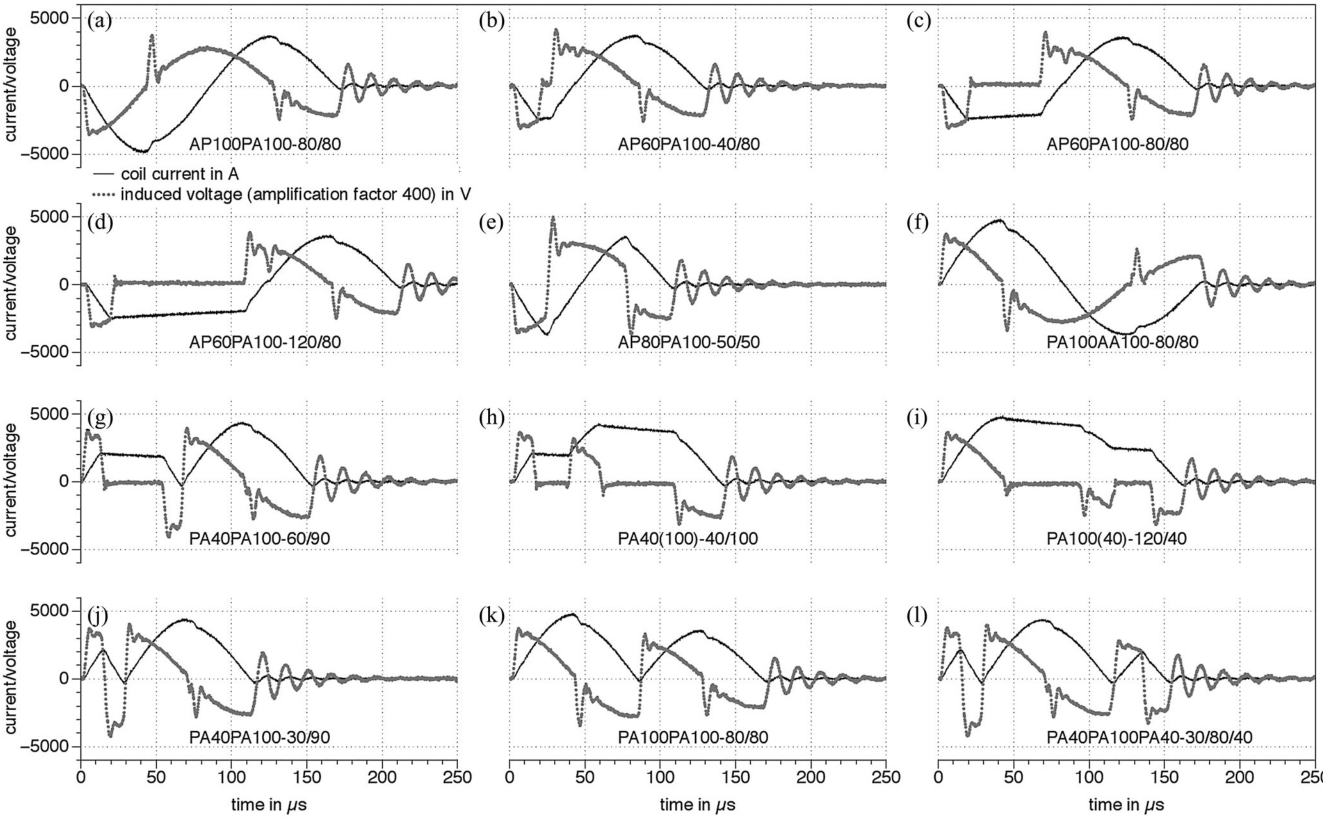

Fig. 3. Choice of possible coil currents (solid line) and induced voltages (dotted line); all pulses were applied at 100% MSO. Biphasic pulses (a)–(f) as well as monopasic pulses (g)–(l) can easily be set. All different pulse shapes can be described with the following encoding pattern: the first block encodes all delivered coil current directions (AP stands for anterior to posterior current flow in the brain and represents a negative coil current in this case; PA thus stands for a positive coil current), followed by its peak value (percent of possible maximum). The second block is separated by a dash line and implies the corresponding time slots in microseconds. Due to inevitable damping effects and switching losses, the possible peak current level degrades over time, which can be clearly seen in inlay (*k*).

