INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	Nilay Mondal
Roll Number	:	156123021
Programme of Study	:	Ph.D.

Thesis Title: Mathematical Modelling of Drug Delivery in Tissue Cells by Electroporation

Name of Thesis Supervisor(s)	:	Prof. Durga Charan Dalal
Thesis Submitted to the Department/ Center	:	Mathematics
Date of completion of Thesis Viva-Voce Exam	:	23/05/2022
Key words for description of Thesis Work	:	Mathematical modelling, Drug delivery, Electroporation, Thermal effects

SHORT ABSTRACT

Electroporation method is a useful tool for delivering drugs into various diseased tissues in the human body. In this thesis, mathematical models are developed to demonstrate how to deliver drugs into the diseased cells using tissue electroporation. A detailed study is carried out on reversible electroporation, thermal effects resulting from pulse application, and on drug elimination and metabolism. The present dissertation starts with a mathematical model of single cell electroporation for delivering drug into the cell. The model is able to capture non-homogeneous drug transport in the cell due to non-uniform cell membrane permeabilization. Several numerical experiments are conducted to understand the effects of electric field and drug permeability on drug uptake into the cell. Through investigation, the appropriate electric field and drug permeability are identified that lead to sufficient drug uptake into the cell. The second work contributes an improved mathematical model for drug delivery into the electroporated tissue that deals with both reversibly and irreversibly electroporated cells. The time-dependent mass transfer coefficient as a function of pore density is used to find the drug concentrations throughout reversibly and irreversibly electroporated cells as well as in the extracellular space. The effects of permeability of drug, electric field, and pulse period on drug concentrations in extracellular and intracellular regions are discussed. The threshold value of an electric field to initiate drug uptake is identified in this study. Special emphasis is also given on two cases of electroporation, drug dynamics during ongoing electroporation and drug dynamics after the electric pulse period is over. The next work focuses on the development of a mathematical model of drug delivery based on reversible tissue electroporation in order to treat all of the cells at the targeted site. In addition, the thermal effects on the tissue, which is an outcome of Joule heating, are also considered. The model optimizes the electroporation parameters for the required drug uptake into the cells with no thermal damage. This model can be used in clinical experiments to predict the drug uptake into the infected cells by controlling the model parameters according to the nature of infections.

The subsequent work emphasizes the tissue boundary where the drug is injected as a point source. Drug loss from the tissue boundaries through extracellular space and its reaction on drug transport are examined. The effects of electric field on tissue conductivity is studied. Multiple pulses are applied to deliver a sufficient amount of drug into the targeted cells. The final work concentrates on the process of drug metabolism in the cells in our modified model. The main objective is to examine the combined effects of drug loss across tissue boundaries and drug metabolism within cells. A detailed analysis of the effects of metabolism parameters on cellular drug uptake is presented. The model is able to calculate the amount of drug metabolites in cells at the end of drug transport.