THE WIDEBAND ULTRASONIC PULSER FOR SONOPORATION

L. Svilainis[1], A. Chaziachmetovas[1], R. Jurkonis[2], D. Kybartas[1], N. Lamanauskas[3] and S. Satkauskas[3]

[1]Signal processing department, Kaunas University of Technology,
Studentu str. 50, LT-51368 Kaunas, Lithuania
[2] Biomedical Engineering Institute, Kaunas University of Technology,
Studentu str. 65, LT-51369 Kaunas, Lithuania
[3] Department of Biology, Faculty of Natural Sciences, Vytautas Magnus University.,
Vileikos str. 8. LT-44404, Kaunas, Lithuania

T. +370 37 300532; F. +370 37 753998;E. linas.svilainis@ktu.lt / rytis.jurkonis@ktu.lt / darius.kybartas@ktu.lt / andrius.chaziachmetovas@ktu.lt / nlamanauskas@gmail.com / s.satkauskas@gmf.vdu.lt

Abstract

The transient nature of membrane permeability requires extensive study to develop the most efficient sonoporation parameters: the ultrasound energy, frequency content or signal shape. Other investigators use the arbitrary function generator and linear RF power amplifier. We consider such setup expensive and oversized. More compact design can be achieved if binary or unipolar pulser is used in excitation. Dedicated hardware was developed and the performance investigated. We achieve up to 500 Vpp voltages, frequencies beyond 3 MHz, ability to have both unipolar and bipolar pulses, burst lengths up to 40 periods and pulse repetition frequency up to 3 kHz on transducers with capacitance of 3000 pF.

1. INTRODUCTION

Sonoporation has some advantages over electroporation in modifying the permeability of the cell membrane for drugs or foreign genes delivery: nonbactericidity, safety, ability for specific volume are named [1]. It is assumed that the acoustic field causes the inertial cavitation which in turn develops some microstreaming facilitating the membrane permeability. Alternative hypothesis propose that microbubble's rupture can be the cause of the sonoporation. Assuming that excitation parameters can be fine tuned to inhibit the most bioeffective [2,3] oscillations, there is a need for extensive study to develop the most efficient sonoporation parameters: the ultrasound energy, frequency content or signal shape. Such experiments where the arbitrary function generator and linear RF power amplifier are used we consider expensive and oversized. More compact design can be achieved if binary/unipolar pulser is used for excitation. Design of the dedicated electronics hardware and performance investigation is presented below. Such system could be applied for ultrasound contrast agent microbubble properties investigation.

2. PULSER REQUIREMENTS

Results of Apfel and Holland presented in [4] indicate that at 1 MHz frequency the inertial cavitation threshold is 0.25 MPa of peak negative pressure; 0.6 MPa at 5 MHz and 0.85 MPa at 10 MHz. Assuming high ultrasonic transducer impedance and low coupling, we aimet at to achieve the variable, up to 300 V output voltages, frequencies beyond 3 MHz, ability to have both unipolar and bipolar pulses, burst lengths up to 40 periods and pulse repetition frequency up to 3 kHz for relatively high capacitance (up to 3000 pF) transducers. Experimental system (Figure 1) used hydrophone HNP-1000 from Onda and digital storage oscilloscope Yokogawa DLM2054 for sound pressure waveforms registration.

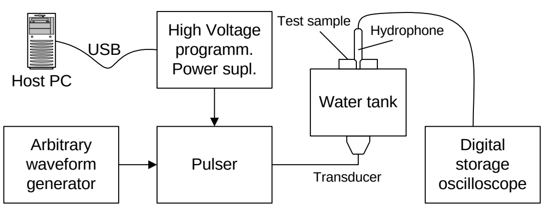

Figure 1. Hardware setup

The excitation signal generation was planned to be performed by arbitrary waveform generator generating low voltage CW bursts. These signals were fed into pulser input and positive and negative waves selected to drive different output channels. Our own design high voltage source was used for excitation voltage supply.

3. TOPOLOGY SELECTION

Main part of the piezoelectric transducer impedance is capacitive. This capacitance has to be charged and discharged every excitation cycle. Then, half bridge topology with two active elements (Figure 2, left) should offer and advantage in achieving both high efficiency and high frequencies.

