

High Frequency Electroporation for Biomedical Applications Using GaN Gate Injection Transistors

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Abstract—Electroporation is a promising technique for cancer treatment consisting on applying a high electric field in order to induce selective cell death in those tumors with difficult treatment with alternative therapies. In order to achieve successful results, recent studies have discovered the need of high voltage and high frequency pulses to achieve the desired results without neurostimulation. This paper takes advantage of advances in GaN devices to build a high frequency generator for biomedical applications of electroporation. To achieve the desired performance, the latest generation of Gate Injection Transistors from Panasonic has been used in the experimental prototype.

Index terms—Wide band-gap devices, Gallium Nitride, Electroporation.

I. INTRODUCTION

Electroporation [1, 2] consist on applying an electric field to living tissues in order to generate biological changes that may be temporary or permanent (Fig. 1). If the applied electric field is low, typically $< 1\text{ kV/cm}$ for mammalian cells, the phenomena is reversible, and it can be used to improve drugs absorption or gene therapy. When the electric field is higher, $> 1.5\text{ kV/cm}$ in mammalian cells, the process is irreversible and leads to cell apoptosis, i.e. tissue death [3]. The latter technique, called irreversible electroporation (IRE) [4, 5] can be used as an effective non-thermal treatment for tumors with difficult access where other therapies are not appropriate, such as liver or pancreas cancer. Besides, IRE has additional benefits compared with radiofrequency or microwaves ablation in terms of recovery time and treatment of highly irrigated areas.

Currently, research on IRE is severely constrained by the limitations of commercially available generators, which limit the maximum voltage, current and frequency. Besides, recent studies have highlighted the need of high-voltage and high-frequency generators in order to obtain the desired effects while avoiding undesirable neurostimulation [6]. These techniques are known as high frequency IRE (H-FIRE) [7] or ultrasteep IRE and require the use of high-voltage short pulses, typically in the range of $1\ \mu\text{s}$, an/or high dv/dt to avoid undesired muscular stimulation and

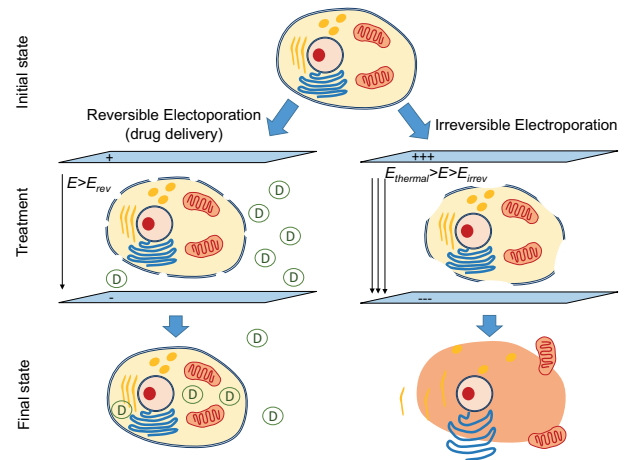


Fig. 1. Electroporation: (a) reversible and (b) irreversible phenomena.

amplify the biological effects in cells. Considering these requirements, current technology relying in silicon devices do not meet the requirements to provide the required generators for research and clinical purposes.

In order to enable new and promising therapies, this paper takes advantage of the latest generation of Gate Injection Transistors from Panasonic [8, 9] to design and implement a high-voltage and high-frequency generator for biomedical applications of electroporation. A structure providing high-voltage fast-transitions is proposed and built, and the preliminary experimental results prove the feasibility of this proposal.

The remainder of this paper is organized as follows. Section II present the proposed power converter taking advantage of GIT GaN devices. Section III shows the main implementation and experimental results, including transition details as well standard treatment pulse delivery. Finally, Section IV summarizes the main conclusions of this paper.

