

Flexible Pulsed Power Generator to Create Wide Range of Pulses for Cancer Treatment

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Abstract: In this paper, a flexible pulsed power generator (FPPG) based on the solidstate Marx Structure is designed to create a wide range of pulses for cancer treatment. Pulse with different characteristics is needed to treat different samples depending on their type, dimensions, and impedance. Also, with the change in pulse widths, the pulse characteristics suitable for treatment change widely. With conventional semiconductor base Marx generators, due to the limitations in their rise time, current level, and impedance characteristics, it is not possible to generate a wide range of pulse characteristics, especially for low impedance loads. The FPPG by changing the connection mode of two Marx generators, can decrease the generator impedance for low impedance loads, increase the output current and voltage amplitude and repetition rate, and generate pulse width from nanosecond to several hundred microseconds. The simulation of FPPG in OrCAD-PSpice software shows its proper functioning.

Keywords: Bioelectric, Biomedical applications, Flexible pulsed power generator, Variable series-parallel Marx generator.

1 Introduction

I NDUCTION of the electroporation phenomenon on cells is one of the cancer treatment methods that have been used recently [1]. Applying an electric field to cells, by applying short and high-amplitude electrical pulses, increases the permeability of the cell membrane and creates holes in it which eventually leads to cell death that is called electroporation [2].

Most electroporation and bioelectric studies are focused on the effects of pulse electrical parameters, ignore environmental conditions such as culture and buffer, and select the cell culture medium and buffer according to the pulsed power generator conditions, resulting in a large number of different treatment protocols [3]. Also, in different studies, different values for the electrical impedance of cancer tissues and cells are mentioned and the different pulsed power generators are designed for loads with different impedance [4], [5]. The main reason for these differences in the impedance of the sample is the difference in the dimensions of the tissue and the treatment chamber, and the type of tissue and buffer which may have impedances from a few ohms to several hundred ohms.

The excitation frequency of the pulse is related to the inverse of the pulse width [6]. At different frequencies, different parts of the cell structure are excited [4]. Therefore, by changing the pulse width, the cell impedance is changed. Also, the deviations in the distance between the electrodes, changes in blood flow in the tissue, and tissue movement can lead to changes in the impedance of the sample during treatment [7].

As a result, the appropriate pulse characteristics (voltage and current amplitude, width, repetition rate and the number of pulses) of the treatment can be very different according to the different conditions

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mentioned. Therefore to have a sufficient effect on the treatment under different conditions, a pulsed power generator must have a flexible enough structure to be able to generate a wide range of pulse parameters [8].

To adapt the pulse generator to the application of cancer treatment, different flexible structures have been proposed in different studies [3], [5], [9]-[13]. A pulse generator is designed based on a switchable capacitor array and a SiC MOSFET switching array [9]. With this design, pulses with a width of 100 ns to 100 μ s can be achieved. In this study, the minimum load impedance of 50 Ω is considered, while in this application, loads with lower impedance are possible. The main limitations of pulse formation lines and networks are the limited pulse width, the impossibility of increasing the pulse amplitude, and the limitation in applying appropriate pulses to loads with an impedance different from the impedance of the generator. To match the pulsed power generator impedance to loads with impedance lower than 50 Ω , parallel transmission lines have been used [3], [10]. Three microstrip transmission lines with 10, 50, and 133 Ω impedances have been used to create flexibility for impedance matching of the pulse generator and load [11]. Solid-state linear transformer drivers (SSLTD) bipolar circuit topology is proposed for electroporation to aggregate voltage and current [12]. SSLTDs are suitable for generating short pulses and for applications with low impedance loads. In this design, due to the saturation of the transformer, a pulse width of up to 8 μ s is possible.

Marx generator with the modular and simple structure it will be easily possible to increase the pulse voltage amplitude and change the pulse width. A Marx generator is designed based on semiconductor switches capable of generating bipolar pulses for cancer treatment [5]. In this design, 100-ohm load impedance is considered. Also, a flexible design of a pulse generator with the structure of two Marx generators in series together is presented for medical application [13]. In this structure, due to the rise time limitation of the semiconductor switches, it will not be possible to generate narrow pulses.

