

AFOSR MURI

“Nanoelectropulse-induced Electromechanical Signaling and Control of Biological Systems”

Instrumentation for Studying Cancellation Effects Caused by Nanosecond Pulses

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Engineering Core in this MURI

Pulse Generators *(Developed from scratch)*

- **Multiphase pulser (>80 ns)**

A series of capacitor switch modules are distributed to produce pulses in a synchronized way.

UP1k: uniphasic 1 kV pulse generator

BP1k: biphasic 1 kV pulse generator

MP1k: multiphase 1kV pulse generator

UP5k: uniphase 5 kV pulse generator

MP5k: multiphase 5 kV pulse generator

- **Uni-bipolar converter (<20 ns)**

A passive inductor is charged in parallel with the load resistor and release its charge after initial phase.

CAN-CAN: Novel Electrode Configurations

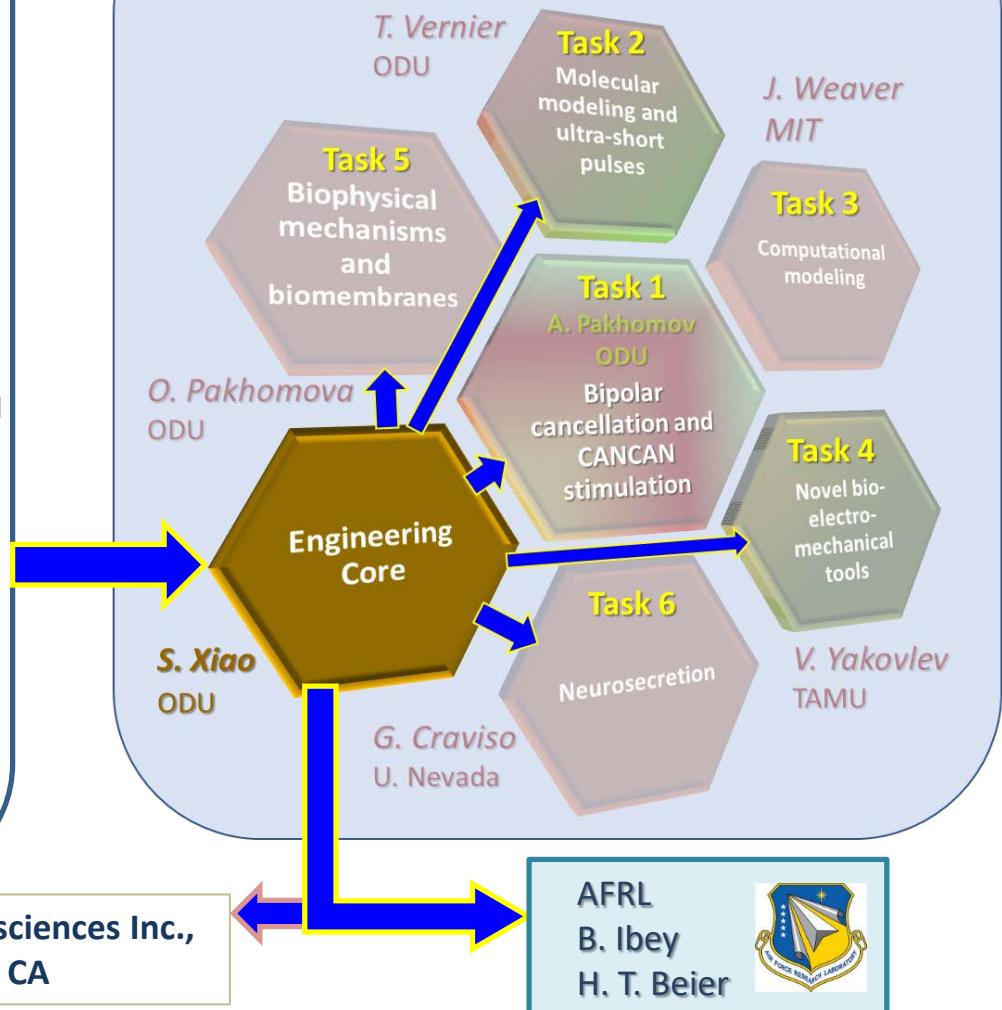
(in 3D tissue culture)

- **Linear CAN-CAN electrodes**
- **Quadrupole CAN-CAN electrodes**

Remote CAN-CAN Stimulation

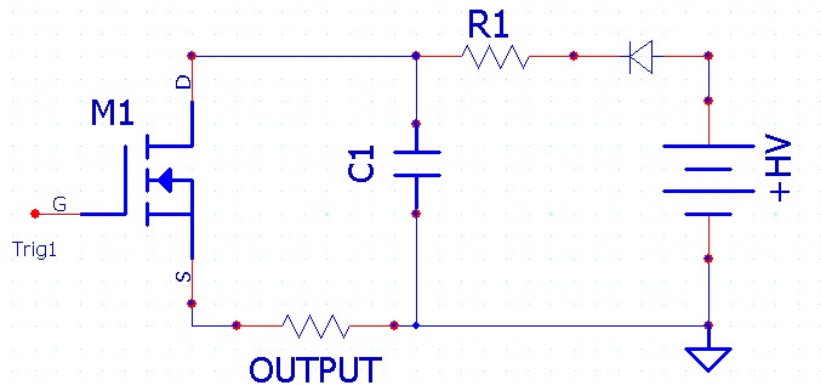
Surface electrodes incorporating CAN-CAN concept
Antennas (free field)

MURI Team Structure

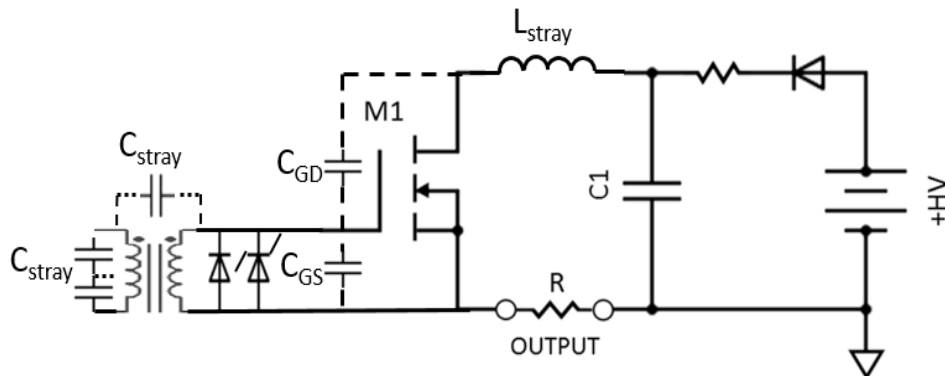
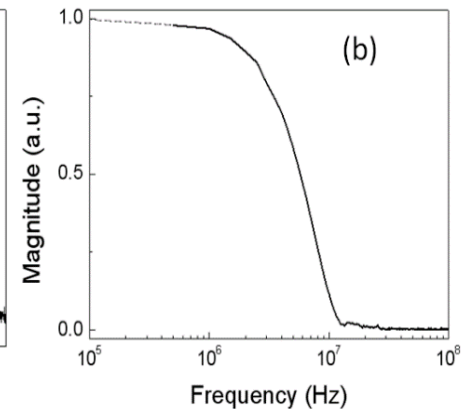
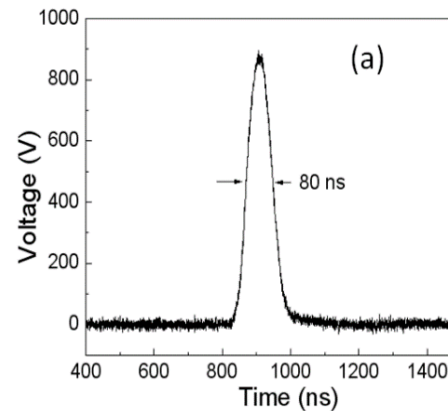


Modular Pulse Generator: Uniphasic Pulse with MOSFET Switches (UP1K)