pulse power of a PowerMAG stimulation device (MAG & More GmbH, Munich, Germany). Its first, negative half-sine wave induced a current which flows from anterior to posterior (AP) in the brain. The following second, positive half-sine wave resulted in an induced current flowing from posterior to anterior (PA). As each half-wave of the reference pulse has a length of 80 μs, it was named as AP100PA100-80/80. The three biphasic testing stimuli only differed from the reference pulse in the duration and intensity of their first, negative current half-wave. Thus, their first half-wave always consisted of a trapezoidal pulse shape, limited to 60% of the peak current flow of the reference pulse, but had different lengths. Fig. 3(b)–(d) represents these waveforms with their initial half-wave lengths of 40 μs (AP60PA100-40/80), 80 μs (AP60PA100-80/80), and 120 μs (AP60PA100-120/80).

A. Subjects

The involved researchers as well as members of our work group participated in the experiment (mean age 32 years with a standard deviation of $\pm$13.3 years; two females, five males; six right-handed subjects). All subjects were familiar with TMS, had no history of brain disease, and fulfilled no exclusion criteria for TMS [16]. The study was carried out according to the *Declaration of Helsinki*.

B. Experimental Design

The TMS experiment was designed to assess how different biphasic stimulation pulses affect the efficacy of TMS to evoke a motor response in the contralateral hand. It was performed with the aforementioned *flexTMS* device with an assembled pulse capacitor of 66 μF in combination with a standard figure-8 coil (P/N 510519, MAG & More GmbH, Munich, Germany). To achieve lowest possible threshold intensities, the initial polarity of the biphasic coil current was chosen to be negative, so that the induced current in the brain initially flowed anteromedial to posterolateral across the motor strip [4], [7], [17], [18]. Stimuli were applied to left M1-HAND and motor-evoked potentials (MEPs) were recorded with surface electrodes from the relaxed right *abductor pollicis brevis* muscle. As cutoff value, an MEP amplitude of 300 μV peak-to-peak was chosen. The order of MEP measurements was identical across all blocks. First, we assessed the selected threshold for each pulse type using a maximum-likelihood threshold-hunting procedure [19], [20]. As recommended for the use in research projects, threshold determination was based on a set of 16 stimuli [21]. We then measured the stimulus response curve (SRC) for each of the four different pulse shapes, reflecting the increase in MEP amplitude with increasing stimulus intensity. Stimulus intensity of TMS was gradually increased in 10% steps from 90% determined threshold to 130%

TABLE II
NEUROPHYSIOLOGIC GROUP DATA

Pulse Shape	AP100PA100-80/80	AP60PA100-40/80	AP60PA100-80/80	AP60PA100-120/80
Pulse Shape shown in	figure 3a	figure 3b	figure 3c	figure 3d
Threshold in % MSO	71±6.92	64±7.19	66±7.49	66±7.78
MEP latency in ms	23.87±1.73	23.57±1.73	23.67±1.62	23.6±1.7
Energy Consumption in J	55.23±8.09	33.18±6.42	36.81±7.04	38.11±7.67
Stimulus Response Curve shown in	figure 4a	figure 4b	figure 4c	figure 4d

threshold [22]. Ten MEPs were recorded at each intensity level. All stimulation conditions were randomly applied, leading to a total set of 200 pulses, each consisting of four different pulse shapes applied with five stimulation intensities each.