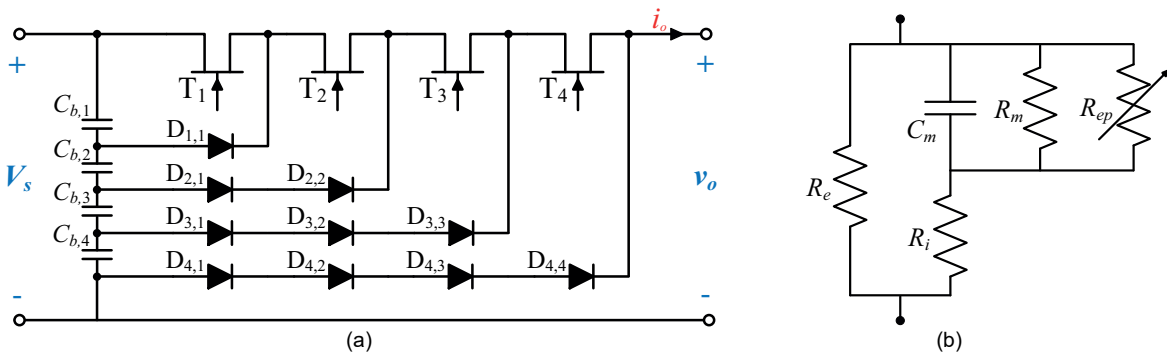


Fig. 2. Proposed power converter (a) and electrical equivalent of the electroploration load (b).

II. HIGH-VOLTAGE GATE INJECTION TRANSISTORS

Power electronics plays a major role in many biomedical applications [10] and it is essential to enable new IRE therapies. The proposed power converter topology aims at providing faster high-voltage generators to enable research on H-FIRE therapies. Wide bandgap devices (WBG) [11, 12] will be fundamental in these advances due to its superior performance in terms of higher blocking voltage and faster switching.

Fig. 2 (a) shows the proposed converter to achieve high-voltage high-frequency operation. It is based on a multi-level approach which, in combination with latest high-voltage GaN devices, obtains the required output voltage. In this paper, a 4-level converter is considered, where each device, T_i , D_i , C_i must block only 1/4 of the output voltage. Consequently, this structure enables to provide high voltage output while using fast GaN devices. Besides, the development of high-voltage GaN devices significantly improves the benefits of this proposal.

Fig. 2 (b) shows the electrical equivalent of the electroploration load. Essentially it behaves as a capacitive load during transitions, with a time constant in the range of 0.1-1 μ s, and a variable parallel resistance R_{ep} which depends on the electroploration process. This resistance R_{ep} decreases during the electroploration process, increasing the current through the devices and serving as an indicator of the electroploration process.

Fig. 3 shows the main expected converter waveforms during the electroploration process. During the IRE treatment, pulse width, frequency, and burst configuration are variable parameters to consider in order to optimize the electroploration process. Typically, in H-FIRE treatments pulses in the range of μ s are grouped in pulse trains with tens of pulses, with a frequency of 1 to 10 Hz to avoid thermal damage [13].

In this application, it is essential to ensure high frequency operation as well as high dv/dt to provide the

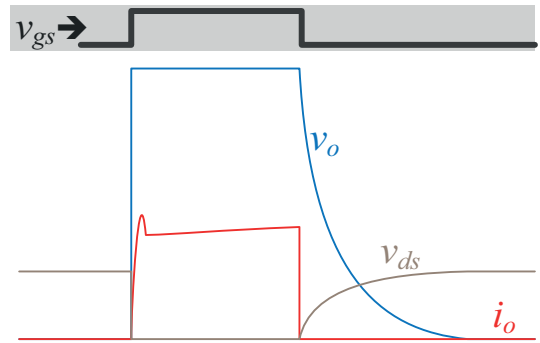


Fig. 3. Main converter waveforms.