With decreasing load resistance, pulse voltage and power efficiency are decreased for solid-state Marx generators [14]. In the Marx generator, in applications with very low load impedance, parallelization of Marx generators will be necessary to reduce the characteristic impedance of the generator and to apply the maximum voltage and power [15], [16]. If the generator impedance is not small enough, the total output voltage of the generator will not be applied to the load and the applied waveform will be affected. As the load impedance decreases, the load voltage drop and waveform distortion become more acute. The most important limitation of Marx conventional structures is the impossibility of generating narrow pulses [9], [17]. It has been shown that for a Marx generator based on semiconductor switches, the pulse rise time increases by decreasing the load resistance (increasing the generator current) [14]. This is due to the dependence of the rise time of the semiconductor switches on their current passing through. Therefore, in cancer treatment applications whit a low impedance load and increased current, conventional Marx generators cannot create narrow pulses and apply pulses with designed specifications, especially with the appropriate voltage, power, and waveform.

By parallelizing Marx generators, in addition to the possibility of reducing the characteristic impedance of the generator, the current applied by each generator is also reduced, by dividing the current between the two generators. So that by reducing the current of each generator, the rise time of the switches located on each stage of the Marx generator is reduced, as a result of which it is possible to produce narrow pulses.

Another limitation of Marx generators is the need to increase the capacity of the capacitors to increase the energy level to generate wide pulses. Large capacitors increase the parasitic inductance and reduce the compression of the circuit [9]. It is more difficult to produce short pulses with this structure.

In this paper, due to the importance of the electrical characteristics of the sample, impedance spectroscopy was performed. Then, a flexible pulsed power generator (FPPG) based on a variable seriesparallel Marx generator (VSPMG) is designed. The flexibility in the FPPG structure is obtained by changing the connection mode of the two Marx generators from series to parallel and vice versa. In series connection mode, the FPPG can increase the output voltage. In parallel connection mode, the FPPG can decrease the generator impedance and increase the output current for low impedance loads. To reduce the effects of parasitic inductance, the capacitance of Marx stages is chosen small enough. The pulse aggregation in the parallel connection mode is used to generate wide pulses or high repetition pulses. This structure is capable to generate a wide range of appropriate pulses for

cancer treatment, especially for low impedance applications of it.

2 Impedance Spectroscopy of Cell

The electrical model of a cell is justified by the capacitance property of the cell membrane and the resistance property of the cytoplasm [4]. In this paper, the impedance spectroscopy of human cells under different buffers has been performed with the Agilent impedance analyzer model 4395A and a standard connector (Agilent 16192A fixture) at a frequency of 1 to 100 MHz with electroporation cuvettes. According to Eq. (1), the frequency of 1 MHz to 100 MHz will be approximately equal to the excitation frequency of pulses with a width of 3 ns to 300 ns [6, 18]. Where f is the pulse excitation frequency and T is the pulse width.

$$f = \frac{1}{\pi \times T} \tag{1}$$

2.1 Impedance Spectroscopy of the Bone and Lung Cancer Cell

The impedance spectroscopy of the bone cancer cell (MG 63) suspension and RPMI buffer in a standard 2 mm cuvette is shown in Fig. 1. In addition to, the impedance spectroscopy of lung cancer (MRC5) and normal (A549) cell suspensions in RPMI and DMEM buffers, and RPMI and DMEM pure buffers in a 1 mm cuvette is shown in Fig. 2. These measurements confirmed the results of the other similar studies [13, 18].



Fig. 1 The impedance of MG 63 and RPMI buffer in 1 mm cuvettes. (a) impedance magnitude, (b) impedance phase.



Fig. 2 The impedance of MRC5, A549, RPMI and DMEM in 2 mm cuvettes. (a) impedance magnitude, (b) impedance phase.

2.2 RC Series Model of Cells

In this paper, the RC series model according to Fig. 3 is proposed for load including the cuvette and its contents. In this method, in each pulse width, the values of parameters R and C are selected according to the excitation frequency of the pulse width.



Fig. 3 The RC series model of the sample.