C. Electromyographic Recording

The subjects were seated comfortably in an armchair with their stimulated hand resting on a cushion. MEPs were recorded from the right *abductor pollicis brevis* muscle at rest by surface electromyography (EMG) with Ag–AgCl surface electrodes using a bipolar belly tendon montage. The EMG amplifier was triggered by the magnetic stimulator. Raw EMG signals were band-pass filtered between 2 and 2000 Hz, notch filtered at 50 Hz, amplified by a factor of 500, and digitized at 20 kHz sampling frequency. The data were stored on a standard PC for online visual display and later offline analysis using MATLAB R2010b (The Mathworks Company, Natick, MA). Peak-to-peak amplitudes of each MEP were measured and mean MEP amplitudes were calculated for each condition.

D. Results

We did not observe any adverse effects or any kind of spreading activity to neighboring muscles in the course of the experiments.

1) Determined Threshold: The mean threshold for each pulse shape as well as the MEP amplitude and latency is given in Table II.

2) SRC: First, the mean MEP response at different threshold-related stimulator output levels was determined for each of the applied waveforms. Among others, [23] and [24] showed that if stimulus intensity is plotted onto the x-axis and if stimulus response of a neural population is plotted onto the y-axis, the resulting SRC will be of sigmoidal appearance. However, as we did not observe any saturation effects of the MEP response within our performed span of stimulator output levels, we decided to carry out a linear fit. In our case, stimulus intensity is equivalent to the stimulator output level and was denoted as a percentage of the MSO.

For a better visualization, each of the tested waveforms is plotted in its own inlay. Each plot shows the measured MEP data (dots), its belonging error bars, and the fitted SRC (solid line). Fig. 4(a) represents the data of the biphasic sinusoidal reference stimulus of Fig. 3(a). Arranged clockwisely, Fig. 4(b)–(d) visualizes the response data of the three aforementioned biphasic testing stimuli [see Fig. 3(b)–(d)]. Although no significant differences in intensity between the four tested waveforms were determined, pulse energy losses differ (see Table II).

VI. DISCUSSION

Currently, the only commercially available pulse shapes are biphasic (sinusoidal) and monophasic ones. In their review article, Pell *et al.* summarize that both waveforms do not necessarily activate a population of neurons to the same degree [9]. Maybe even entirely different populations are excited for both monophasic and biphasic pulses, with a wider range of inhibitory and facilitatory neuronal circuits excited by the biphasic pulse [3], [9]. As parameters for the pulse capacitance C and coil inductance L vary from manufacturer to manufacturer (e.g., The Magstim Company, MagVenture, Neuronetics, MAG & More), pulse duration varies as well. However, not only the pulse duration changes, but even the usage of the same kind of coil from different manufacturers changes the geometry of the magnetic field resulting in possibly different functional effects [3], [25]. As there is some indication, different pulse durations might be an option to selectively target different neuronal populations on the basis of different membrane time constants [3], [9].

A. Pulse Characteristics and Circuit Topology

To the best of our knowledge, there is only one kind of TMS device available allowing the control of pulse parameters in a wide range. Peterchev *et al.* first described a novel *cTMS* device, which is able to generate monophasic current pulses that lead to nearly rectangular induced electric fields [10], [11] and expanded this topology to a repetitive *cTMS* device which can apply monophasic and biphasic pulses, respectively [12], [13]. In contrast to Peterchev *et al.*, we decided to use commonly used sinusoidal pulse shapes as a basis and tried to widen their control capability. Our circuit topology enables us to easily apply biphasic, trapezoidic, and even monophasic pulses with selectable polarities. Yet, compared to the monophasic *cTMS* device, our design uses a much smaller pulse capacitor of currently 66 μF and no explicit damping circuitry (the pulse capacitor for the monophasic cTMS device is 716 μF [11]). However, as indicated in Fig. 5, our device allows similar pulse shapes to *cTMS*. To have a closer look at this special case, one has to admit that the pulses last longer and, compared to [11], cause a higher thermal heating of the coil. Yet, the weaker the damping, the smaller the slew rate and, as such, the smaller the induced electric field. This means that our *flexTMS* device permits us to set monophasic *cTMS*-like pulses with a strongly unipolar induced electric field.

