Design and Optimization of Pulsed Magnetic Field Generator for Cell Magneto-Permeabilization

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***Abstract*—Biological cell magneto-permeabilization is the phenomenon when the membrane of the cell increases permeability to molecules to which it was initially impermeable due to the exposure to high pulsed magnetic fields. Flexible high power electronics systems are required for triggering this effect. In this work, we have designed a high power (938 A, 2 kV) pulsed magnetic field generator (up to 5.5 T), which generates 10 µs–100 µs pulses with predefined repetition frequency of 1 Hz–100 Hz. We have applied SPICE and COMSOL Multiphysics modelling for design and development of the system, which showed a good agreement with the experimental results. The snubber and crowbar circuitry has been implemented for compensation and dampening of the transient processes on the switches, which allowed limiting the overvoltage to 0.25 kV. The multilayer inductor structure and design considerations are also presented in the study.**

***Index Terms*—Pulsed power; transient process; magnetoporation; inductor.**

I. INTRODUCTION

Application of pulsed power technologies for transdisciplinary research in areas such as material science, biomedicine, aerospace or plasma science has expanded widely in the past 25 years, accompanied by the development of new specific pulsed power setups to meet the requirements of the experiments [1], [2]. At the same time the technologies of high magnetic field generation are of particular interest, especially in the area of biotechnology, due to the capability of the contactless treatment [3], [4]. As a result, a new method of treatment of biological cells has been proposed recently, which results in transient contactless membrane permeabilization (magnetoporation), therefore is highly relevant in the area of drug delivery, DNA vaccination, cancer treatment or gene therapy [5], [6]. However, at the current state the availability of the high pulsed magnetic field generators (> 3 T) is low – there are no commercially available setups, while the existing self-made laboratory prototypes are typically stationary and not adaptable for biological experiments [7].

The most straightforward approach for development of a pulsed magnetic field generator is a spark gap switch based circuit topology, which discharges a high power capacitor through a multilayer inductor [8], [9]. However, this approach does not allow a flexible control of the pulse shape and the pulse is bipolar (fading sinusoidal oscillation), which further increases the complexity of interpretation of the biological effect [8]. A more sophisticated approach is to use a thyristor as switch, which introduces the capability to generate a half-sine pulse, while still offers only limited capability to control the pulse shape [10], [11]. Ultimately, application of IGBT's and MOSFET's is advantageous, however the high current (> 500 A) and voltage (> 2 kV) ratings, transient processes during pulse shaping (inductive load), all form a challenging electronics and electrical engineering problem. At the same time the capability to control the pulse amplitude (> 3 T), duration (microsecond range), number of pulses and pulse frequency, while maintaining the high dB/dt (rise time < 5 µs) should be introduced.

Therefore, in this work we design a flexible high magnetic field generator, which has a direct application in the area of magnetoporation. We optimize the circuit for inductive load handling by damping the transient processes (limiting the overvoltage and overcurrent), which allows application of an array of high power MOSFET switches.

II. IDENTIFICATION OF GENERATOR'S PARAMETERS

Biological effects of pulsed magnetic field (PMF) are pulse dependent [12], [13], therefore in this case the biological phenomenon (magnetoporation) determines and raises the requirements for a pulsed system that is needed for research. At the current state of knowledge, it is believed that the PMF permeabilization phenomenon is triggered by means of contactless induction of voltage on the cell membrane, causing electroporation [5], [12], [13]. Nevertheless, the dose-dependent pulsed magnetic field

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effect has been also confirmed [14], therefore the prototype should be capable to generate high magnetic field (range of several T) and feature a high *dB/dt* pulse (for induction of transmembrane voltage). At the same time the capability to control the pulse duration should be introduced for parametric study of the phenomenon, however taking into account the high energy of the pulses, the duration should be limited in microsecond range to prevent Joule heating [15].