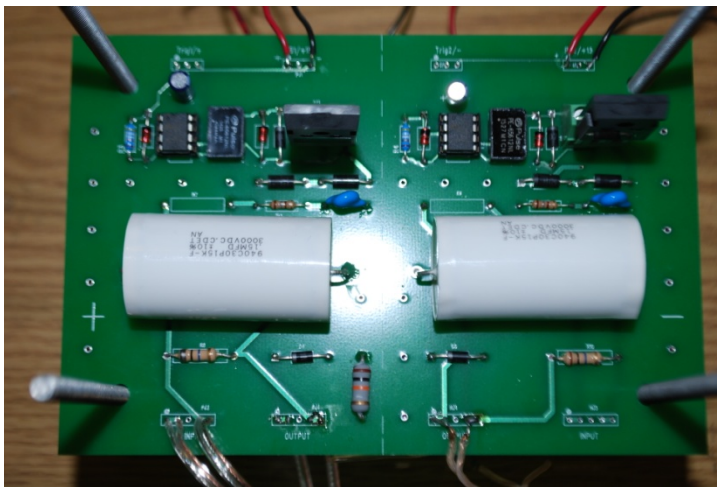
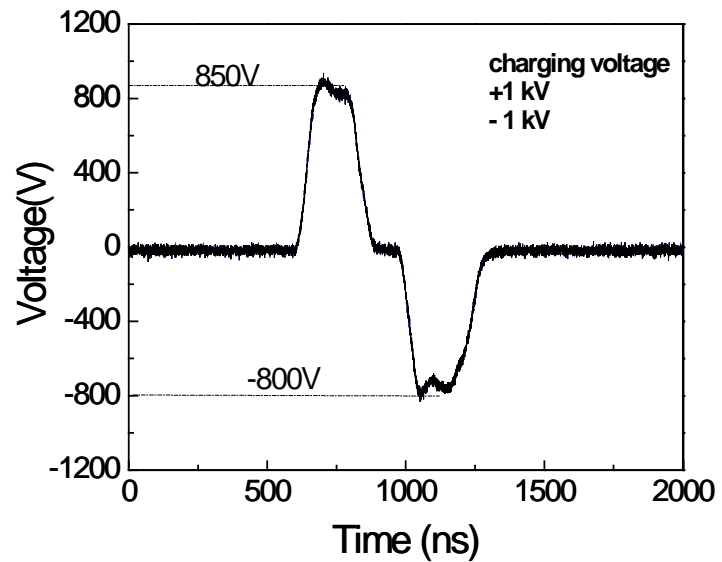
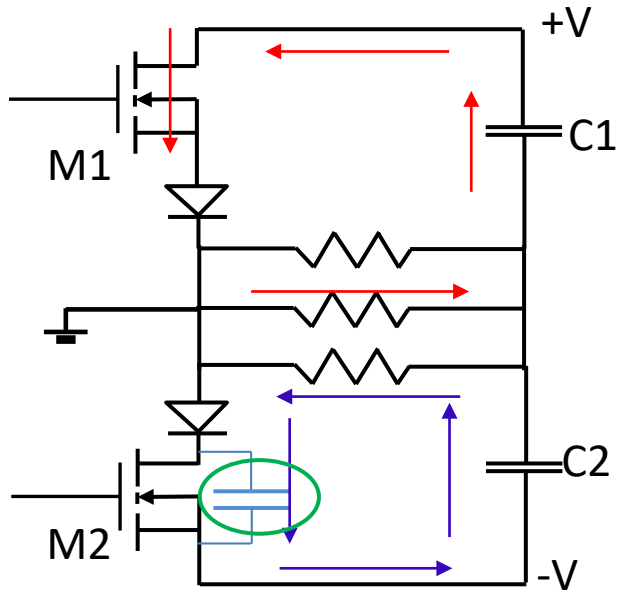
Fundamental module:
RC in series switched by a MOSFET



Shortest pulse: 80 ns



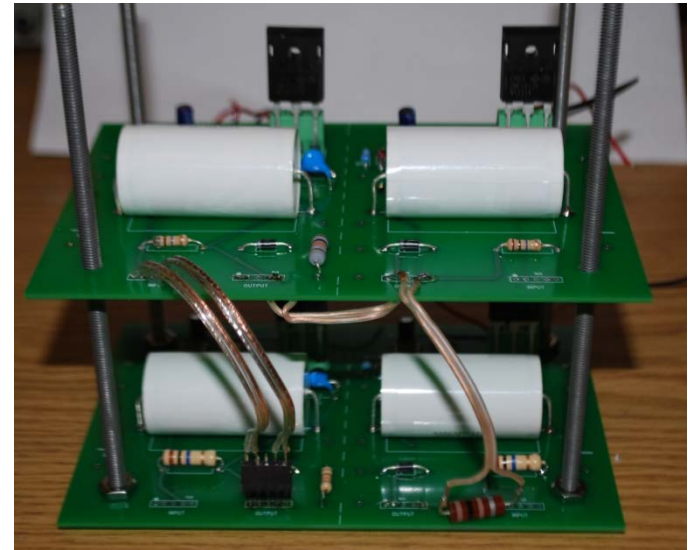
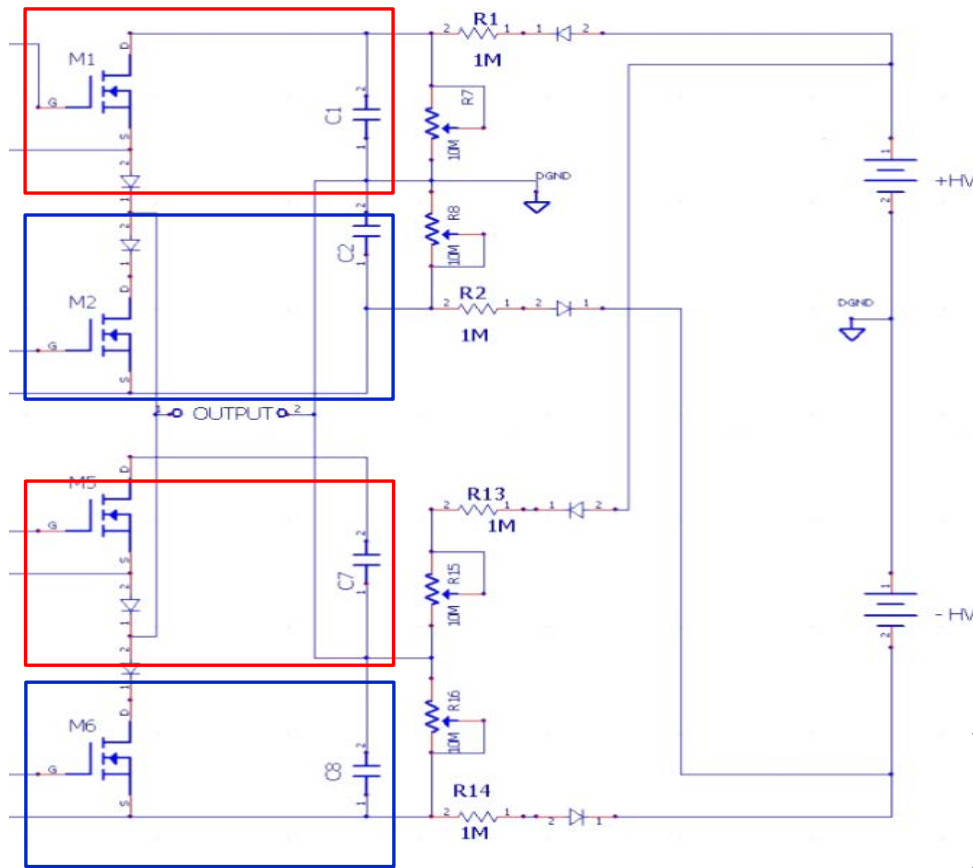
Pulse Generator (BP1K): Biphasic Pulse



Biphasic pulses were produced by combining two fundamental modules to supply the same load.