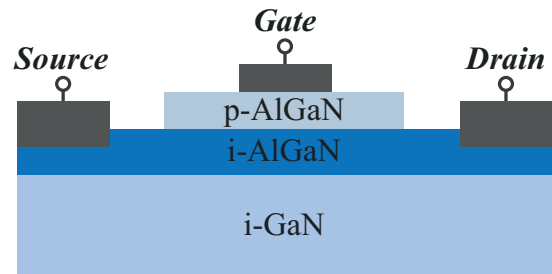


Fig. 4. Gate Injection Transistor© device from Panasonic.

required electrical field without neurostimulation. These requirements are in line with recent advances in high-voltage GaN devices [14-16], which enables smooth high frequency operation up to 650 V with increasing levels of output current capability. In this paper, the latest version of Gate Injection Transistors [17] from Panasonic has been used Fig. 4, which are an evolution of HEMT transistors with optimized performance avoidance of current collapse issue.

III. IMPLEMENTATION AND EXPERIMENTAL RESULTS

In order to prove the feasibility of this proposal, an experimental prototype has been designed and built. 600-V and 30-A PGA26F04DV devices from Panasonic have been selected, which exhibits a remarkable 40 mΩ and 470 pF C_{oss} . To enable a versatile control and generation of variable modulations, an FPGA is used to control the converter.

Fig. 5 shows a 3D render of the experimental prototype whereas the main experimental results obtained during IRE experiments with plant cells are shown in Fig. 6 and Fig. 7. Firstly, Fig. 6 (a) and (b) show the intentionally slow turn-on transition to avoid overcurrent as well as the fast turn-off transition typical of GaN devices. Besides, Fig. 6 (c) and (d) show the proper operation with single 9-μs and 1-μs pulses. Finally, Fig. 7 shows the proper operation of the converter with different train pulses used in IRE therapies. These results prove the proper operation of the power converter and opens new possibilities for future cancer therapies using irreversible electroporation.

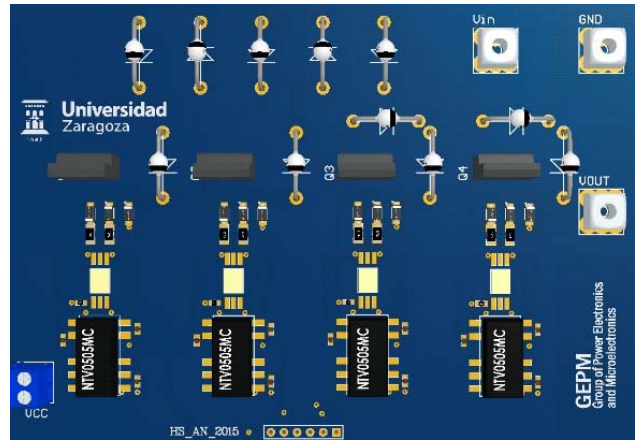


Fig. 5. 3D render of the experimental prototype.

