High voltage pulse generation

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A new topology of a high voltage source with a variable output pulse pattern and featuring an independent adjustment of the magnitude, repetition frequency and pulse duration is presented. The power stage of the source consists of eight individual unipolar sources that can be arbitrarily connected in series to obtain the desired output voltage pulse of several amps and with extremely high du/dt.

Introduction: Owing to the tremendous increase of applications in oncology, genetics and cell biology, high voltage pulse sources capable of delivering AC or DC currents of several amps are the subject of intensive investigations. Several authors have reported that the application of short high voltage pulses transiently increases the permeability of the cell membrane [1–3]. The so-called electroporation, or electropermeabilisation, has become an effective tool for the internalisation of various molecules, especially anti-cancer drugs and gene material, into the biological cells. The efficiency of such applications depends on many parameters: defining the state of the cell, electrode type and, of course, the applied electric field [4]. The shape, and other parameters of the electric pulse (magnitude, pattern, duration, number of pulses and repetition frequency), are chosen so as to achieve a reversible electroporation with a minimum side effect on a cell. For *in vitro* and *in vivo* experiments on tumours and for gene therapy, rectangular electric pulses have proven to be the most advantageous. With the first, short ($\sim 100\,\mu s$) and high voltage pulses (300–1300 V) are used, whereas for the latter, longer (several ms) pulses of lower magnitude (100–250 V) are used. In both cases, it is often necessary to apply several pulses with a certain repetition frequency (from 1 Hz up to several kHz) to increase the efficiency of the permeabilisation. In these above-mentioned studies, special commercially available pulse voltage sources, electroporators [5], are used. Unfortunately, the flexibility of their pulse parameter settings is not sufficient, especially when the effect of different pulse parameters is to be investigated [6]. Another drawback appears owing to the lack of available energy when several high voltage (~ 1 kV), as well as high current (several amps) pulses with high repetition frequency, need to be delivered to the electrodes. The scope of this Letter is to present a new topology of a modular high voltage pulse source capable of delivering currents of several amps and fulfilling the demands for the flexible magnitude, pulse duration and repetition frequency setting.

Proposed topology: The proposed high voltage pulse source consists of several (n) individually controlled voltage sources, modules (Fig. 1). Their magnitudes form a binary logic-like set of values, where a particular source has the magnitude U_n twice as high as the predecessor ($U_n = 2 \cdot U_{n-1}$). The voltage of the individual source is constant and therefore at any instant available to participate in a generation of a common output pulse. With an appropriate control of output transistors T_1–T_n that operate as switches and connect the sources in series, a total of 2^n different output voltage levels with the resolution of U_1 are obtained. The total voltage range on the output of the combined source therefore spans from 0 V up to $U_1 \cdot (2^n - 1)$. Voltage sources that do not participate in the output voltage generation share no current, since the load current i_L is forced through their freewheeling diodes.

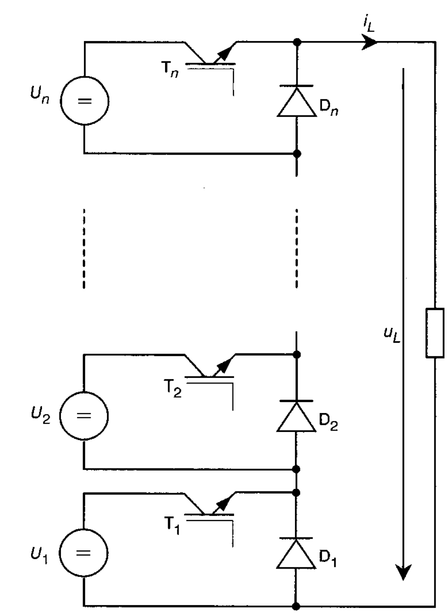

Fig. 1 *Modular high voltage source*

Rise and fall times of the pulse depend strictly on the speed of the power transistors used in the application. With the proposed solution, there is no additional delay, repetition frequency limit or nonlinearity-related problems on the output as is the case with the conventional solutions using a function generator-based input signal and analogue voltage and/or current amplifiers to generate the desired output pulse.