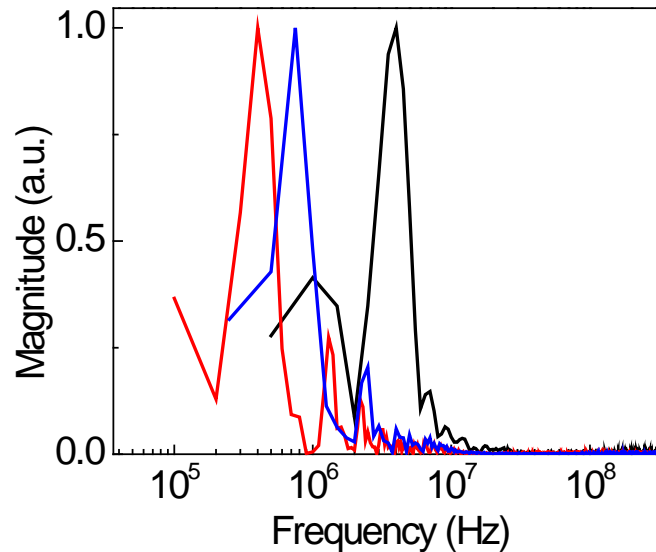
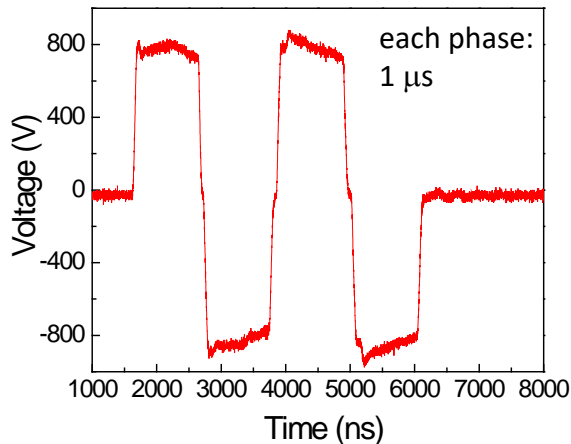
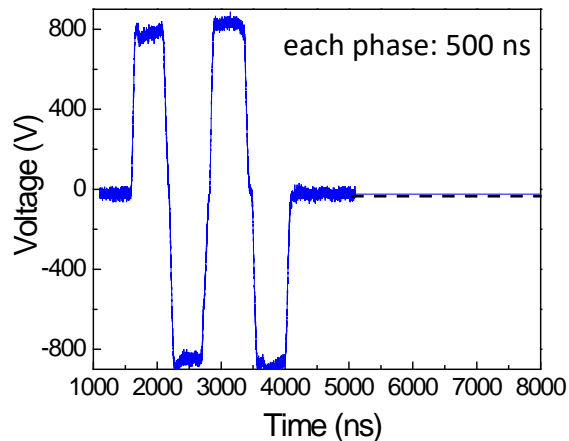
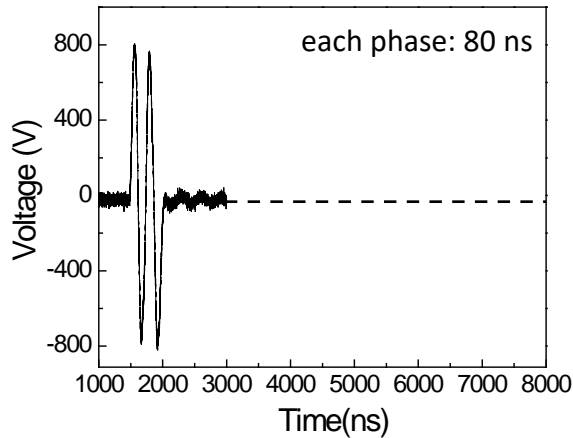
The coupling between the positive and negative phase of the bipolar pulse generator causes 10%-20% voltage loss.

Multiphasic Pulses: Parallel Operation of Multiple Modules (MP1K)



Multiphasic pulses can be produced by combining four fundamental modules to supply the same load. Each module can be charged with different voltages and is responsible for producing one phase of the pulse. In this diagram, a multiphasic wave that has two positive phases and two negative phases is generated.

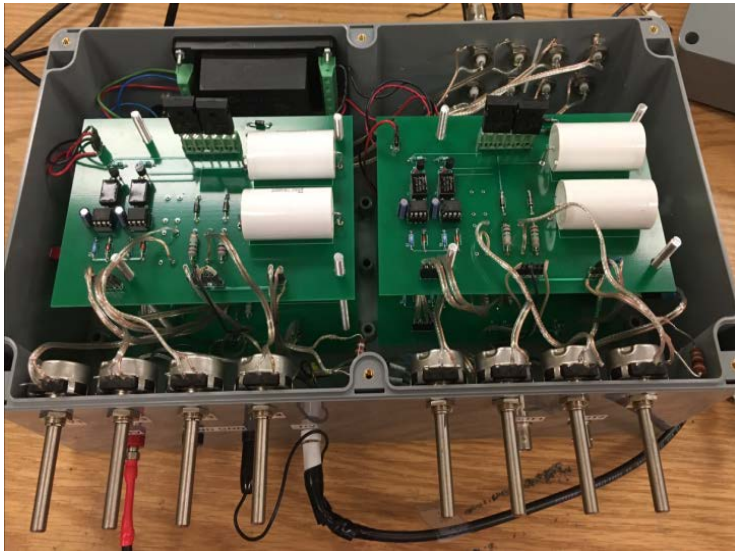
Pulse Generator: Multiphasic Pulses



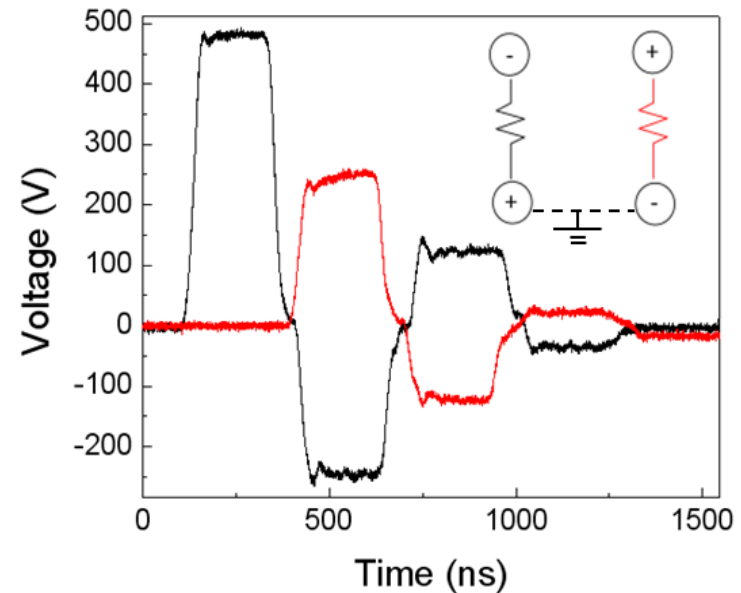
The multiphasic pulses consisting of 4 phases of alternating polarities. The phase width is 80ns, 500 ns and 1000 ns as well as the spectra of the multiphasic pulses.

The center frequency shifts as the phase width changes.

Two Parallel Multiphasic Pulse Outputs (2 MP1K)



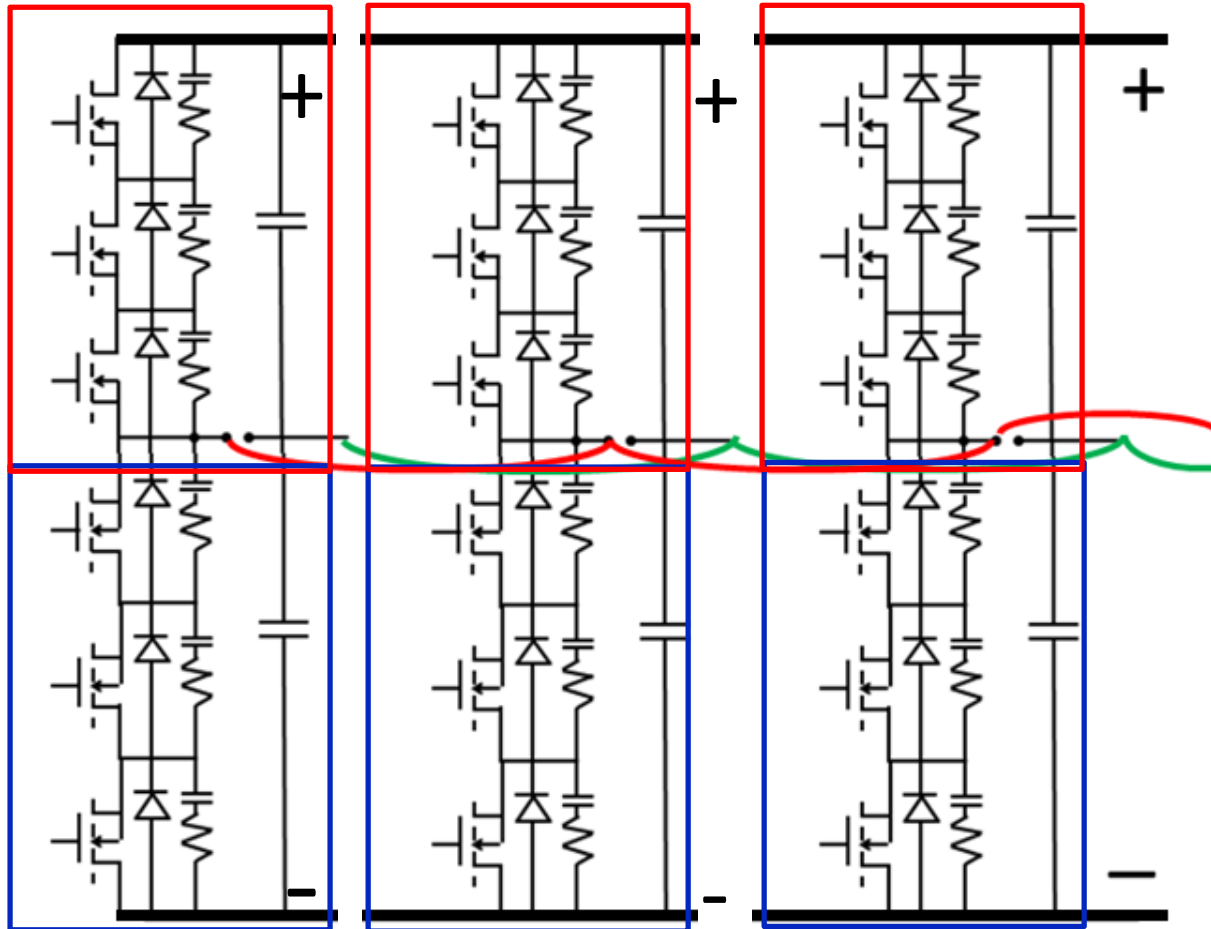
A multichasic pulse generator that has two independently-controlled outputs. Each output delivers four phases with alternating polarities. The pulse width and delay are controlled by an external delay generator. The amplitude of each phase is varied by a potentiometer.