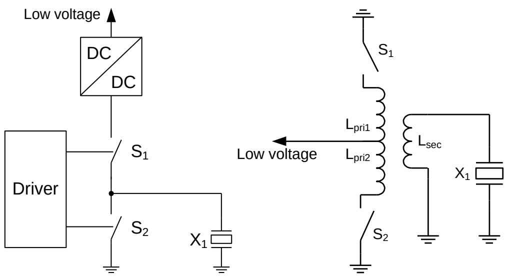

Figure 2. Half bridge (left) and transformer push-pull (right) topologies

Such topology was presented in [5], where also the analysis and theory for components selection is given. But driving the high side switch presents a challenge: high *dV/dt* will be present on floating driver. Therefore, such topology is limited to 3-4 MHz operating frequencies. Though, it has an advantage in achieving high excitation voltages [6]. Another, transformer coupled push-pull topology (Figure 2, right), is using only low side drivers and transformer coupling [7].

On the other hand such design requires (Figure 3) careful transformer construction and material selection.

Figure 3. Pulser photo

But the result is the simple and compact design.

3.1. High voltage source

The high voltage power source was designed using a DC/DC converter CA05P from EMCO. Main control tasks including consumed current, supply voltage monitoring, USB connectivity, and control know encoder servicing, indication is accomplished (Figure 4) by MSP430 microcontroller. Whole high voltage source is encapsulated into separate box and power supplied from 24V wall-plug SMPS.

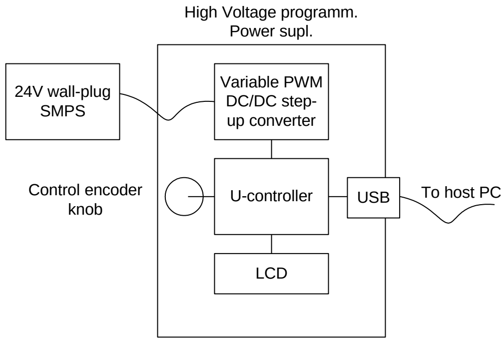

Figure 4. Programmable high voltage power source structure

Voltage control is either manual, using control know (Figure 5) or via USB interface.

Figure 5. High voltage source photo

Such design allow for reuse of the high voltage source.

4. EXPERIMENTAL PULSER PERFORMANCE EVALUATION

Comparison to commercially available standalone sonoporation generator from Medelcom was performed. Same load and operation conditions were used: 3 MHz at 50 Ω and 3nF load at 500 Vpp programmed voltage. Results for 50 Ω output are presented in Figure 6.

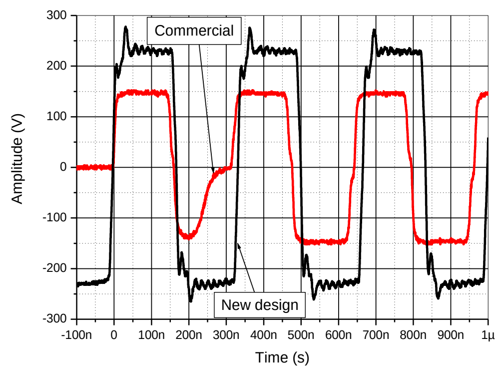

Figure 6. Generators output comparison at 50 Ω load

It can be seen that commercial device does not adhere to the frequency stability requirement. Furthermore, output voltage is lower than specified in control software.

Refer Figure 7 for generators output for 3000 pF load case.

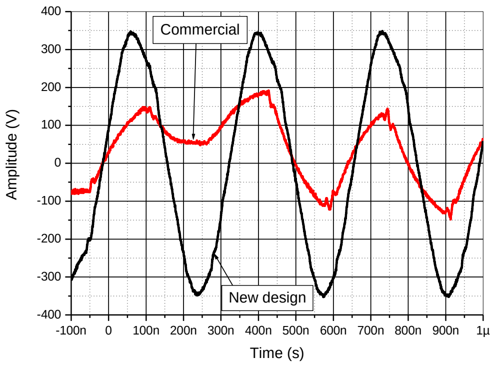

Figure 7. Generators output comparison at 3000 pF load

Results indicate that commercial device is not capable to deliver the signal to capacitive load. New design pulser is capable of programmed output delivery.

5. CONCLUSIONS

Push-pull topology with symmetric transformer output was used. Such approach allows for N-channel MOSFETs application for both positive and negative wave, avoiding complicated high side driver structure. New solution allows for high voltage yet high speed pulse trains generation into capacitive load. Voltages up to 500 Vpp and frequencies *beyond* 3 MHz can be achieved. Pulser is capable of both unipolar and bipolar pulses, burst lengths beyond 40 periods and pulse repetition frequency up to 3 kHz on transducers with capacitance up to 3000 pF.

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