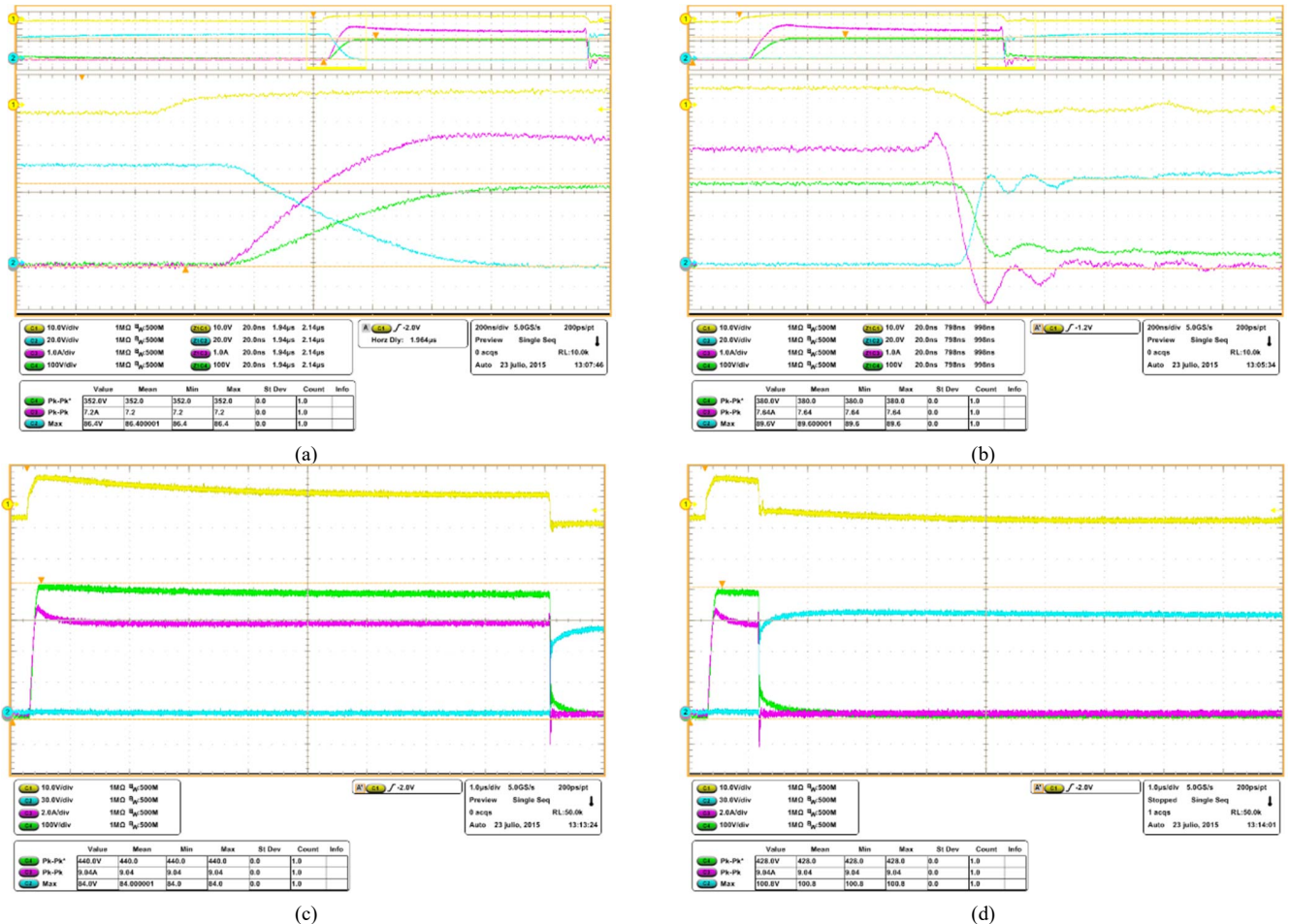


Fig. 6. Main experimental results using electrodes in an electroporation experiment with plant cells and single pulse.