Two multiphasic pulses were applied to two resistors that shared the same ground. They were programmed so that the addition of these two complementary pulses creates a uniphasic pulse. The resistors were used to simulate the solution resistances between the electrodes in the CAN-CAN

A total of 8 phases!

High Voltage, Multiphase, Nanosecond Pulse Generator



Arbitrary Nanosecond, High Voltage Pulses

Uniphasic

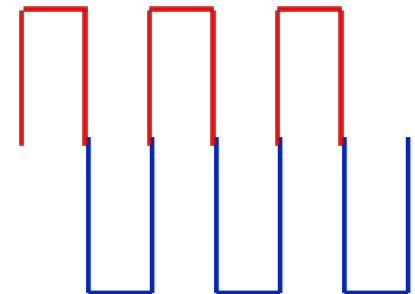
Uniphasic train

Biphasic

Biphasic train

Multiphasic

Multiple multiphasic outputs



Major Issues of High Voltage Multiphasic Generator

1. Multiple switches stacking causes a jitter and some switches are turned on & off differently

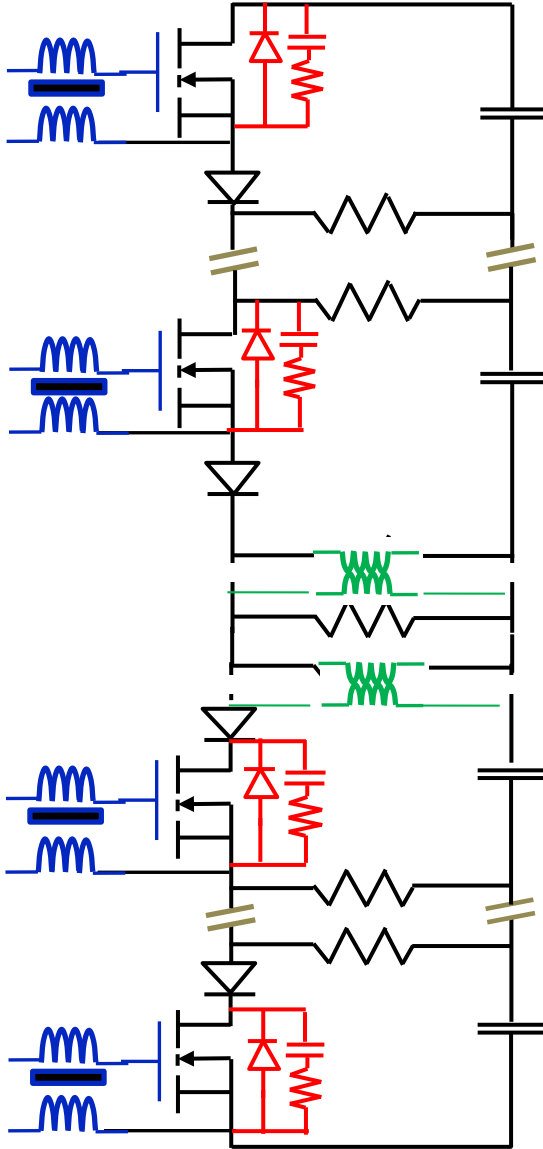
Solution: Snubber circuit

2. High voltage common mode is generated when the switch is turned on, which causes overvoltage of the ground-isolated optoisolators, power supplies

Solution: Choke

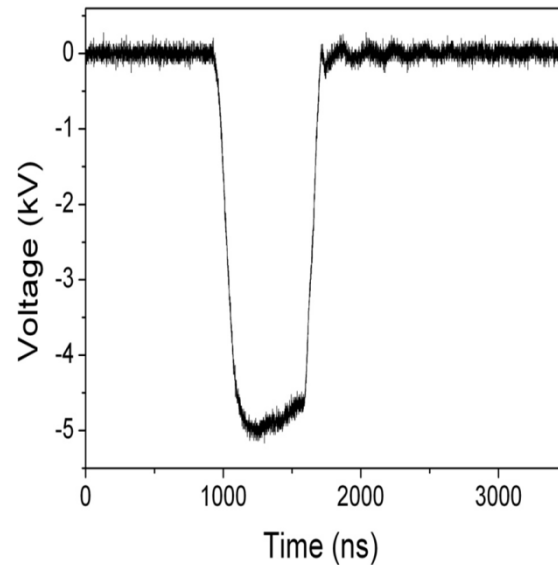
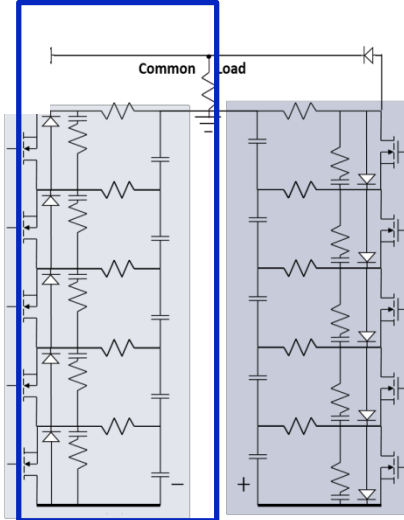
3. A voltage loss occurs among different modules, because of the coupling of the snubber circuit, stray parameters of the switches.

Solution: High voltage, wideband output transformer

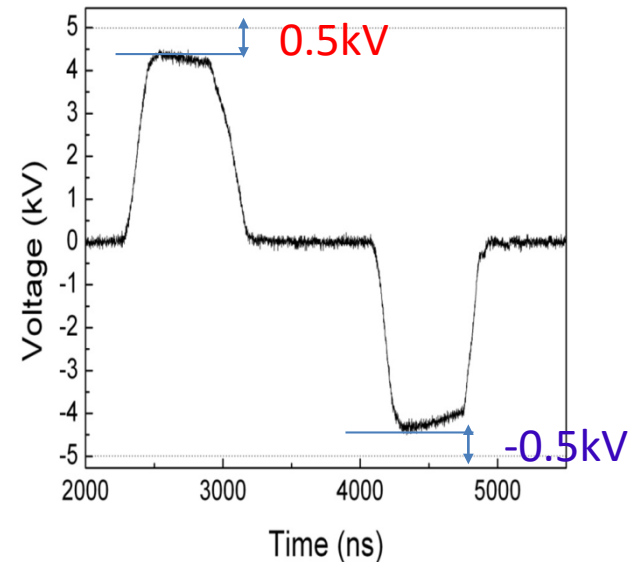


A Biphasic Nanosecond Pulse Generator (BP5K)