Taking into account that the phenomenon is considered to be non-separable from conventional electroporation [14], the capability to control the frequency of pulse repetition should be also introduced [16], [17]. The summary of the generator's parameters is presented in Table I.

TABLE I. REQUIRED GENERATOR PARAMETERS.

Parameter	Value	Denotation	Units
Magnetic field	4–6	B	T
Current	900	I_P	A
Voltage	2000	U_C	V
Duration	10–100	T_P	µs
Pulse number	1–10	n	-
Repetition frequency	1–100	f	Hz
Volume	10	V	µl

The amount of energy that is required for pulsed magnetic field generation is dependent on the volume of effect [18]. Taking into account that the generator is developed for *in vitro* studies, the volume has been limited to 10 µl.

III. Development and Optimization of the Pulsed Generator

A. High Power Pulse Generator Structure

For high power pulse forming, an array of MOSFETs connected in parallel and series has been used. We have selected the APTM120U10SAG devices (Microsemi, USA) due to the high frequency performance, sub-microsecond range rise time and integrated three high power diodes in each module, which offers additional flexibility and introduces simplicity in the snubber circuit design. Series and parallel circuit connection topology has been selected in order to increase the voltage (up to 2.4 kV) and pulsed current (up to 938 A) of the generator. The principle circuit of the generator is shown in Fig. 1.

The generator consists of the 1 – high voltage power supply; 2 – power capacitors, where C1 = 4.7 mF and C2 = 100 µF; 3 – divider for voltage measurement; 4 – pulse shaping module; 5 – crowbar circuit; 6 – load and 7 – the control unit based on XMEGA (Atmel, USA) family 8 bit microprocessor. The load of the generator is a multilayer inductor with a plastic container for cells (L1) and a power resistor (R9 = 2.2 Ω) for maintaining the over damped circuit conditions.

B. Design of the Pulsed Inductor

The load of the generator is an inductor (Fig. 1, L1), however the structure of the inductor may vary, i.e. the number and cross-section of windings (Fig. 1, L1d), the inner (L1b) and outer diameter (L1a) and the height of final coil (L1c) may be altered, thus the generator should be suitable for handling different inductive loads. Typically, the loads in the 1 µH–4 µH range will be used. However, as it was mentioned above, during magneto-permeabilization both the high magnetic field amplitude and the induced electric field value are required.

Taking into account the maximum current value of 938 A, that is supported by the proposed generator, we have designed an inductor that will allow generation of magnetic field in the range of 4 T–6 T. The structure of inductor and the resulting pulsed magnetic field amplitude have been simulated using finite element method analysis [19] in COMSOL Multiphysics (COMSOL, Sweden).

It has been determined that the 4 layer coil structure with a total of 40 windings (0.35 mm wire) and 1.2 mm inner radius is sufficient to generate pulsed magnetic field in the range of 4 T–6 T. The resultant spatial magnetic field distribution and induced electric field inside the effective volume of the inductor are presented in Fig. 2.