The purpose of the RC Series model is to provide a simple and accurate enough model to design and simulate a pulsed power generator. Since cancer tissue and cells have capacitive and resistance properties, with this model under different frequencies or pulse widths, the values of resistance and capacitance are calculated and their values are used to design and simulate the pulse generator in various pulse widths. Table 1 lists the values of the series RC model parameters of cell samples at different excitation frequencies and their corresponding pulse widths.

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Pulse Width (ns)		3	10	100	200	300
Frequency (MHz)		100	31.8	3.18	1.59	1.06
MG63+ RPMI (2 mm)	R (Ω)	8.83	9.59	10.1	10.29	10.73
	$X(\Omega)$	-0.4	-0.37	-0.96	-1.24	-1.95
	C (nF)	4	13	52	80	77
RPMI (2 mm)	R (Ω)	9.4	10.23	10.76	10.95	11.41
	$X(\Omega)$	-0.46	-0.4	-1	-1.3	-2.05
	C (nF)	3.5	12	50	77	73
MRC5+ RPMI (1 mm)	R (Ω)	7.67	8.22	8.3	8.31	8.33
	$X(\Omega)$	-0.22	-0.01	-0.99	-0.14	-0.26
	C (nF)	7	575	50	715	577
MRC5+ DMEM (1 mm)	R (Ω)	9.86	10.75	10.86	10.87	10.9
	$X(\Omega)$	-0.98	-0.42	-0.14	-0.17	-0.29
	C (nF)	1.6	12	358	590	518
A549+ RPMI (1 mm)	R (Ω)	8.8	9.16	9.23	9.24	9.27
	$X(\Omega)$	-0.25	-0.14	-0.16	-0.22	-0.39
	C(nF)	6.4	36	312	455	385
A549+ DMEM (1mm)	R (Ω)	9.58	9.85	9.95	9.97	10.02
	$X(\Omega)$	-0.16	-0.1	-0.02	-0.29	-0.52
	C (nF)	10	50	2384	345	289
RPMI (1 mm)	R (Ω)	12.62	13.5	13.64	13.65	13.71
	$X(\Omega)$	-1.46	-0.57	-0.27	-0.36	-0.63
	C (nF)	1	9	185	278	238
DMEM (1mm)	R (Ω)	96.6	10.25	10.35	10.38	10.44
	$X(\Omega)$	-0.48	-0.22	-0.23	-0.31	-0.54
	C (nF)	3	23	217	323	278

Table 1 The RC Series Model Parameters of the Samples

As shown in Table 1, low impedance loads of about 8 ohms are expected in this application. In addition, depending on the other conditions mentioned about samples, the possibility of the smaller impedance of the samples will not be far from expectation.

3 Structure of FPPG

The FPPG must be able to generate a wide range of suitable pulses for cancer treatment under all conditions of samples. Changing the impedances and dimensions of the load will change the voltage and current required for effective treatment. Therefore, the VSPMG is proposed as shown in Fig. 4 (a). Each of the Marx generators in VSPMG is based on the solid-state Marx generator [19]. Fig. 4 (b) shows the charging mode of the capacitors of two Marx generators, which are charged through diodes and the closing switches at the bottom of each floor. The VSPMG is possible to select the series connection (SC) mode and the parallel connection (PC) mode of two Marx generators.

3.1 The SC Mode of Marx Generators

The SC mode of Marx generators shown in Fig. 5 will be possible to increase the pulse voltage amplitude to generate stronger fields for large dimension samples. The advantage of using two Marx n-stage generators in series compared to a 2n-stage Marx generator is to increase the voltage efficiency of its generated pulse due to a decrease in the charge path impedance.



Fig. 4 The VSPMG consist of two Marx generator. (a) Schematic of the main circuit, (b) Charging mode of two Marx generators.



3.2 The PC Mode of Marx Generators

In the PC mode shown in Fig. 6 (a), two n-stage Marx generators are parallel to each other and their generated pulses are aggregated. In this mode, two aggregation cases can be achieved due to the simultaneous or non-simultaneous pulses applied to the load by two generators.

A: Simultaneous Pulses (SP) Case

In the SP case shown in Fig. 6 (b), the pulses generated by the two Marx generators are applied to the load simultaneously and without a time difference. In this case, in the treatment of samples with low impedance, the equivalent impedance of the generators in parallel will be reduced, so it is possible to create pulses with the appropriate voltage, power and waveform.