2-phase generator



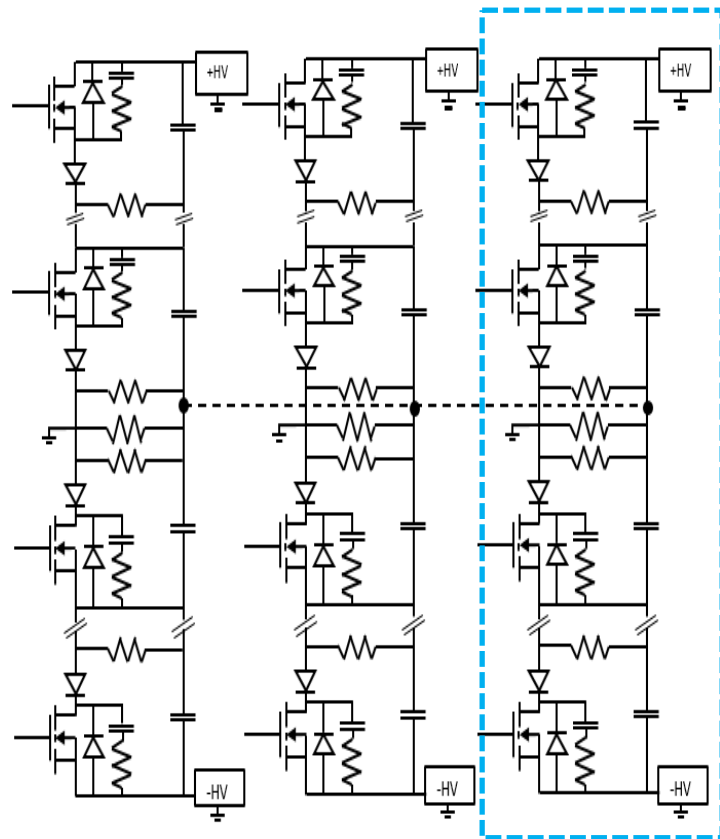
1 phase



2 phases

10% voltage loss

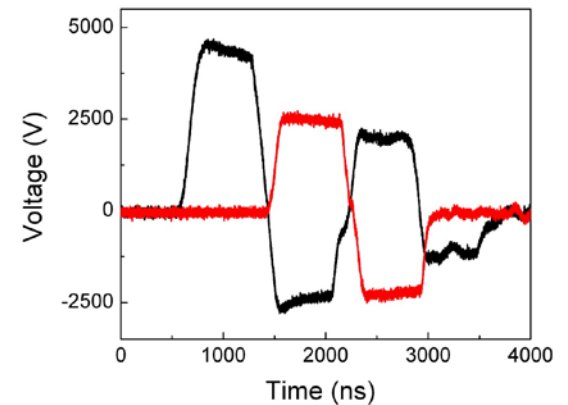
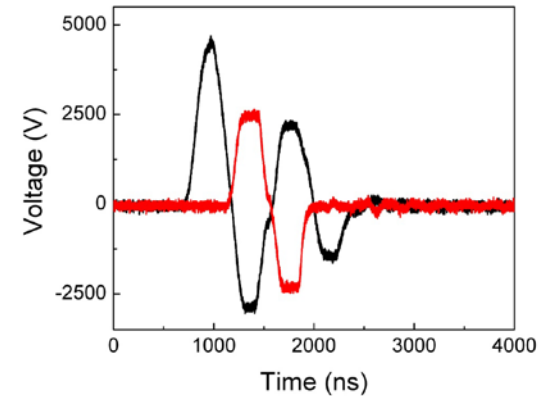
A Multiphase Nanosecond Pulse Generator (MP5K)



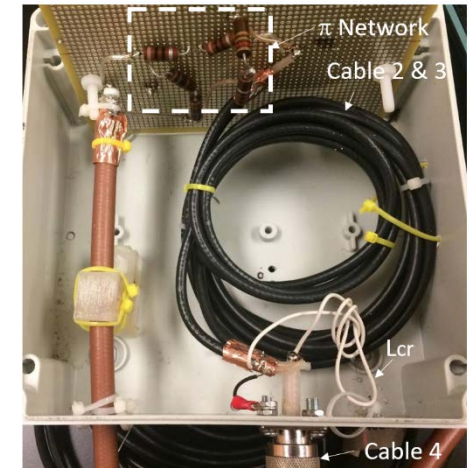
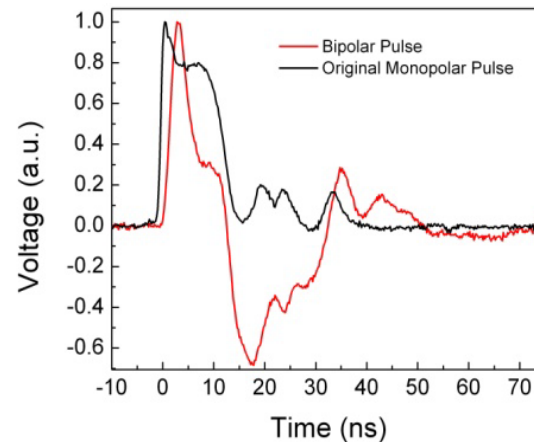
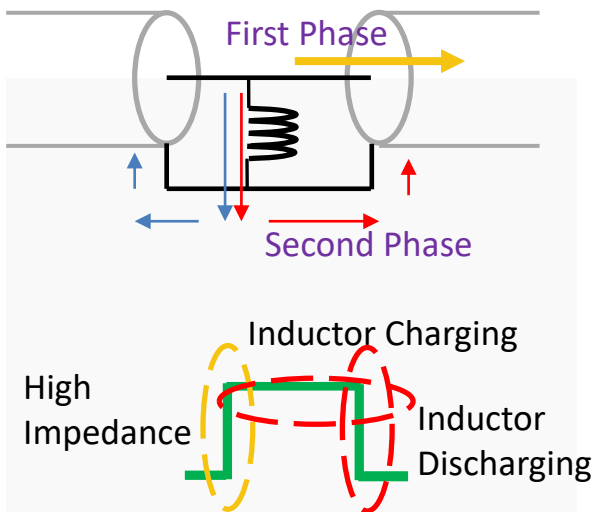
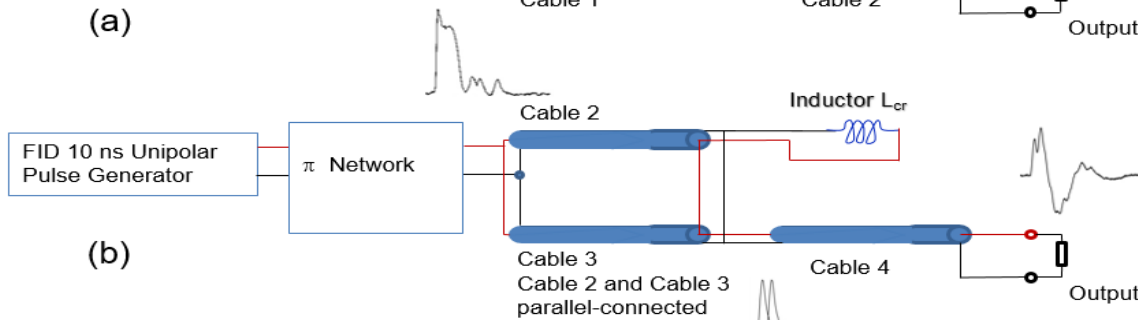
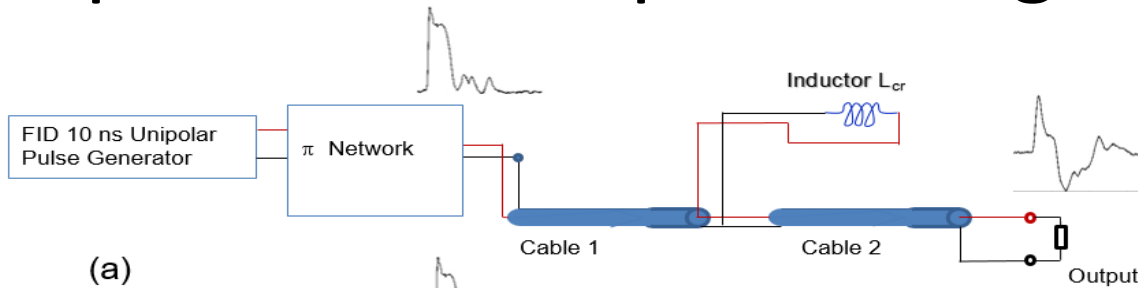
2-phase generator



