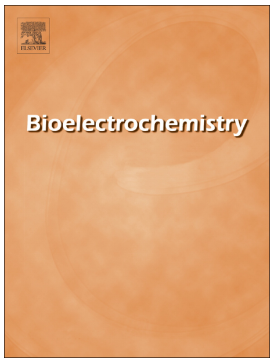

The second phase of bipolar, nanosecond-range electric pulses determines the electroporation efficiency

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PII: S1567-5394(18)30051-3
DOI: doi:10.1016/j.bioelechem.2018.03.014
Reference: BIOJEC 7133

To appear in: *Bioelectrochemistry*

Received date: 28 January 2018
Revised date: 21 March 2018
Accepted date: 28 March 2018

Please cite this article as: Andrei G. Pakhomov, Sergey Grigoryev, Iurii Semenov, Maura Casciola, Chunqi Jiang, Shu Xiao , The second phase of bipolar, nanosecond-range electric pulses determines the electroporation efficiency. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Biojec(2017), doi:10.1016/j.bioelechem.2018.03.014

The second phase of bipolar, nanosecond-range electric pulses determines the electroporation efficiency

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Abstract

Bipolar cancellation refers to a phenomenon when applying a second electric pulse reduces ("cancels") cell membrane damage by a preceding electric pulse of the opposite polarity. Bipolar cancellation is a reason why bipolar nanosecond electric pulses (nsEP) cause weaker electroporation than just a single unipolar phase of the same pulse. This study was undertaken to explore the dependence of bipolar cancellation on nsEP parameters, with emphasis on the amplitude ratio of two opposite polarity phases of a bipolar pulse. Individual cells (CHO, U937, or adult mouse ventricular cardiomyocytes (VCM)) were exposed to either uni- or bipolar trapezoidal nsEP, or to nanosecond electric field oscillations (NEFO). The membrane injury was evaluated by time-lapse confocal imaging of the uptake of propidium (Pr) or YO-PRO-1 (YP) dyes and by phosphatidylserine (PS) externalization. Within studied limits, bipolar cancellation showed little or no dependence on the electric field intensity, pulse repetition rate, chosen endpoint, or cell type. However, cancellation could increase for larger pulse numbers and/or for longer pulses. The sole most critical parameter which determines bipolar cancellation was the phase ratio: maximum cancellation was observed with the 2nd phase of about 50% of the first one, whereas a larger 2nd phase could add a damaging effect of its own. "Swapping" the two phases, i.e., delivering the smaller phase before the larger one, reduced or eliminated cancellation. These findings are discussed in the context of hypothetical mechanisms of bipolar cancellation and electroporation by nsEP.

Keywords: Nanosecond pulses; Electroporation; Electropermeabilization; Nanopores; Membrane permeability; Bipolar cancellation