In the SP case, by reducing the load impedance, the required current amplitude increases, due to the current limiting of semiconductor switches, the parallelization of Marx generators can be useful [20]. Also, the current of the load is divided between the two Marx generators, and the current passing through the switches of each Marx generator will be reduced. As a result, the rise time of the switch is reduced, and it will be possible to generate narrow pulses.

B: Non-Simultaneous Pulses (N-SP) Case

In the N-SP case shown in Fig. 6 (c), considering the appropriate time between the pulses applied by the two Marx generators, only the pulses of one of the Marx generators are applied to the load at a time. In this case, one of the Marx generators will be in charge mode and the other in discharge mode of its capacitors. In the N-SP case, due to the choice of the different time difference between the application of pulses of two generators, it is possible to produce both interconnected and consecutive pulses.

Interconnected pulses: if the time interval between the pulses generated by the two Marx generators is equal to the width of these pulses, a

pulse with twice the width is applied to the load. By increasing the number of pulses of each Marx generator, it will be possible to increase the pulse width to several times the pulse width generated by each Marx generator. The low-width pulses of the two Marx generators are combined to generate highwidth pulses. This will be very effective in reducing the required capacitance of Marx stages. In this method, the charging time of the capacitors must be less than the width of the applied pulses.





In conventional Marx structure, the choice of large capacitance to store sufficient energy and to maintain the voltage amplitude during high-width pulses is essential. In the proposed structure of the pulsed power generator, by reducing the capacitance required by each Marx stage, in addition to reducing the parasitic inductance of the capacitor, the circuit is also more compact and as a result, the parasitic inductance of the overall circuit is reduced and faster pulses can be generated. It should be noted that as the Marx stages capacitance decreases, the pulse repetition rate also increases due to the reduced charging time of the capacitors.

Consecutive pulses: if the time interval between the output pulses of the two Marx generators is greater than the width of these pulses, consecutive pulses are applied to the load. In this method, when a pulse is applied by one generator, the other generator is charging its capacitors. It will increase the number and the repetition rate of the pulses.

3.3 The Process of Changing the Connection Mode of Marx Generators

To change the connection mode of Marx generators in the VSPMG from series mode to parallel mode and vice versa, three switches U_1, U_2 and U_3 are used according to Fig. 4(a). The task of these switches is to create the ground connection required for the two types of series and parallel connections of Marx generators. switches U_1 , U_2 and U_3 are selection switches of the connection modes of the Marx generators. If U_1 is closed and U_2 and U_3 are opened, the two Marx generators are in the SC mode according to Fig. 5. In this mode, two Marx generators with n stages operate similar to a 2n stages Marx generator. And if U_1 is opened, and U_2 and U_3 are closed, the two Marx generators will operate in the PC mode according to Fig. 6 positively polarized pulses are applied from the terminal B of the lower Marx generator.

In the N-SP case, each time the generated pulse by one of the Marx generators is applied to the load. So, the selection switches must connect the load to one of the generators and disconnect from the others at a suitable time and alternately. Therefore, using the same Marx stages switch for switches U_1, U_2 and U_3 would be the most appropriate choice for similar performance with Marx stages switches in terms of rise time and turn-on delay time. Since in both SC and SP mode, a maximum voltage equal to the voltage of a Marx generator is applied to these switches, so to withstand the applied voltage, it will be necessary to use several switches in series with the minimum number equal to Marx stages.

3.4 The Advantages of the VSPMG

The SC mode is used to apply the high voltage pulses. The parallel connection mode of Marx generators is used to 1- adapt the impedance of the generator for low impedance loads, 2- increase the current level, and 3- aggregate the pulses of the two generators for generating either wide pulses or high repetition rate pulses. The capabilities of the proposed structure in different modes are shown in Fig. 7 which indicate its high flexibility and the optimal use of Marx generator stages.



Fig. 7. The capabilities of the FPPG in different modes.