Apart from potentially stimulating different neuronal populations by different waveforms or pulse durations [9], the pulse shape has a large impact on the coil generated impulse noise (click noise). The TMS pulses are accompanied by a click noise of more than 120 dB sound pressure level [26], [27]. The

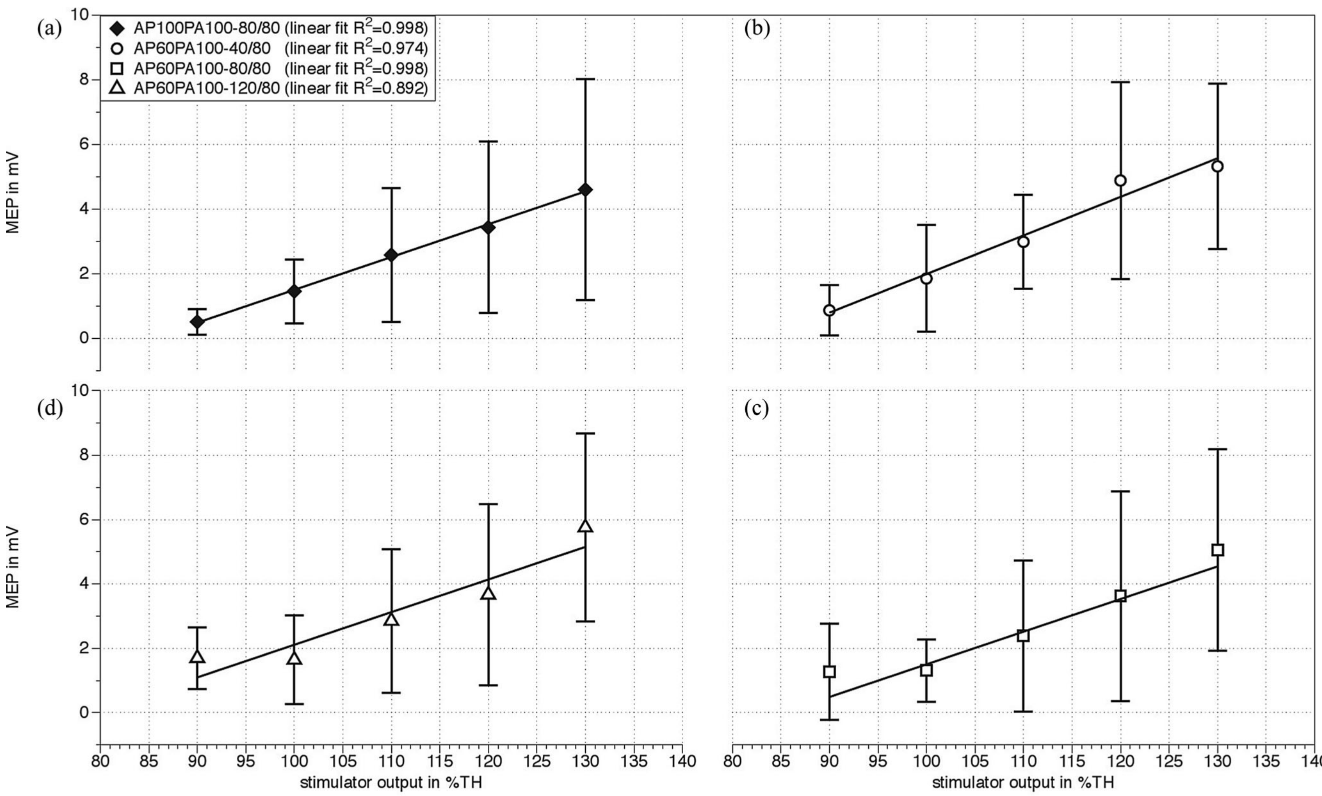

Fig. 4. Stimulus–response curves (SRCs). (a)–(d) show, in a clockwise arrangement, the measured MEP response as well as the fitted SRC for each of the four tested pulse shapes. MEPs were recorded relatively to the previously determined threshold (TH). The four fitted SRCs show no significant difference.

