Analysis of the Role of Cellular Heating in Microsecond Irreversible Electroporation*

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Irreversible electroporation (IRE) involving tumor ablation presents a minimally invasive treatment and has found a niche in oncological applications. It has proven to be a safe and effective procedure for treating many unresectable tumors. However, the use of a series of high frequency sinusoidal bipolar electric pulses, in the context of cellular drug delivery and/or irreversible electroporation, has not been studied to the best of our knowledge. This scheme, similar to the High Frequency Irreversible Electroporation (HFIRE) protocol, could prove to be of utility and synergistic effects of local membrane heating might well be beneficial in the context of this long wavetrain. In the present simulation study, two aspects of interest will be probed: (i) the role of cell heating in possibly promoting the successful uptake of drugs for treatment, and (ii) the possible synergistic interplay between the electric field and local membrane heating in reducing the required electroporation threshold.

In this work, membrane electroporation will be simulated based on a Smoluchowski continuum analysis discussed elsewhere by our group, together with spatio-temporal heating due to the power dissipation from the external bi-phasic source. We will consider two-dimensional transient heat flow with azimuthal symmetry in a single spherical cell. The following aspects will be analyzed and discussed in this presentation: (i) Changes induced by including heating, especially effects on pore formation dynamics. (ii) Quantitative assessment of the magnitude of heating caused by the applied electric fields and its dependence on wavetrain and field characteristics. This could define safe-operating limits and/or provide guidance towards optimum parameter space. Given that the vast parameter space depends on multiple factors, including cell size, pulse characteristics, electrical and thermal parameters of the biological system, applied waveforms, and number of pulses, only a few test cases will be probed. (iii) The present simulations will allow predictions and mechanistic insights into the level of electric field threshold reductions possible due to synergistic heating. (iv) And finally, the possibility of establishing large thermal gradients at the membrane for thermo-diffusive transport will also be quantitatively assessed.

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