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Electroporation of Tissue and Cells: a Three-Equation Model of Drug Delivery☆

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Abstract

The exposure of the cell membrane to electric pulses of sufficient intensity is known to result in an increased permeability due to the formation of microscopic pores. This is electroporation, and it has been implemented to increase the efficacy of targeted drug delivery. In this study we introduce a novel three-equation model of transport that is able to distinguish the drug uptake in reversibly electroporated cells from that in irreversibly electroporated cells. In order to relate the permeability increases and the cell survival to the local electric field, sigmoidal functions are fit to published experimental data. The resealing of reversibly electroporated cells is also considered. A numerical study is presented that considers two different electrode configurations with different initial drug distributions. This model is able to capture the existence of an optimal applied voltage above which any increases in voltage act to decrease the total drug delivery to the surviving cells, illustrating the competing influences of increased cell permeability and decreased cell survival.

Keywords: electroporation; drug delivery; theoretical; reversible; mass transport

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1 Introduction

Electroporation is used in medical applications such as electro-chemotherapy, DNA transfection for DNA vaccination and gene therapy, and tissue ablation [1-4]. During electroporation, the application of short duration (generally ~ 1 μs to 100 ms) – high voltage electric fields (~ $kV \cdot cm^{-1}$) results in the formation of nanometer-sized water filled pores within the cell membrane [5-8]. When these electropores are long lived, they provide the sustained permeability increases that are required to facilitate the relatively slow process of the diffusion of a drug into the cell. This study develops a macroscale theoretical representation of transport associated with the permeability increases resulting from electroporation. Before presenting this model, we begin with a brief description of the fundamental physiological points that should be considered and then provide a short review of the highlights and deficiencies in current modelling approaches.

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