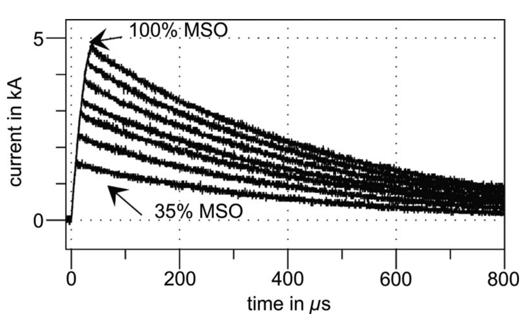

Fig. 5. *cTMS*-like pulses with *flexTMS* device.

maximum peak energy was measured to be in the range of the highest sensitivity in human ears, namely between 2 and 5 kHz [28]. Therefore, Counter *et al.* encourage to use ear plugs to prevent subjects from any damage of the cochlea [28]. Nikouline *et al.* tried to find out how air- and bone-conducted sounds from the TMS coil affect the cochlea and also the cortical excitation [29]. They conclude that brain activation elicited by TMS is greatly affected by the coil click, propagated both via air and via head tissues. Besides, they mention that both the acoustic click noise and the somatosensory scalp stimulation have a side effect on neural excitation [29], [30]. First measurements with *flexTMS* in our laboratory showed that TMS click noise is affected by pulse shape and pulse duration and, thus, might be an optimization criteria for some TMS applications.

B. Pulse Patterns

Not only the efficacies of single applied pulses are of interest, the arrangement of stimuli in certain patterns which can strongly modulate neuronal activity attracts a great deal of attention [4], [5], [9], [31], [32]. The theta burst pattern of repetitive TMS was developed in 2004, based on the physiologic pattern of neural firing found in the hippocampus of animals by *in vitro* experiments [30], [33]. Basically, theta burst stimulation (TBS) consists of three stimuli given every 20 ms and repeated every 200 ms. On the basis of this pattern, several theta burst paradigms have been developed [4], [5]. Nowadays, many commercially available magnetic stimulation devices support the application of theta burst patterns, using a biphasic waveform, because of its charge recovery option. Among others, Arai *et al.* reported that monophasic and biphasic pulses given at a certain pattern do not necessarily lead to the same neuronal response [32]. They point out that at a given and constant repetition rate of 2 and 3 pps, monophasic rTMS had a marked faciliatory influence on the motor cortex, whereas biphasic rTMS evoked relatively stable responses [30], [32]. As George *et al.* sum up, a wider opportunity of setting stimulus parameters might help for further understanding the ways by which TMS changes neuronal function and, therefore, will improve its ability both to answer neuroscience questions and to treat diseases [31]. *FlexTMS* and its appendant software enable us to directly compare resulting neural excitation of different stimulus waveforms arranged in completely user-defineable patterns.

C. Limitations

The loss of energy per pulse depends on the pulse duration, the current amplitude, and the number of switching operations of the power IGBTs. All other stimulus energy can be recovered for the following stimulation pulse due to the single-capacitor circuit topology. Thus, the waveform itself directly affects the amount of recovered pulse energy and limits the maximum repetition rate. All waveforms shown in Fig. 3 can be applied repetitively up to 30 pps and even up to 100 pps in *thetaburst* mode. As no energy can be recovered from the coil when applying *cTMS*-like pulses, this waveform is inapplicable for high-repetition pulse patterns or continuous repetition rates of more than 3 pps.

As already discussed in [11] and [13], a further limitation is the lack of IGBT performance for fast pulsed currents that exceed manufacturers' specifications. Yet, as the IGBT's duty cycle is very beneficial and temperature measurements showed no alarming condition, we were able to apply more than 10 000 pulses with different waveforms and different intensities without any IGBT damage.