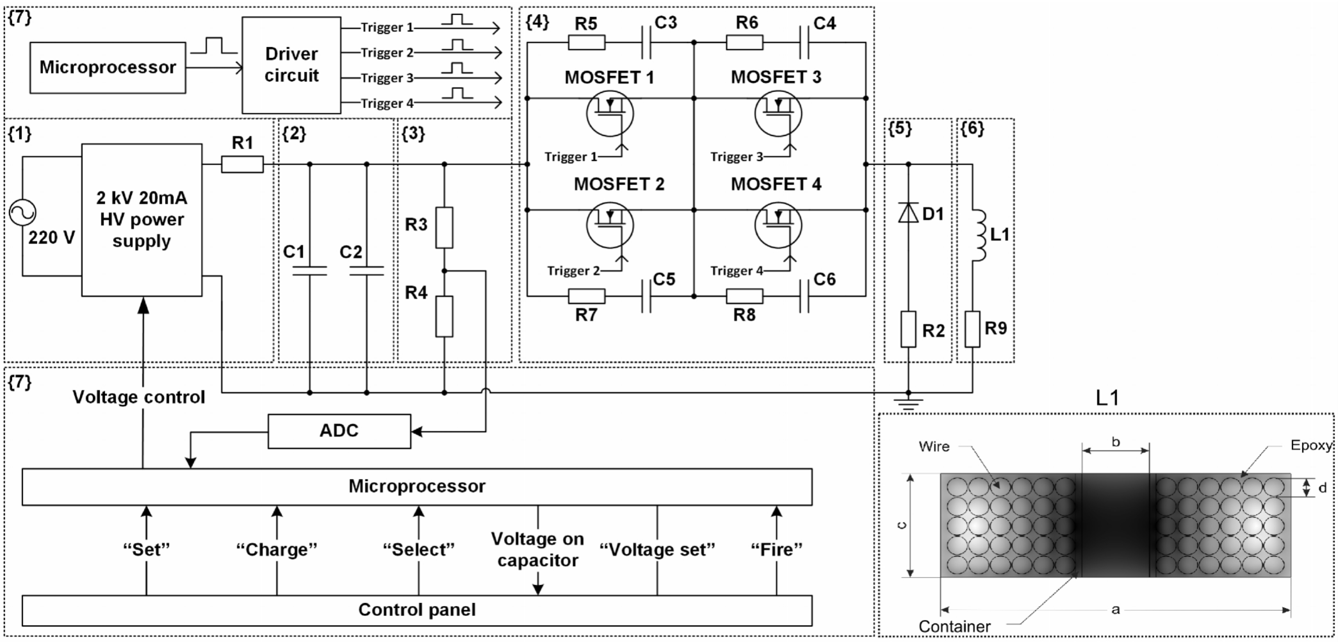

Fig. 1. The principle circuit of the pulsed magnetic field generator, where 1 – high voltage supply; 2 – power capacitors; 3 – divider for voltage measurement; 4 – MOSFET array; 5 – crowbar diode circuit; 6 – generator load; L1 – high magnetic field inductor.

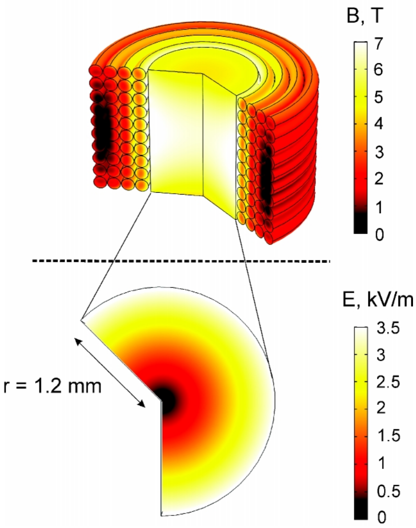

Fig. 2. Spatial distribution of the pulsed magnetic field (top) and the induced electric field distribution in the effective volume of the inductor (bottom); COMSOL Multiphysics model.

As it can be seen in Fig. 2 (bottom) the induced electric field value is in the range of 3.5 kV/m, which is sufficient for magneto-permeabilization studies [12].

A. Transient Process Compensation

The biggest challenge for high power (> 900 A, 2 kV) and high frequency inductive load switching is the control of the transient processes [20], [21], i.e. the damping of the reverse voltage and overcurrent. In our case the breakdown voltage is 2.4 kV, which creates only a 0.4 kV reserve for induced reverse-biased voltage on the MOSFETs.

Therefore, in order to estimate and compensate the overvoltage on the switches, the SPICE model of the generator was introduced, which corresponds to the principle circuit shown in Fig. 1 (SPICE model circuit not shown).

It has been decided that the RC snubber and crowbar circuit for overvoltage and overcurrent protection will be introduced. The maximum load of 4 µH for the model has been selected and the parametric analysis of the circuit was performed. The results are presented in Fig. 3.

