A Novel Device for In-Vitro Electromagnetic Modulation

Bryon Eckert[1], Huan Truong[1] and Mina Izadjoo[2]
[*]Trideum Biosciences, Frederick, MD, USA, mizadjoo@trideumbiosciences.com
[**]Chiscan LLC, Tempe, AZ, USA, bryon@chiscan.com

ABSTRACT

Numerous published papers have noted biological effects based on the modulation frequency of plasma and radio frequency fields, as well as the frequency of electric and magnetic near-field emitters. However, clinical studies in energetic medicine are difficult to justify because the physical mechanism behind the biological interaction is not well understood. Clinical studies are also very expensive and the protocol for selecting an optimum frequency is poorly defined. These problems can be mitigated by studying a bacterial, fungal or viral culture *in vitro* in the laboratory. An array of 96 emitting elements is placed underneath a 96 well culture plate. The array is connected to an FPGA, which generates a set of 96 separate frequencies simultaneously. This speeds the frequency search. The array is also thermally controlled to incubate the culture. Arrays are designed for non-thermal plasma, RF 2.4 GHz, electric, magnetic and optical (LED) stimulation.

Keywords: plasma, electromagnetic, in vitro, incubate, biological

1 INTRODUCTION

Previous authors have noted biological effects and cancer therapies based on the modulation frequency of non-thermal plasma [1], modulation frequency of an RF carrier [2], frequency of an electric near-field emitter [3], and pulse frequency of LED light sources [4].

Modern experiments echo the earlier work of Royal Rife, but clinical studies are difficult to justify because the physical mechanism behind the biological interaction is not well understood.

Clinical studies are also very expensive and the protocol for selecting an optimum frequency is poorly defined. These problems can be mitigated by studying a bacterial, fungal or viral culture *in vitro* in the laboratory, to create a more solid foundation for the science.

The key to reducing the cost of laboratory study in a frequency search is to apply many different frequencies to the culture simultaneously. A good starting point for laboratory use is a standard 96 well culture plate. The instrument should be designed to incubate the culture as well as apply modulated energy to each well.

A picture of the modulation array instrument with 96-well culture plate is shown in Figure 1.

Figure 1: Modulation Array

The modulation array instrument is designed with a common set of electronics for the following:

- power supply
- memory card socket (for managing control and test data in the laboratory)
- thermal control
- user interface (2 x 20 character OLED and buttons)
- RS-485 communications for connecting multiple units to a PC via MODBUS
- Square wave signal generation on up to 96 signal lines

A block diagram of the modulation array instrument is shown in Figure 2. The array and associated electronics are thermally coupled to a heat sink, with thermoelectric device (TEC, for heating or cooling) and fan.

The heat sink and internal electronics are thermally insulated from the case. The fan draws in air from the bottom of the case, past the heat sink and up past the culture tray on top.

Multiple temperature sensors are used for thermal control, including a sensor on the array element module, a sensor on the metal enclosure, and a sensor on the heat sink.

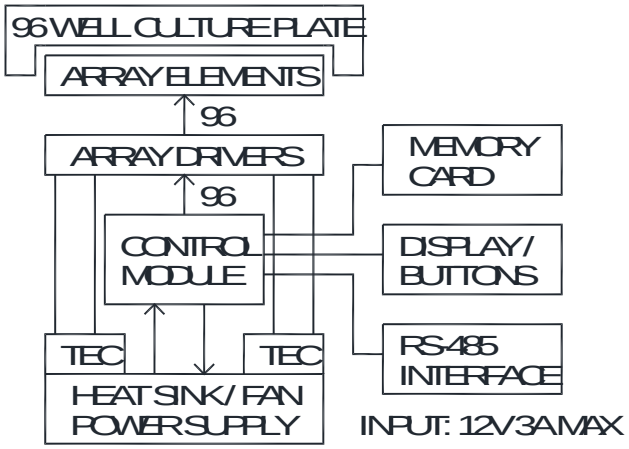

Figure 2: Modulation Array Block Diagram

The FPGA is a Xilinx Artix 7. Each signal generator is implemented in VHDL code as a phase accumulator, or numerically controlled oscillator (NCO). The output consists of the most significant bit of the phase accumulator.

Using only a single bit of the output will add deterministic phase jitter, but allows us to easily define 96 units with reasonable FPGA resources. Using a 200 MHz clock and both edges of the clock, the peak timing uncertainty will be ± 2.5ns.

A typical output frequency will be in the audio range but may go higher. Since the jitter is deterministic, it will manifest as discrete spectra rather than noise and we expect that it will not significantly degrade biological interaction.

2 ARRAY ELEMENTS

There are five different array options:

- 2.4 GHz RF
- electric field
- magnetic field
- LED
- non-thermal plasma

2.1 RF Array

The RF array element is a resonant structure consisting of a printed spiral inductor and series capacitor, which presents a good impedance match at 2.44 GHz. This is not an efficient antenna since most of the power is dissipated in the spiral structure, but it is meant to couple near field energy into the culture well above it.

The matching is relatively narrowband, and the RF frequency may be adjusted to get an optimum match. A circuit for measuring the forward and reverse power on a single element is included, on the assumption that all the other elements will be very similar.

The antenna array is a separate circuit board, fitting inside the bottom well of the culture tray. Below this is a thermal pad to transfer heat through the array driver to the tray.