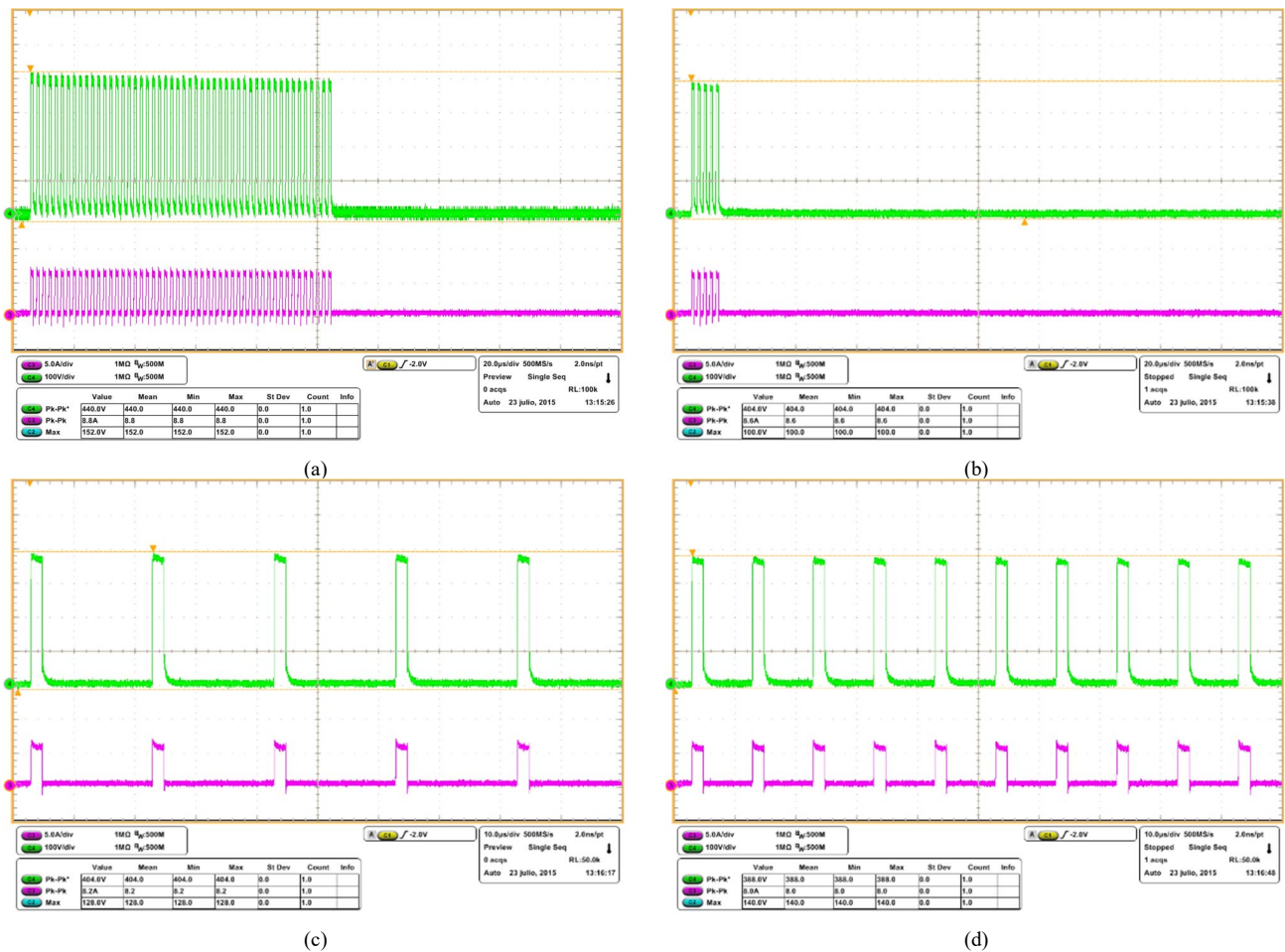


Fig. 7. Main experimental results using electrodes in an electroporation experiment with plant cells and several train pulses.

IV. CONCLUSIONS

In this paper, a high-voltage and high-frequency GaN-based generator for irreversible electroporation has been presented. The proposed design enables improved performance and advanced modulations taking advantage of the latest GaN GIT technology, enabling promising IRE therapies. The proposed design has been implemented and tested experimentally, proving its correct operation and suitability for biomedical applications of electroporation.

ACKNOWLEDGMENT

This work was partly supported by the Spanish MINECO under Project TEC2016-78358-R and Project PI17/00468, and by the DGA-FSE.

REFERENCES

- [1] J. C. Weaver and Y. A. Chizmadzhev, "Theory of electroporation: A review," *Bioelectrochemistry and Bioenergetics*, vol. 41, no. 2, pp. 135-160, 1996.
- [2] T. Y. Tsong, "Electroporation of cell membranes," *Biophysical Journal*, vol. 60, no. 2, pp. 297-306, 8// 1991.
- [3] M. C. Junquera *et al.*, "Electron microscope evaluation of irreversible electroporation on the liver in a porcine model," *Histology and Histopathology*, vol. 32, no. 1, p. 125, 2017.
- [4] A. Ivorra, "Tissue Electroporation as a Bioelectric Phenomenon: Basic Concepts," in *Irreversible Electroporation*, B. Rubinsky, Ed. (Series in Biomedical Engineering: Springer Berlin Heidelberg, 2010, pp. 23-61.