Table 1: Output parameters of modular high voltage source

Parameter	Value		
	Minimum	Maximum	Increment
Pulse magnitude	0 V	1275 V	5 V
Pulse duration	10 μs	10 ms*	10 μs
Number of pulses	1	20*	1
Repetition frequency	1 Hz	50 kHz**	
Pulse rise time		< 200 ns	
Pulse fall time		< 200 ns	
Pulse current		20 A	

*Parameter is software adjustable

**Value for 10 μs pulse; with longer pulses, the repetition frequency is adequately lower

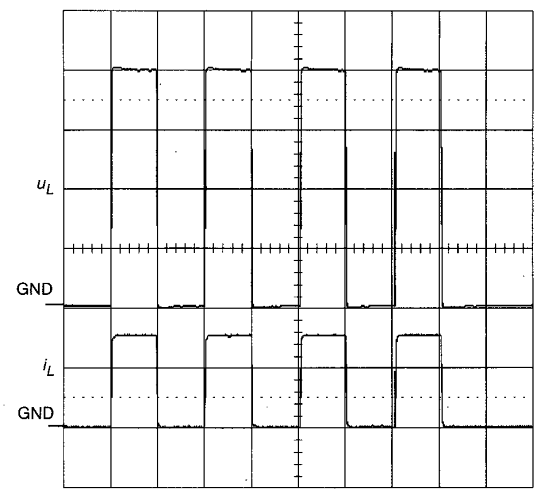

Fig. 2 *Train of four consecutive pulses at 5 kHz repetition frequency, magnitude 800 V, pulse duration 100 μs ($k_u = 200$ V/div, $k_i = 5$ A/div, $k_t = 100$ μs/div)*

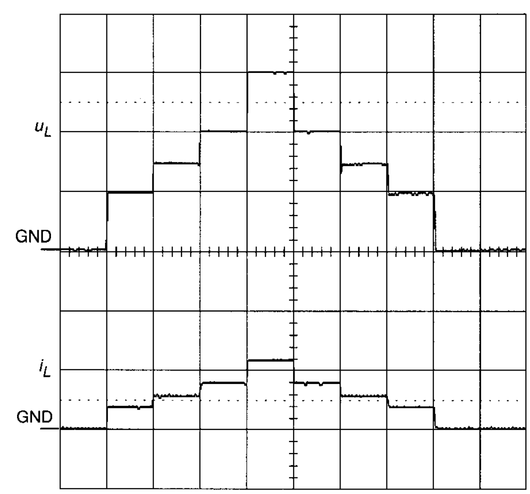

Fig. 3 *Load voltage u_L and current i_L ($k_u = 200$ V/div, $k_i = 5$ A/div, $k_t = 100$ μs/div)*

Performance: In the test setup, we used eight ($n = 8$) voltage sources with the first source magnitude set at 5 V, which is the origin point for each next source up to the magnitude of 640 V for the last source. With the series connection of all sources (5, 10, 20, 40, 80, 160, 320 and 640 V), the maximum magnitude on the output is 1275 V.

Control signals for the IGBT transistors T_1–T_8, which participate in the output pulse generation, are formed according to the pulse parameter specification using a supervisory personal computer (PC) and a subordinative microcontroller. In the latter, a specific application software directly controls the transistor drivers of the eight individual modules by activating each of the eight integrated digital outputs. The minimum pulse duration is therefore a subject of the microcontroller capability of generating the time-dependent control signals and, by all means, the speed of the IGBT transistor switches. In the experiment, the minimum pulse duration was set at 10 μs, thus enabling the maximum repetition frequency of 50 kHz. A complete list of the pulse parameter setting limits is given in Table 1.

The operational behaviour of the modular high voltage source was tested using a 100 Ω load resistor. Figs. 2 and 3 show typical voltage and current waveforms, demonstrating the versatility of the parameter settings and an outstanding dynamic performance of the proposed voltage source.

Conclusions: We have presented a novel method for generation of a high voltage and high power pulse with arbitrary magnitude, duration and repetition frequency. Owing to a modular power stage topology with preset magnitudes of a particular module, output pulses with extremely high *du/dt* were obtained. As shown by the experimental results, besides rectangular pulses with high repetition frequency, modulated pulses with arbitrary waveform can also be formed (Fig. 3). The experimental high voltage pulse source demonstrated an outstanding dynamic performance and is already being successfully used in the laboratory studies of the *in vivo* cell electropermeabilisation.

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