The array driver consists of a large number of Wilkinson power splitters, RF switches and load resistors. The digital signals from the FPGA are routed to this module and create a distinct modulation frequency underneath each well.

The RF array driver also contains a TCXO and frequency synthesizer, as well as amplifiers and attenuators for controlling the RF level. The power into the modulation section is -10dBm to +17dBm, but the maximum radiated power from the array is expected to be about 1 mW.

2.2 Electric Field Array

The electric field array is a separate circuit board, fitting inside the bottom well of the culture tray. Below this is a thermal pad to transfer heat through the array driver to the tray.

The array driver consists of a set of high voltage amplifiers generating 190V p-p up to 100 kHz. The peak electric field in the culture well should be ± 100V/cm, decreasing to zero in the center of the cell.

The electric field array driver also contains a voltage boost converter to generate the 200V bias for the amplifiers. It is possible to redesign the driver for lower voltages and higher frequencies. For example, 5V AHCT logic would operate past 50 MHz, with a field strength similar to a current cancer therapy.

2.3 Magnetic Field Array

The magnetic element consists of a ferrite bar, with a length of 7.5mm and diameter of 0.8mm. The coil winding around the bar consists of 200 turns of #36 wire, presenting about 100uH of inductance.

The magnetic field array is a separate circuit board, fitting inside the bottom well of the culture tray, functioning mainly to hold the tops of the ferrite bars. It also contains a temperature sensor. Below this is a thermal pad to transfer heat through the array driver to the tray.

The moderate permeability (ui=125) of the ferrite bar will tend to efficiently couple higher harmonics generated by the driving waveform. The duty cycle of the driving waveform is adjusted to produce a DC bias of 2mA at 5V.

A circuit for monitoring DC bias is connected to a single element, on the assumption that all elements are similar. A calibration routine will determine the required duty cycle for a given frequency.

The heat spreading plate, which is used to conduct heat past the controller board over to aluminum blocks (which conduct heat down to the thermoelectric devices), is constructed of Aluminum Nitride. This keeps metal farther away from the ends of the inductors.

2.4 LED Array

The LED array is a single module, with the LED lenses inside the well of the culture tray. A thermal pad may be added around the LEDs to improve thermal transfer to the tray.

The LEDs are 1206 package with lens. A wide variety of wavelengths are available, from NIR 850nm to UV 395nm.

The LED drivers are designed to run at a fixed current. The average power can be reduced by adjusting the duty cycle.

2.5 Plasma Array

The non-thermal plasma array is a separate circuit board, fitting inside the bottom well of the culture tray. Below this is a thermal pad to transfer heat through the array driver to the tray. This is designed to be replaced by the user at the end of its useful life.

The plasma array driver requires multiple lines from the FPGA to control the plasma driver and high voltage transformer, so there are a total of 24 drivers. Each driver is connected to a set of 4 micro-plasma arrays, which sit underneath the culture wells.

Each set of plasma arrays presents a capacitance of about 20pF. This capacitance resonates with the plasma drive transformer, and the plasma drive frequency is expected to be about 250 kHz.

The plasma modulation frequency is adjusted inside the FPGA up to 10 kHz. The plasma tends to run at a fixed current, and a duty cycle of 10% is recommended to reduce average power and extend the array life.

3 SOFTWARE

Software for the modulation array will generate frequency and temperature control data as part of the research program. At a minimum, this will all be stored in a database, and written to a memory card as well.

Since the lab technician is most likely preparing, staining and monitoring the cultures, handling the data cards as well is a convenient way to run the program.

The software keeps track of program frequencies used. In the case of an observed effect, the location of the modulation frequencies can be shuffled by the software and repeated to see if the effect in the culture is repeatable.

If a large number of arrays need to be managed, connecting up to 128 units in an RS-485 daisy-chain is relatively straightforward. The units set their addresses automatically, and use the MODBUS protocol. The interface is designed so the unit which is first in the cable chain from the PC has the lowest address, and the subsequent units have sequentially higher addresses.

REFERENCES

[1] M Alkawareek, Q Algwari, G Laverty *et al*, "Eradication of Pseudomonas aeruginosa Biofilms by Atmospheric Pressure Non-thermal Plasma," PloS One 7(8), e44289, 2012.

[2] J. Zimmerman, H. Jimenez, M. Pennison, I. Brezovich, D. Morgan, A. Mudry, F. Costa, A. Barbault and B. Pasche, “Targeted treatment of cancer with radiofrequency electromagnetic fields amplitude-modulated at tumor-specific frequencies,” Chinese Journal of Cancer, 32-573, 2013.

[3] M Giladi, R Schneiderman, T Voloshin, Y Porat, M Munster, R Blat, S Sherbo, Z Bomzon, N Urman, A Itzhaki, S Cahal, A Shteingauz, A Chaudhry, E Kirson, U Weinberg & Y Palti, “Mitotic Spindle Disruption by Alternating Electric Fields Leads to Improper Chromosome Segregation and Mitotic Catastrophe in Cancer Cells,” Sci. Rep. 5, 18046; doi: 10.1038/srep18046, 2015.

[4] J Hashmi, Y Huang, S Sharma, D Kurup, L De Taboada, J Carroll, and M Hamblin, “Effect of Pulsing in Low-Level Light Therapy,” Lasers Surg Med., 42(6): 450–466, August 2010.