Fourier Analysis SpecTroscopy for real-time monitoring of tissue impedance, temperature, and treatment outcome during electroporation-based therapies

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Electroporation (EP)-based therapies use pulsed electric fields to enhance cell membrane permeabilization to drugs and molecules [1, 2]; EP results in detectable changes in tissue electrical properties [3, 4]. Here, we introduce a methodology, Fourier Analysis SpecTroscopy (FAST), for monitoring tissue impedance changes during EP-based therapies. High bandwidth impedance spectra are attained by implementing a wide-band chirp signal, subsequent voltage and current capture, and Fourier transform for analysis in the frequency domain.

Firstly, FAST was investigated to monitor impedance changes from irreversible EP in potato. Potato tissue, similar to mammalian tissue, undergo impedance changes due to EP [3]. Two 20-guage stainless electrodes, 1 cm spacing, were inserted into a 7 mm thick ellipsoidal potato section. Impedance spectra were acquired with a potentiostat (Gamry Reference 600) and with FAST (chirp signal 1-50-1-250-10-250 μs, **Figure 1a**) immediately before treatment and after 1, 5, 10, 20, 40, and 80 pulses of 1000 V and 100 µs on-time. Impedance measurements from Gamry (solid) and FAST (circles) are seen in **Figure 1b** and demonstrate good agreement from 2 kHz up to 4.5 MHz. Impedance acquisition time was ~45s for Gamry and <1s for FAST.

Secondly, FAST was investigated to monitor changes in tissue temperature from pulsing. EP-effects heavily influence low frequency impedance measurements due to capacitive cell membrane effects [4]. At high frequencies, the membrane reactance is shorted and EP-effects on impedance are minimized; we postulate that high-frequency impedance measurements can be used to predict temperature rise during EP. From equation 1:

$$\sigma_T = \sigma_0 \cdot (1 + \alpha \cdot \Delta T) \quad (1)$$

a temperature coefficient, α, 2.25%/°C was used and high frequency (1.78 MHz) impedance monitored. Tissue was heated uniformly using plate electrodes and high amplitude pulses; temperature was measured with a FLIR thermal camera. Results show good agreement between measured and FAST predicted temperature (**Figure 1C**). FAST allows for real-time impedance spectroscopy and is easily integrable in existing pulse generators.

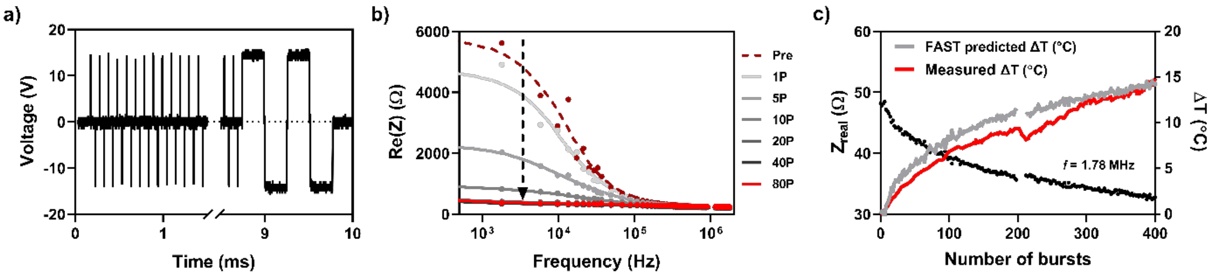

Figure 1. Custom a) FAST waveform and b) resulting impedance measurements before and after irreversible EP. c) Impedance measurements and predicted temperature from FAST compared to thermal measurements.

References

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