- [5] A. Ivorra and B. Rubinsky, "Historical Review of Irreversible Electroporation in Medicine," in *Irreversible Electroporation*, B. Rubinsky, Ed. (Series in Biomedical Engineering: Springer Berlin Heidelberg, 2010, pp. 1-21.
- [6] J. Chunlan, R. V. Davalos, and J. C. Bischof, "A Review of Basic to Clinical Studies of Irreversible Electroporation Therapy," *IEEE Transactions on biomedical Engineering*, vol. 62, no. 1, pp. 4-20, 2015.
- [7] C. Yao *et al.*, "Bipolar Microsecond Pulses and Insulated Needle Electrodes for Reducing Muscle Contractions during Irreversible Electroporation," *IEEE Transactions on Biomedical Engineering*, vol. PP, no. 99, pp. 1-1, 2017.
- [8] Y. Uemoto *et al.*, "Gate Injection Transistor (GIT)-A normally-off AlGaIn/GaN power transistor using conductivity modulation," *IEEE Transactions on Electron Devices*, vol. 54, no. 12, pp. 3393-3399, 2007.
- [9] H. Sarnago, O. Lucía, and J. M. Burdío, "Advanced induction heating appliances using high-voltage GaN Gate Injection Transistors," in *IEEE Applied Power Electronics Conference and Exposition*, 2015, pp. 1375-1380.
- [10] B. Grzesik and M. Stepień, "Power electronics in biomedical applications - An overview," in *Power Electronics and Motion Control Conference (EPE/PEMC), 2012 15th International*, 2012, pp. LS5a.1-1-LS5a.1-4.
- [11] X. She, A. Q. Huang, O. Lucia, and B. Ozpineci, "Review of Silicon Carbide Power Devices and Their Applications," *IEEE Transactions on Industrial Electronics*, vol. PP, no. 99, pp. 1-1, 2017.
- [12] H. Sarnago, O. Lucía, and J. M. Burdío, "A comparative evaluation of SiC power devices for high performance domestic induction heating," *IEEE Transactions on Industrial Electronics*, vol. 62, no. 8, pp. 4795-4804, August 2015.
- [13] B. López-Alonso *et al.*, "Electro-thermal modeling and characterization of irreversible electroporation of large tissues for cancer treatment," in *World Congress on Electroporation & Pulsed Electric Fields in Biology, Medicine, food and environmental Technologies*, 2017.
- [14] D. Reusch and J. Strydom, "Evaluation of Gallium Nitride Transistors in High Frequency Resonant and Soft-Switching DC-DC Converters," *Power Electronics, IEEE Transactions on*, vol. 30, no. 9, pp. 5151-5158, 2015.
- [15] D. Reusch and J. Strydom, "Understanding the Effect of PCB Layout on Circuit Performance in a High-Frequency Gallium-Nitride-Based Point of Load Converter," *Power Electronics, IEEE Transactions on*, vol. 29, no. 4, pp. 2008-2015, 2014.
- [16] Z. Xu, W. Zhang, F. Xu, F. Wang, and L. M. Tolbert, "Investigation of 600 V GaN HEMTs for high efficiency and high temperature applications," in *IEEE Applied Power Electronics Conference and Exposition*, 2014.
- [17] Y. Uemoto *et al.*, "Gate Injection Transistor (GIT)-A Normally-Off AlGaIn/GaN Power Transistor Using Conductivity Modulation," *IEEE Transactions on Electron Devices*, vol. 54, no. 12, pp. 3393-3399, 2007.