6-phase generator

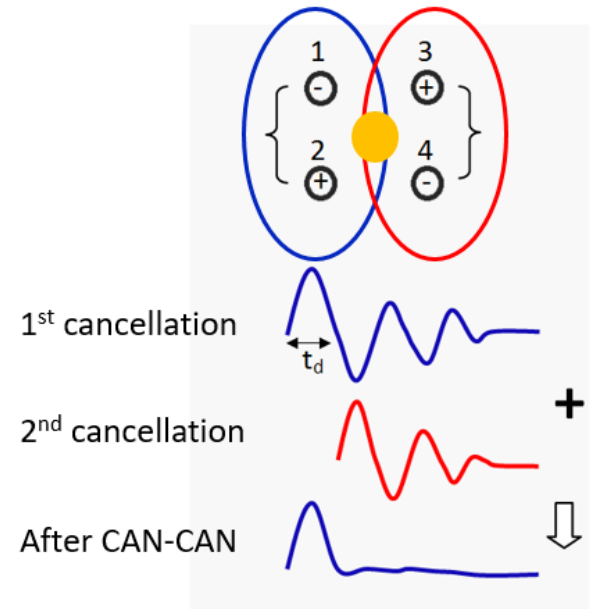
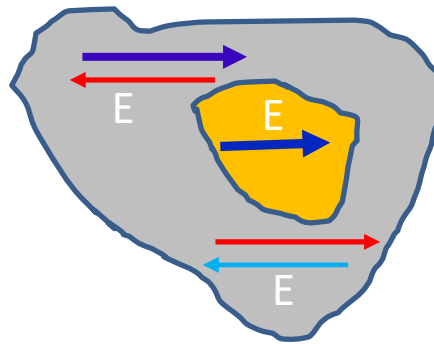
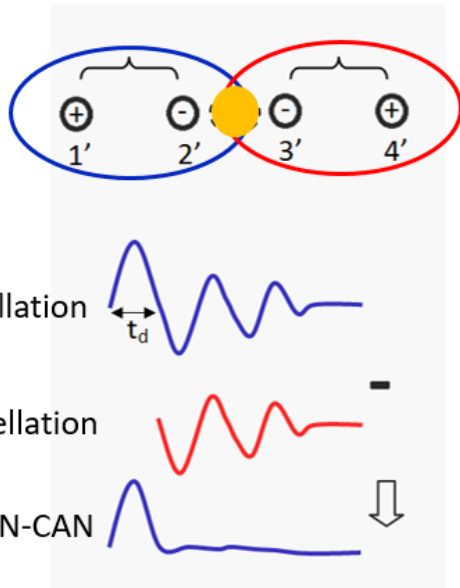


Uni-bipolar Converter: generating bipolar pulses from a preexisting unipolar pulse



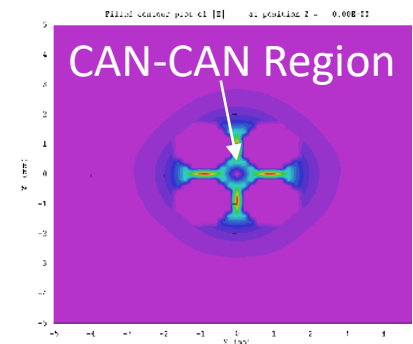
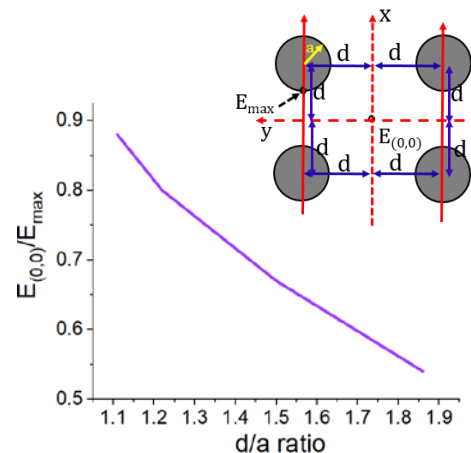
A unipolar pulse source provides a nanosecond pulse, which goes through an impedance matching network (π network) and then arrives at an inductance L_{cr} . A cable (Cable 2) is connected in parallel with the inductance before it connects to the output load. The inductor is charged by the flat part of the unipolar pulse and releases its current in the fall time of the phase.

Cancellation of Cancellation

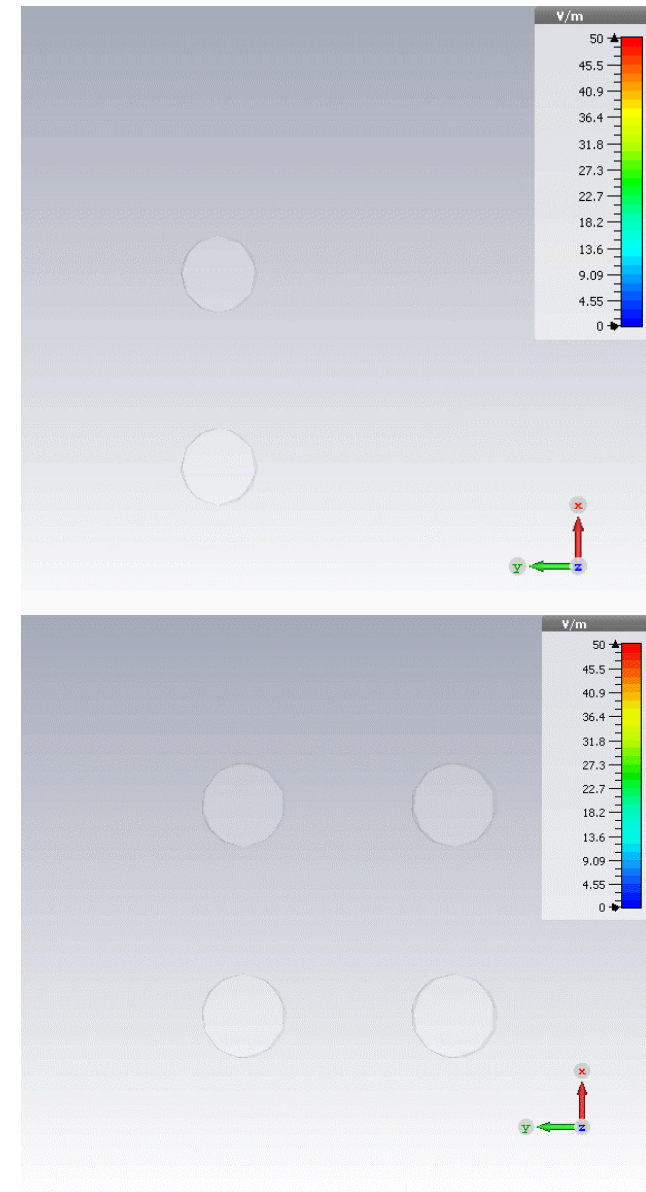
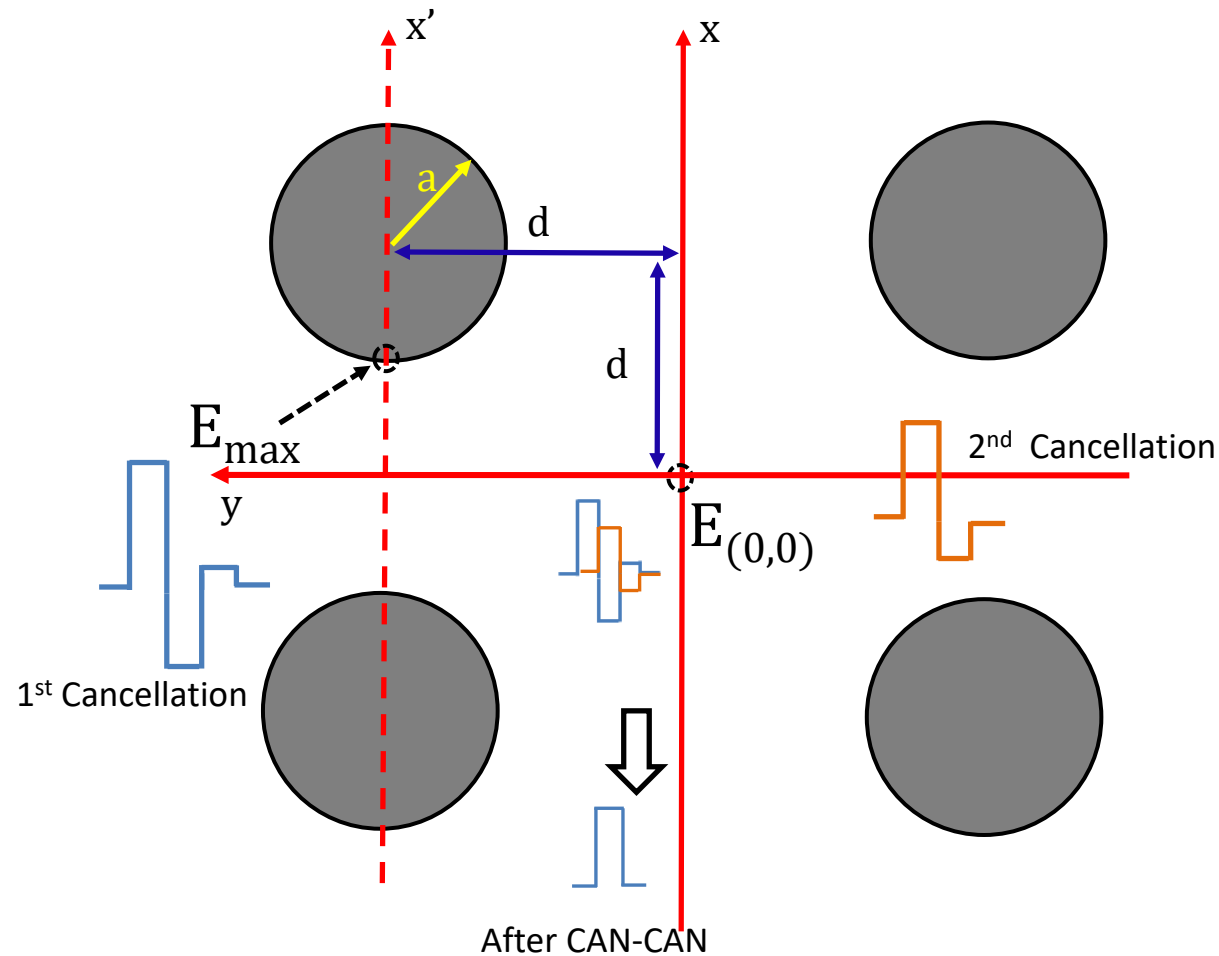


Can-Can may be a revolutionary approach to deliver pulses with increased focality and deeper targeting. Problem is increased complexity of pulse shapes and synchronization.