The benefits of the proposed structure include:

- 1. The possibility to generate narrower and more square pulses, the ability to apply more current, and impedance matching of the generator and low impedance loads, in the SP case of the PC mode.
- 2. The possibility to increase the repetition rate of pulses by adding the pulses generated by each Marx generator in consecutive pulses of the N-SP case of the PC mode.
- 3. The possibility to generate high-width pulses by adding the low-width pulses generated by each Marx generator in interconnected pulses of the N-SP case of the PC mode.
- 4. The possibility of reducing the parasitic inductance of the circuit due to the reduction of the capacitance required and the more compact circuit by using interconnected pulses in the N-SP case of the PC mode to create high-width pulses.
- 5. The possibility to generate pulses with higher voltage magnitude and increase the output voltage efficiency in the SC mode.
- 6. By increasing the number of parallel Marx generators to more than two generators, due to the reduction of current switches, it is possible to generate narrower pulses by using switches with lower tolerable current but faster (Generalization of the proposed structure).

4 Marx Generators Design

The VSPMG will be able to generate narrow and high voltage and current pulses. For a 6-stage Marx generator, a DC power supply with a maximum voltage of 600 V can create a suitable voltage amplitude. This structure, in parallel mode, can generate a pulse with a voltage of about 3.6 kV and in series mode, it can generate pulses up to a voltage of 7.2 kV. According to the mentioned conditions, the IGBT switch model APT90GF100JN with a tolerable voltage of 1000 V and a continuous tolerable current of up to 90 A, and the rise time of a few tens of nanoseconds will be used as Marx generator switches.

The capacitance of each capacitor is determined from Eq. (2) according to the load resistance and pulse time as well as the amount of allowable voltage drop across the pulse [19].

$$C_N = \frac{C}{N} \ge \frac{\tau \times V_0}{\Delta V_d \times R_L} \tag{2}$$

That in Eq. (2) *C* is the capacitance of each capacitor, *N* is the number of capacitors and C_N is the equivalent capacitance, R_L is the load resistance, V_0 is the pulse voltage, ΔV_d is the maximum allowable voltage drop, and τ is the pulse length. The capacitance to maintain the voltage amplitude during the pulse is determined according to the maximum width of the desired pulse.

Since with the PC mode of Marx generators with the aggregation of generated low-width pulses of two Marx generators, it will be possible to generate high-width pulses. In this case, when a pulse is applied by one generator, the other generator is charging the capacitors. Therefore, the maximum capacitance is selected only for a pulse width of 1 μ s. Finally, to generate pulses with a width greater than 1 μ s, the pulses generated by the two Marx generators are combined and high-width pulses will be generated. It will be possible to achieve a pulse width of several hundred microseconds.

The minimum possible impedance of the sample load (1 mm and 2 mm cuvette) at pulses width higher than several microseconds will be about 100 Ω [13, 18]. Assuming a load impedance of 100 Ω , due to the increase in impedance of load with increasing pulse width and the maximum allowable voltage drop equal to 10%, the minimum capacitance of each stage according to Eq. (2) will be calculated equal to 600 nF. The capacitance of Marx stages will be selected equal to 1 μ F.

4.1 Control System and Drive Circuit

Proper operation of the control system and drive circuit will have a great impact on rise and fall time, width pulse, and repetition rate. The control signal generated by FPGA (Altera Company's Cyclone IV series EP4CE6F17C8) is suggested for this design. In the control circuit, it will be possible to use a fiber optic system including an HFBR2521Z optical receiver, HFBR-1521Z optical transmitter, and HFBR-RUS100Z optical cable. The control signal is transmitted to the drive circuit via optical fiber, which also prevents a high-voltage invasion. The drive circuit then converts the control signal to a positive amplitude voltage of 15 V, which has the same time as the control signal to turn the switches on or off. In order not to interfere with the performance of the generator and switches, a small

dead band (a few nanoseconds) is applied between the gate signal applied to the two switches of the Marx stages. Finally, a driver that fits the switches will be necessary for use in this structure to obtain short rise and fall times.

5 Simulation of FPPG

To show the performance of the proposed structure under different conditions, it will be simulated in OrCAD-PSpice software. In this simulation, the resistor of the gate switches was 1 Ω and the voltage source applied to it was 15 V. In all simulations, the impedance load is considered according to the actual conditions. In the following, the simulation results related to different connections mode of generators in different load conditions will be mentioned. In the simulations, the load is modeled as the RC series equivalent circuit according to Table I and the results of the other studies [13, 18]. In the performed simulations, the delay time of 10 nanoseconds is considered as the delay of the control system and the driver circuit.

