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Evaluation of Electrical Pulsing Strategy for Optimizing Cellular Inflows Through Electroporation by Nanosecond, High-Intensity Pulses

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Applications of electric pulses to create nanopores at the membranes of biological cells can modulate the conductivity and permeabilization in a controlled manner. Applications of such membrane poration lies in the field of biomedical engineering, drug/gene delivery, cell fusion, and electrochemotherapy for cancer treatment. In principle, various different electrode shapes and geometries can be used for selecting the target areas and tailoring the spatial electric field profiles, with the over-riding goal of ensuring optimal inflows into the cell through the pores created by the external electric pulsing. The role of pulse shape (e.g., monopolar-vs-bipolar), the rise and fall times, duty cycle and duration (nanosecond versus microsecond) have been the topic of several experimental studies.

The physics behind electroporation and its quantitative analysis appears to be on relative form footing [1,2]. However, for the standpoint of a practical application, it is important to choose the pulse width and the duty cycle (since the use of multiple pulsing seems to suggest a stronger cellular uptake), while allowing for multiple electrodes for more uniform and extensive effects. What is perhaps missing is a more comprehensive predictive analysis of cellular uptake with such pulse trains using multiple electrodes. The pulse characteristics and electrode placement strategies become important issues.

Here in this contribution, we focus on a numerical study of ion inflow in to cells following poration by a pulse train. Many-pronged electrode configurations have been used for spatial flexibility, with pulse sequencing that effectively allows for phased array-like behavior. The membrane electroporation behavior and ionic inflows will be evaluated for both monopolar and bipolar nanosecond pulses. The role of pulse delay times relative to the pore resealing durations will also be analyzed, and the simulations will enable separate evaluations of the electrophoretic versus diffusive transport. Relevant comparisons to experimental data will also be provided, and the role and dependencies on diffusion rates, pore closing times, pulse durations, duty cycles and repetitive frequency will be gauged.

[1] W. Krassowska and P. D. Filev, Modeling electroporation in a single cell, Biophys. J., vol. 92, 404-417, 2007.
[2] R. P. Joshi and K. H. Schoenbach, Bioelectric Effects of Intense, Ultrashort Electric Pulses, Critical Reviews in Bio-Medical Engineering, vol. 38, 255-304, 2010.

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