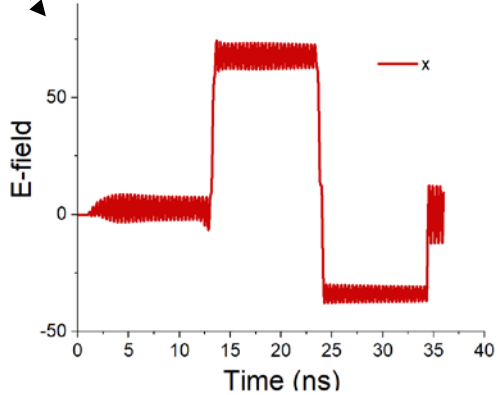
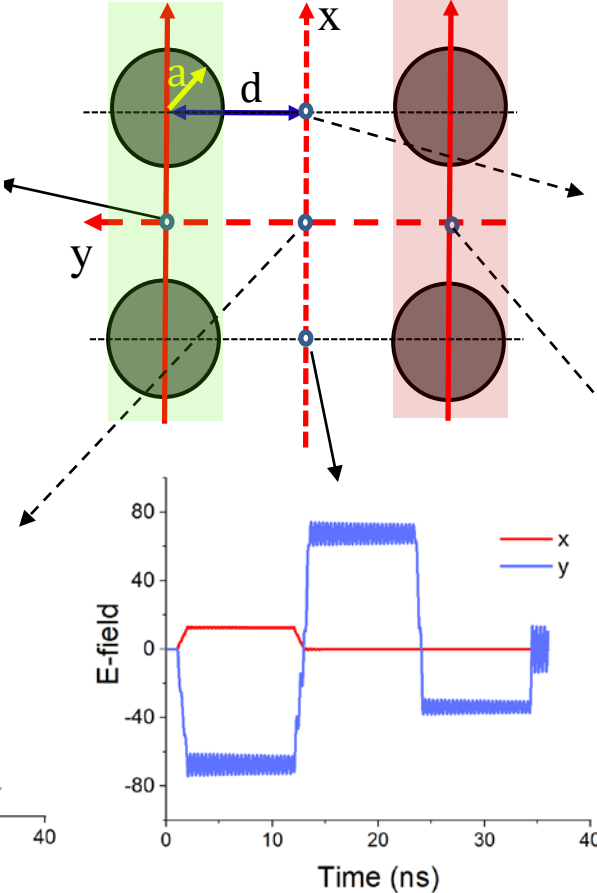
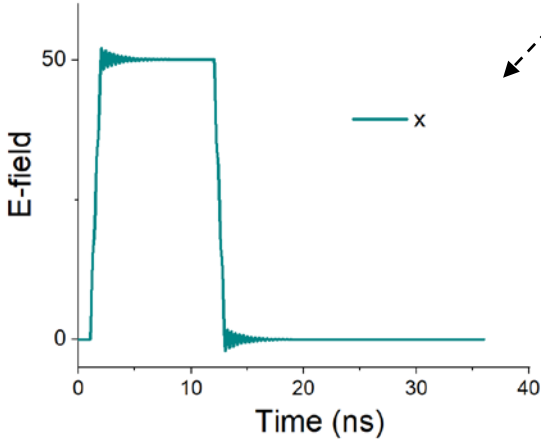
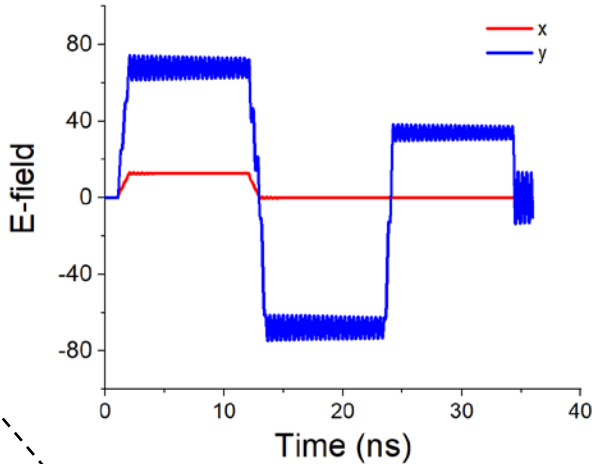
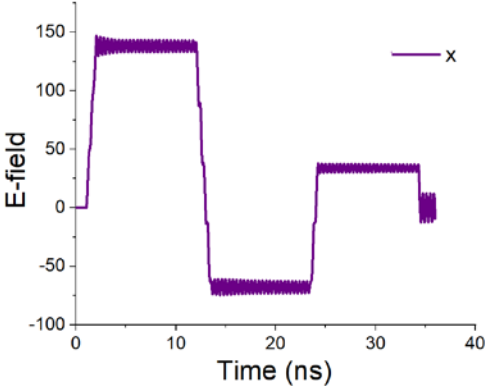
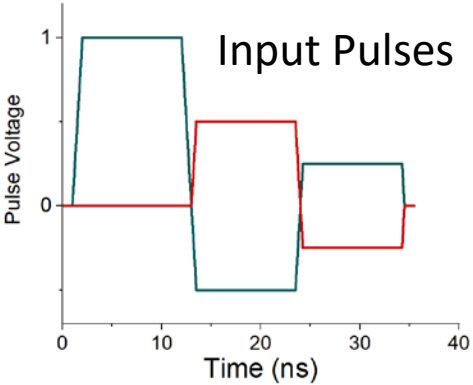
Advantages: **better focality**
useful for remote stimulation