5.1 Simulation Results in SC Mode

In applications that require high voltage pulses, it is possible to connect the two Marx generators in series, to increase the voltage amplitude of the pulses. In Fig. 8, a 100 ns pulse with a voltage of about 7.2 kV has been applied to the RC series load $(R = 100 \Omega, C = 800 \text{ nF})$ in the SC mode of Marx generators. These pulses are generated using a power supply voltage of 600 V. In this case, the applied voltage was the sum of the voltages of the two generators. The operation will be suitable for generating a pulse width of several microseconds for high impedance loads. The SC mode is used for high impedance applications to increase the pulse voltage amplitude and create a suitable electric field for the tissue.



5.2 Simulation Results in PC Mode

In Fig. 9, a 100 ns pulse with a voltage of about 2.4 kV has been applied to the RC series load (R =

8.3 Ω , C = 50 nF), in the SP case of the PC mode, without applying a time difference between the pulses generated by the two Marx generators. Also, in figure 10, the rise time of the pulse in figure 9 is shown. These pulses are generated under a DC power supply voltage of 400 V. In this case, the total current of low impedance load is applied by two generators that it cased to reduce the current of the stage switches. Thus, the rise time of the switches has been reduced to less than 30ns and the pulse is square and has an acceptable rise and fall time.



Fig. 9 A 100 ns pulse in SP case of PC mode, applied to the RC series load ($R = 8.3 \Omega$, C = 50 nF).



Fig. 10 The rise time of a 100 ns pulse in SP case of PC mode (the pulse is show in figure 9), applied to the RC series load ($R = 8.3 \Omega$, C = 50 nF).

In Fig. 11 and 12, the VSPMG operates in the N-SP case of the PC mode, with applying a time difference between applying the pulses generated by the two Marx generators. These pulses are generated under a DC power supply voltage of 200 V.



Fig. 11 A 2 μ s interconnected pulse in N-SP case of PC mode, applied to the RC series load ($R = 100 \Omega$, C = 800 nF).



Fig. 12 Two 100 ns consecutive pulses in N-SP case of PC mode, applied to the RC series load ($R = 8.3 \Omega$, C = 50 nF).

In Fig. 11, two pulses of 1 μ s have been applied to the RC series load (R= 100 Ω , C = 800 nF) as an integrated pulse of 2 μ s. In this case, the time difference between applying the pulses of the two Marx generators is 1 μ s, equal to the generated pulse width of each Marx generator. As can be seen, at the simulation time of 1.2 μ s, the pulse of the second Marx generator is applied to the load and the voltage drop across the first pulse is neutralized. With this method, it will be possible to generate wide pulses up to a few hundred microseconds by aggregating a larger number of pulses. Depending on the load impedance, it is possible to increase the pulses voltage amplitude to several kilovolts by increasing the voltage of the DC power supply.

In Fig. 12, two pulses of 100 ns have been applied to the RC series load ($R = 8.3 \Omega$, C = 50 nF). The first pulse is generated by one of the Marx generators and the second pulse is generated by the other. In this case, the time difference between applying the pulses of the two Marx generators is greater than the width of the generated pulse by them and about 250 ns. This time determines the repetition rate of the pulses and the least amount of it depends on the required time to charge the capacitors of the Marx stages. Due to the selection of the capacitors with a small capacity, for each pulse, the capacitors are charged quickly, and therefore pulses without voltage drop are generated even by increasing the number of pulses. Also, the advantage of this method is the increase in pulse repetition rate.

5.3 Simulation Results with Parasitic Parameters

Parasitic parameters such as inductances and capacitances related to the connections and elements that appear in the circuit seriously affect the waveform and fall time of the output pulse of the Marx generator. Parasitic inductances include series inductances of storage capacitors and inductances of connections, and parasitic capacitances include capacitances between Marx stages and earth and capacitance of two electrodes and the load between them. To consider these parasitic parameters in simulations, 10 nH inductors series with DC source, 15 nH inductors series with capacitors of each Marx stage, and 20 pF capacitors for each Marx stage in parallel to the earth are considered [19].