It can be seen that the crowbar circuit allows controlling the fall time of the magnetic field pulses (Fig. 3(a)) and thus limit the *dI/dt*, which influences the reverse biased voltage in the inductor. Similarly, the RC snubber circuit allows controlling the pulse shape (Fig. 3(b)). The C3 = C4 = C5 = C6 = 0.33 µF were not altered.

The purpose of the proposed circuit combination is to limit the overvoltage on the MOSFETs (by limiting the *dI/dt* in the inductor) therefore the induced voltage on the switches with and without the proposed circuit has been evaluated and is presented in Fig. 3(c).

Based on the simulation results the snubber resistance of 15 Ω and the crowbar resistance of 5 Ω were selected, which allowed reducing the overvoltage on the switches to 0.25 kV (< 0.4 kV, which was reserved).

Based on the SPICE model results the prototype of the generator has been created.

IV. EXPERIMENT

The generator has been tested with a coil prototype, which was developed based on the COMSOL simulation results (Fig. 2). The coil has been wounded using 0.35 mm cross-section enameled copper wire and fixed with additional epoxy encapsulation (Fig. 1, L1).

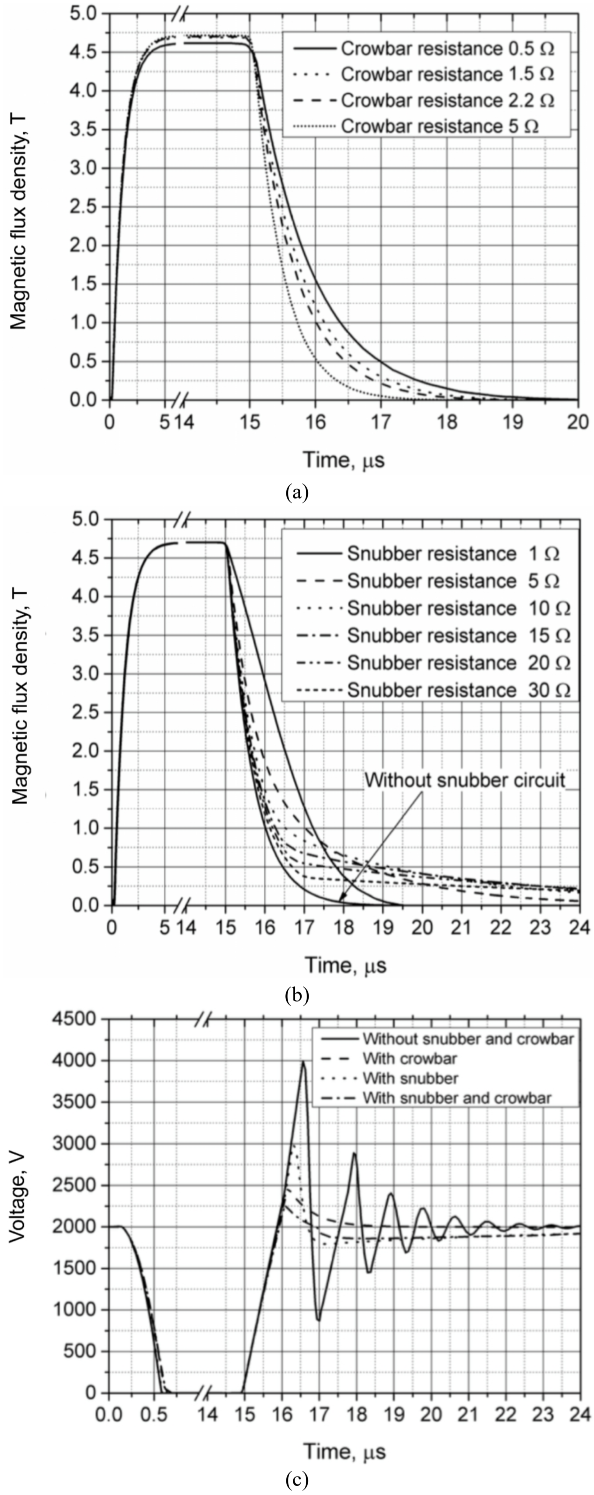

Fig. 3. Transient processes in the generator's circuit, where A: waveform dependence on the crowbar resistance; B: waveform dependence on the snubber resistance and C: the resultant induced overvoltage on the switches.

