Computational Model of Apoptosis Induction by Nanosecond Pulsed Electrical Fields (nsPEF) in Biological Cells

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Effects of pulse power technology using high intensity (up to 300 kV/cm) nanosecond pulsed electrical fields (nsPEF) on biological cells have not been reported till recently, although the technology has been applied for decontamination and amelioration of biofouling (S. J. Beebe, P. M. Fox, L. J. Rec, K. S. Somers, R. H. Stark, and K. H. Schoenbach, IEEE Transactions on Plasma Science, 30, 286-292, 2002). Recent studies have reported that nsPEF modulates cell signaling from the plasma membrane to intracellular structures and functions with decreasing pulse durations (S. J. Beebe, P. M. Fox, L. J. Rec and K. H. Schoenbach, The FASEB Journal expresses article, June, 2003). NsPEF was shown to induce apoptosis within tens of minutes, depending on pulse duration, which is caspase- and mitochondria- dependent, but independent of plasma membrane electroporation and thermal changes (S. J. Beebe, P. M. Fox, L. J. Rec and K. H. Schoenbach, The FASEB Journal expresses article, June, 2003). We develop a mathematical model of apoptosis induction by nsPEF using mass-conservation principles with kinetic rate laws, based on an existing model of caspase function in apoptosis (M. Fussenegger, J. E. Bailey, and J. Varner, Nature Biotechnology, 18, 768-774, 2000). The model focuses on caspase activation induced by stress-related factors mediated by rectangular pulse nsPEF stimulation. Experimental research shows that the kinetics of nsPEF-induced apoptosis depends on the pulse duration and higher electrical fields are required for apoptosis induction as the pulse duration is decreased (S. J. Beebe, P. M. Fox, L. J. Rec and K. H. Schoenbach, The FASEB Journal expresses article, June, 2003). In our model, special attention is also given to the positive feedback loop between the release of cytochrome *c* and the active executioner caspases, which accounts for the rapidity of apoptosis progression. The model will attempt to show why caspases are activated in 5-20 min following nsPEF treatment while it requires hours for the appearance of apoptosis markers for other physiologically apoptotic stimuli like Fas, UV light and toxic chemicals. Qualitative strategies for promoting or retarding apoptosis are simulated by controlling the duration or amplitude of the nsPEF stimulation. Our model thus extends the existing apoptosis model and can help in better understanding the mechanisms of nsPEF-induced apoptosis which can potentially be utilized to provide a unique, high-power, energy-independent tool to remove aberrant cells.