According to the proposed PC mode of Marx generators using capacitors with smaller capacities, it is possible to generate wide pulses by adding lowwidth pulses. The use of capacitors with smaller capacities will reduce the series parasitic inductance of the capacitors and further compress the circuit, and as a result, reduce the inductance of the Marx generators circuit. As a result, it will be possible to generate smoother pulses with less fall time. The results of simulation in SC and PC modes of Marx generators are shown in Fig. 13. Finally, to reduce the effect of the parasitic parameters, in the manufacturing process, efforts are made to compress the circuit as much as possible.



Fig. 13 A 100 ns pulse to the RC series load ($R = 100 \Omega$, C = 800 nF) considering parasitic parameters (line: SC mode, and dotted line: PC mode).

6 Conclusion

Loads of pulsed power generator in medical applications are tissues or cell suspension inside treatment chambers (cuvettes). Due to the strong dependence of the pulsed power generator structure on the load, the pulsed power generator design has been done according to the real loads. In this research, by presenting the RC series model, the impedance of the cells will be achieved in frequencies proportional to the applied pulse width, and these impedances are used for the design and simulation of the pulsed power generator.

In this paper, an FPPG with a structure based on Marx generators with semiconductor switches is presented. In the FPPG, by changing the connection of two Marx generators in series and parallel with each other, the possibility of generating a wide range of pulses is provided. In fact, in cancer treatment, due to the existence of many variables in the treatment conditions and the need for unique and appropriate pulse characteristics, the proposed structure has increased the flexibility against these variables. Also, the pulse aggregation cases generate wide pulses or higher repetition rate pulses. The FPPG can create a wide range of pulse parameters by the conditions affecting the treatment for clinical and research applications of cancer treatment. Finally, the FPPG, in addition to the possibility of using semiconductor switches in the generation of narrow pulses (several nanoseconds), is possible to generate the suitable pulses for applications with variable load impedance especially applications with low impedance loads in cancer treatment.

Intellectual Property

The authors confirm that they have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing to publication, with respect to intellectual property.

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A. Aziznia: Idea & Conceptualization, Research & Investigation, Analysis, Software and Simulation.
M. S. Akhavan Hejazi: Idea & Conceptualization, Project Administration, Revise & Editing, Supervision

Declaration of Competing Interest

The authors hereby confirm that the submitted manuscript is an original work and has not been published so far, is not under consideration for publication by any other journal and will not be submitted to any other journal until the decision will be made by this journal. All authors have approved the manuscript and agree with its submission to "Iranian Journal of Electrical and Electronic Engineering".

References

- N. Jourabchi, K. Beroukhim, B. A. Tafti, S. T. Kee, and E. W. Lee, "Irreversible electroporation (NanoKnife) in cancer treatment," *Gastrointestinal Intervention*, Vol. 3, No. 1, pp. 8-18, 2014.
- [2] Y. Lv, X. Cheng, S. Chen, H. Liu, Y. Wang, C. Yao, and B. Rubinsky, "Analysis of the Electric Field-Dependent Current During Electroporation Pulses," *IEEE Access*, Vol. 8, pp. 93850-93856, 2020.
- [3] W. H. Baldwin, B. W. Gregory, C. J. Osgood, K. H. Schoenbach, and J. F. Kolb, "Membrane permeability and cell survival after nanosecond pulsed-electric-field exposure—significance of exposure-media composition," *IEEE*

Transactions on Plasma Science, Vol. 38, No. 10, pp. 2948-2953, 2010.