The effective inner volume of the coil was 15 µl, which is in agreement with the requirements that were set in the study (Table 1). As a container for the cells the sterile 0.1 ml PCR tubes (STARLAB International GmbH, Germany) have been used.

The coil has been connected as a load of the generator.

The proposed generator has been controlled with a microprocessor. The pulse amplitude, duration, repetition frequency and number of pulses could be controlled, which allowed flexible parametric analysis of the biological effects of pulsed magnetic fields.

The maximum duration of the pulse or sequence of pulses has been limited to 100 μs, mainly due to the Joule heating. The minimum duration of the pulse has been limited to 10 μs. Therefore, up to 10 pulses of 10 μs could be generated with a predefined pulse repetition frequency, which was limited in the 1 Hz–100 Hz range.

The resultant magnetic field pulse has been measured using a calibrated B-dot sensor, which was positioned in the center of the coil for the axial magnetic field measurement. For pulse acquisition the DPO4034 digital oscilloscope (Tektronix, Oregon, USA) was used, the data was post-processed using OriginPro software (OriginLab, Northhampton, MA, USA). The waveform is presented in Fig. 4.

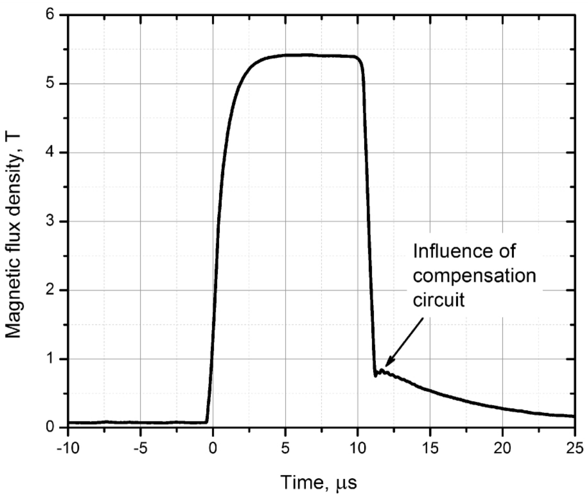

Fig. 4. Measured magnetic field pulse waveform.

As it can be seen in Fig. 4 the pulse has and amplitude of 5.5 T, which is in acceptable agreement with the simulation data. We believe that the difference in amplitude was influenced by the defects in the multilayer coil structure, i.e. the variation of pitch in the windings and different epoxy layer thickness between separate layers, which has a direct influence on the pulsed magnetic field value.

The applied snubber and crowbar circuitry allowed to successfully damp the transient process on the MOSFET, thus limit the overvoltage. However, as a trade-off the alteration of the pulse waveform due to the compensation circuit took place (see Fig. 4), which is in full agreement with the simulation data (see Fig. 3B).

V. CONCLUSIONS

We have designed a flexible pulsed magnetic field generator for biological applications, i.e. research of the magneto-permeabilization phenomenon. The generator circuitry has been optimized for inductive load handling and damping of the transient processes on the MOSFET switches. Subsequently, the proposed solutions allowed developing a system, which is capable of forming high power pulses (938 A, 2 kV) and generation up to 5.5 T magnetic fields in the multilayer inductor (4 layers, 40 windings) that has been also designed in the study.

We have adapted the inductor to be compatible with commercial plastic PCR vials for the cells. Even higher pulsed magnetic field can be generated with the setup, but the inductor structure should be changed, which in any case will be a trade-off between the effective volume, magnetic field amplitude and induced electric field.

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