Next, one has to keep in mind that current gradients are only dependent on both the fundamental *RLC* oscillation frequency and the stimulus intensity. Hence, lengthening the pulse duration to a desired value by adding free-wheeling segments does not affect current gradients. Consequently, the induced electric field of, e.g., a trapezoidal biphasic wave with a pulse period of 200 μs differs from the induced electric field of a biphasic sine wave with a fundamental period of 200 μs.

Finally, due to the quite small pulse capacitance C, *flexTMS* is sensitive to changes of the coil inductance L as it alters the fundamental *RLC* oscillation frequency and, thus, the maximum current rise $\mathrm{d}I/\mathrm{d}t$.

D. Safety

As the *flexTMS* pulse capacitor is not larger than the ones already used for conventional rTMS devices (e.g., PowerMAG), the stored pulse energy can be treated as uncritical. Due to a defect of the pulse switches within the *flexMAG* device, energy not more than in normal use can be transferred to the coil. The maximum of energy is 160 J for the used 66 μF capacitor. So far, we have tested coils from two manufacturers: MAG & More (double coil P/N 510519, MAG & More GmbH, Munich, Germany) and Magstim (70 mm double coil, The Magstim Company Ltd., Whitland, U.K.). As we used approved coils for our testing and neither exceeded the specified operating voltage nor its peak current capability, safety considerations are the same as for conventional rTMS devices.

Once designed on a PC, new stimulation waveforms have to be transferred via a USB data storage to the stimulation device, which from now on works self-sustaining. While reading out the pulse information from the USB flash drive, pulse parameters are checked according to feasibility and faulty pulse configurations are ignored.

Apart from the commonly used monophasic or biphasic pulse shapes, new and user-defined waveforms are available with *flexTMS*. Possible neuromodulating effects are unknown, which is why caution should be exercised since the standard safety guidelines for preventing seizure induction were developed for conventional rTMS pulse shapes [16]. Additional attention should be paid while testing established pulse patterns with established pulse shapes; in case the combination of both has never been tested, which, for example, is the case for monophasic high frequency rTMS [9].

E. Experiments

In a first proof of principle experiment, we showed on the example of four waveforms that *flexTMS* is able to elicit a clear MEP response, even with a relatively small pulse capacitance of 66 μF. Most commercial devices have larger pulse capacitors, for example, the Magstim 200 device with 185 μF and the BiStim device with 370 μF, both manufactured by The Magstim Company Ltd., Whitland, U.K. (capacitor values have been taken from [11]). As the four used biphasic waveforms only differed in the first phase and as we did not notice any remarkable difference in SRC, this outcome slightly supports the assumption that the influence of the second phase of the biphasic pulse dominates over its initial phase [9], [30], [34]. Since, at a given intensity, the conventional biphasic pulse and the three testing stimuli showed no statistically evident difference in MEP value, but differed in their energy consumption and thus in the resultant thermal coil heating, trapezoidic pulses might be a good option to reduce thermal coil heating during rTMS pulse application. However, this experiment is surely only a clue in finding efficient pulse shapes.

VII. Conclusion

We introduced a new *flexTMS* device which, for the first time, uses a power-IGBT H-bridge in a transcranial magnetic stimulator. This circuit topology enables the use of a polarized pulse capacitor instead of a big and expensive unpolarized film capacitor, even when applying biphasic pulses. The main advantage is that now one single stimulation device can set biphasic, polyphasic, half-sine, trapezoidic, and—with some limitations—even monophasic current waveforms. Thereby, the pulse polarity can be chosen in any order without changing the coil position. The possibility to control the pulse duration, the polarity, and the pulse shape of TMS with our device might help to get a deeper knowledge of how TMS actually works and how the efficacy of both waveforms and pulse patterns can be improved [3], [9], [30]. A first proof of principle experiment showed that the system is strong enough to elicit clear MEP response, when applying single TMS pulses over the M1 motor cortex. As the stimulation system is designed carefully and as neither operating voltages nor transient voltage peaks exceed the maximum ratings of the used components, the system can be seen as safe as any other commercial device.

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