- [4] R. Kageyama, Y. Kobayashi, K. Tamura, K. Saito, and Y. Minamitani, "Difference of cell death of budding yeast for frequency components of pulsed electric field," *IEEE Transactions on Plasma Science*, Vol. 44, No. 5, pp. 877-884, 2016.
- [5] L. Redondo, M. Zahyka, and A. Kandratsyeu, "Solid-state generation of high-frequency burst of bipolar pulses for medical applications," *IEEE Transactions on Plasma Science*, Vol. 47, No. 8, pp. 4091-4095, 2019.
- [6] A. Silve, A. G. Brunet, B. Al-Sakere, A. Ivorra, and L. Mir, "Comparison of the effects of the repetition rate between microsecond and nanosecond pulses: Electropermeabilizationinduced electro-desensitization?" *Biochimica et Biophysica Acta (BBA)-General Subjects*, Vol. 1840, No.7, pp. 2139-2151, 2014.
- [7] C. Bernal, Ó. Lucía, H. Sarnago, J. M. Burdío, A. Ivorra, and Q. Castellví, "A review of *pulse* generation topologies for clinical electroporation." *In Iecon 2015-41st Annual Conference of the IEEE Industrial Electronics Society*, pp. 000625-000630, 2015.
- [8] S. Romeo, M. Sarti, M. R. Scarfi, and L. Zeni, "Modified Blumlein pulse-forming networks for bioelectrical applications," *The Journal of Membrane Biology*, Vol. 236, No. 1, pp. 55-60, 2010.
- [9] X. Rao, X. Chen, J. Zhou, B. Zhang, and Y. Alfadhl, "Design of a high voltage pulse generator with large width adjusting range for tumor treatment," *Electronics*, Vol. 9, No. 6, pp. 1053, 2020.
- [10] Y. Mi, C. Bian, J. Wan, J. Xu, C. Yao, and C. Li, "A modular solid-state nanosecond pulsed generator based on Blumlein-line and transmission line transformer with microstrip line," *IEEE Transactions on Dielectrics and Electrical Insulation*, Vol. 24, No. 4, pp. 2196-2202, 2017.
- [11] S. Romeo, C. D'Avino, O. Zeni, and L. Zeni, "A Blumlein-type, nanosecond pulse generator with interchangeable transmission lines for bioelectrical applications," *IEEE Transactions* on *Dielectrics and Electrical Insulation*, Vol. 20, No. 4, pp. 1224-1230, 2013.
- [12] G. Sun, X. Wang, S. Shen, L. Li, T. Shang, and W. Ding, "All-solid-state bipolar pulsed generator based on linear transformer driver and push-pull circuit," *Review of Scientific Instruments*, Vol. 92, No. 9, pp. 094709, 2021.

- [13] A. L. Garner, A. Caiafa, Y. Jiang, S. Klopman, C. Morton, A. S. Torres, A. M. Loveless, and V. B. Neculaes, "Design, characterization and experimental validation of a compact, flexible pulsed power architecture for ex vivo platelet activation," *PLoS One*, Vol. 12, No. 7, pp. e0181214, 2017.
- [14] C. Yao, X. Zhang, F. Guo, S. Dong, Y. Mi, and C. Sun, "FPGA-controlled all-solid-state nanosecond pulse generator for biological applications," *IEEE Transactions on Plasma Science*, Vol. 40, No. 10, pp. 2366-2372, 2012.
- [15] H. Akiyama, and R. Heller, Bioelectrics: Springer, 2017.
- [16] H. Bluhm, and M. Sack, "Industrial-scale treatment of biological tissues with pulsed electric fields," *In Electrotechnologies for extraction from food plants and biomaterials*, *New York NY: Food Eng. Rev Springer.*, pp. 237-269, 2009.
- [17] F. Song, F. Li, B. Zhang, M. Zhu, C. Li, G. Wang, H. Gong, Y. Gan, and X. Jin, "Recent advances in compact repetitive high-power Marx generators," *Laser and Particle Beams*, Vol. 37, No. 1, pp. 110-121, 2019.
- [18] A. Silve, R. Vezinet, and L. M. Mir, "Nanosecond-duration electric pulse delivery in vitro and in vivo: experimental considerations," *IEEE Transactions on Instrumentation and Measurement*, Vol. 61, No. 7, pp. 1945-1954, 2012.
- [19] S. Dong, C. Yao, N. Yang, T. Luo, Y. Zhou, and C. Wang, "Solid-state nanosecond-pulse plasma jet apparatus based on Marx structure with crowbar switches," *IEEE Transactions on Plasma Science*, Vol. 44, No. 12, pp. 3353-3360, 2016.
- [20] Z. Li, H. Liu, S. Jiang, L. Guo, and J. Rao, "A high-current all-solid-state pulse generator based on Marx structure," *IEEE Transactions* on Plasma Science, Vol. 48, No. 10, pp. 3629-3636, 2020.



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