Quadrupole Electrode Configuration for CAN-CAN



The fields are bipolar everywhere except the CAN-CAN region



Biological effects predicted from CAN-CAN coefficients

Various CAN-CAN Coefficients

$$\eta_1 = \frac{E_{p1} + E_{p2} + E_{p3}}{\max_{i=1,2,3} |E_{pi}|}$$





max|E| in the same pulse

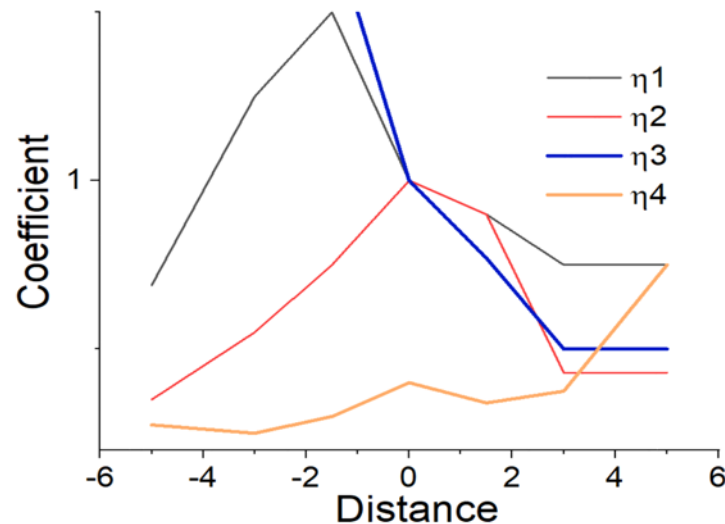
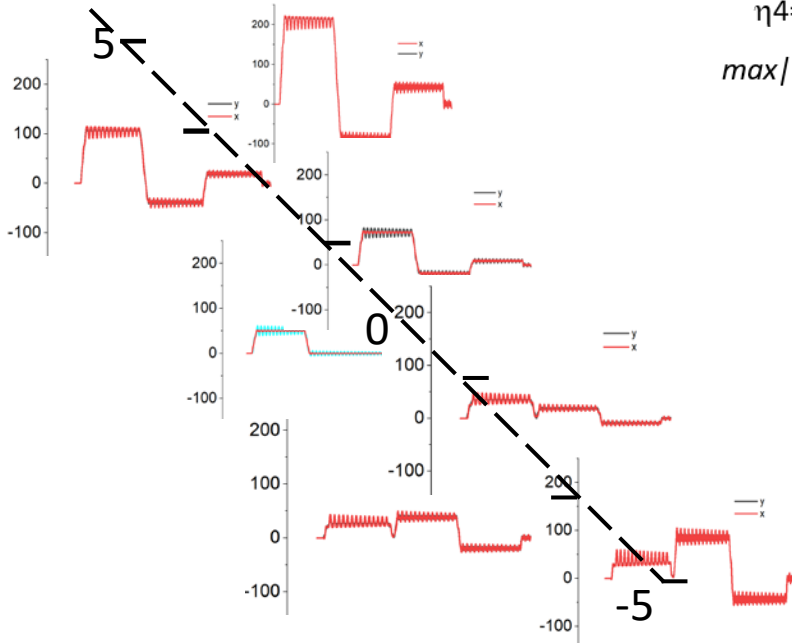
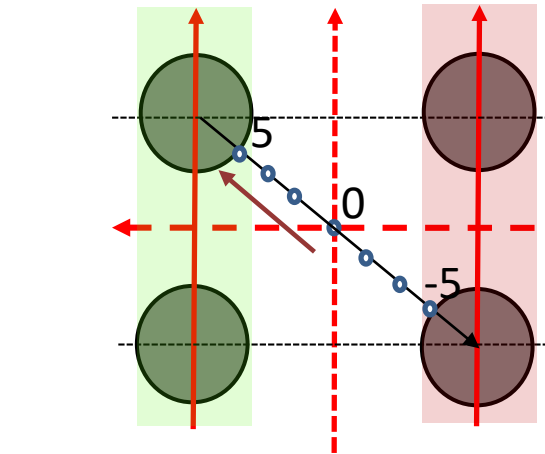
$$\eta_2 = \frac{E_{p1} + E_{p2} + E_{p3}}{|E_{p1}| + |E_{p2}| + |E_{p3}|}$$

$$\eta_3 = \frac{E_{p1} + E_{p2}}{|E_{p1}|}$$

$$\eta_4 = \frac{E_{p1} + E_{p2} + E_{p3}}{\max |E|}$$

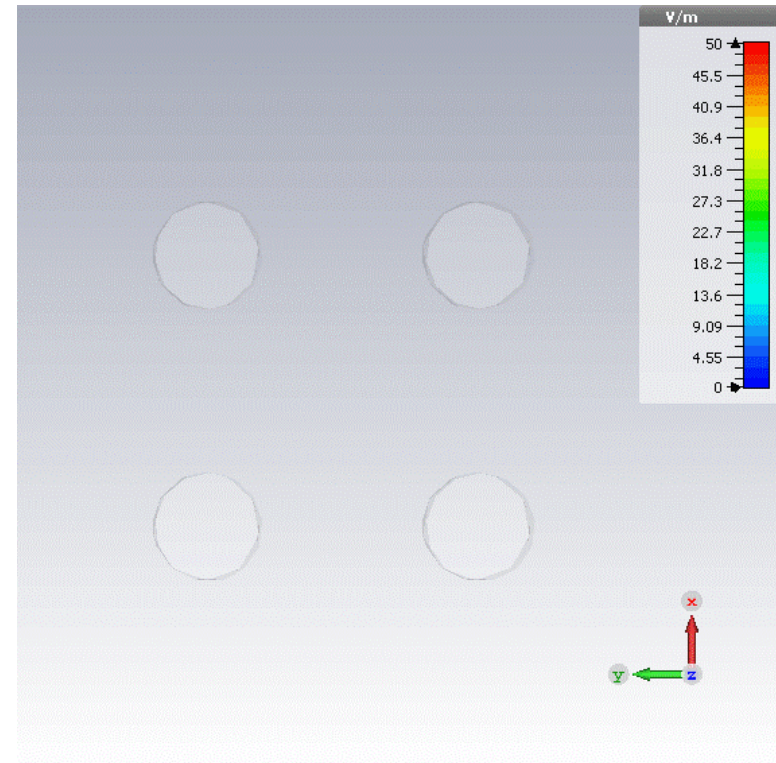
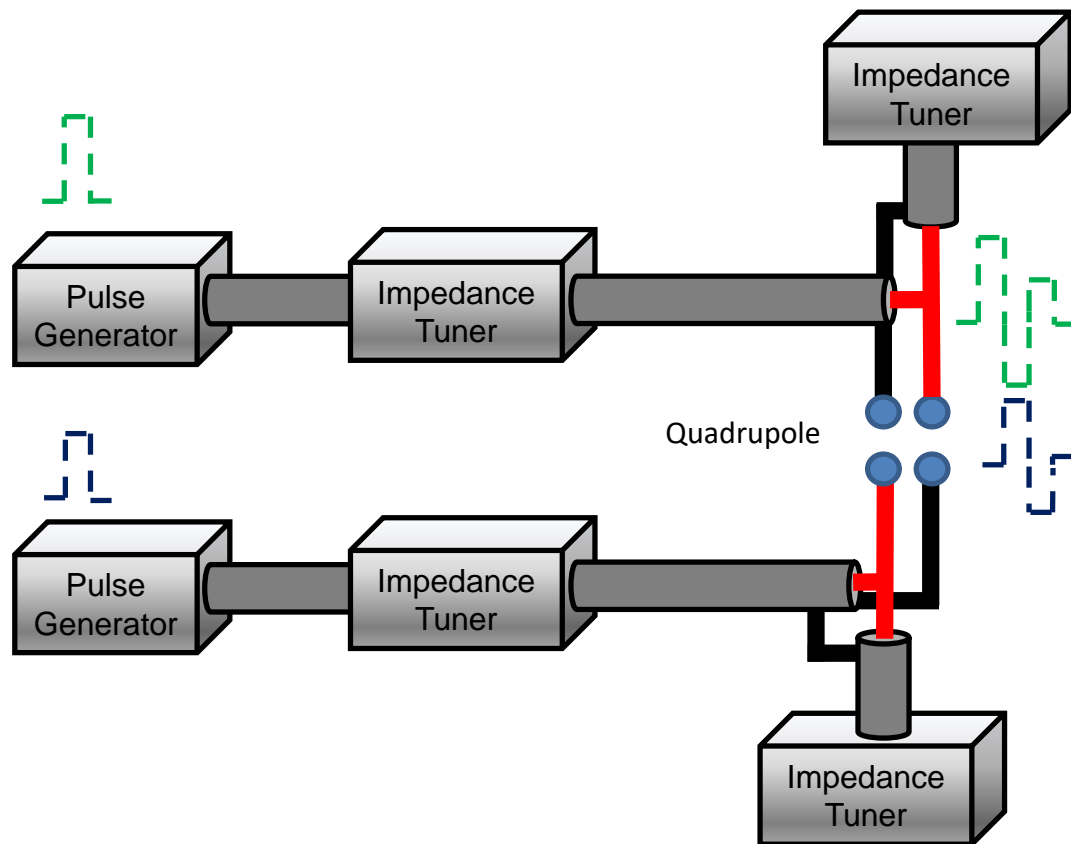
max|E| through out the region

	η_1	η_2	η_3	η_4
	1	1	1	
	0.5	0.33	0.5	
	0.75	0.42	0.75	
	0.4	0.5	6	



CAN-CAN coefficients predict the effective stimulation region and spatial resolution.

A quadrupole electrode configuration energized by two independently-controlled pulse generators for CAN-CAN Stimulation in 3D tissue culture



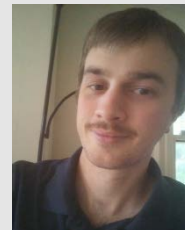
- *Bipolar electric pulses are produced by reflections at impedance tuners.*
- *The quadrupole has 2 electrodes that share the same ground (non-isolated case)*

Acknowledgements

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Chris Venning



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Andrei Pakhomov

Support:

*AFOSR MURI, “Nanoelectropulse-induced electromechanical signaling and control of biological systems”



Summary

- Engineering core has served a critical role in the MURI for providing various pulse sources that are not commercially available. Novel, high voltage, nanosecond pulse generators allow for the study of **nanosecond bipolar cancellation effect**
- New pulse generators and exposure systems have been developed towards the **implementation of CAN-CAN** remote stimulation for increased focality
- Future development will focus on **remote, noninvasive CAN-CAN** stimulation using radiators for nanosecond, bipolar, synchronized pulsing

