An Improved Electrical Model of a Biological Cell Taking Electroporation into Account

N. Citro, **V. Tucci**, **B. de Vivo**, **and P. Lamberti**
University of Salerno, Italy

Electro-permeabilization of biological cells has been proposed as a very efficient pasteurization method in food technology, in biotechnology for gene transfer, in medicine for gene therapy, cancer chemotherapy, and drug delivery. Although the molecular processes involved in the permeabilization mechanisms are very complex, the formation of "pores" in the plasma membrane, under the influence of an electric field, is deemed responsible of the cellular responses. Electric field intensity and duration are the fundamental parameters in the modulation of the occurring phenomena. The effects of the application of an electric field can be evaluated by adopting either a lumped parameters circuital model or a continuous field based description of the cell structure. In both cases one of the main parameters affecting the cell response is the voltage across the membrane (trans-membrane voltage-TMV). If trans-membrane voltage is greater than a critical value, structural changes in the surface membrane occur that cause pore formation and, in turn, increased permeability. Recently, it has been shown that for pulses in the ns range, intracellular structures may be affected without appreciable modifications in the plasma membrane. However, in modelling the electro-permeabilization process, several physical constants need to be approximated in order to obtain realistic results from the numerical scheme approximating the theoretical model (circuital or field based).

In this work we have developed an electric model for living cells in order to predict an increasing probability for electric field interactions with intracellular substructures of cells when the electric pulse duration is reduced to the nanosecond range. Our model consist of a modified Hodgkin-HuxleyCtype non linear equivalent circuit for the outer cell membrane, pore formation and the effect of pores on the conductivity of the outer cellular membrane are taken into consideration. Moreover, the accumulation or depletion of ions in a restricted space surrounding the outer cell membrane (variable concentration), coupled with a linear R_C equivalent circuit for the nuclear membrane is considered.

The pore formation is governed by the so called Smoluchowski equation, which determines, together with the modified nonlinear equivalent circuit, a non linear behaviour of the conductivity of the outer cell membrane with the applied field. In order to take into account the parameters variations and/or uncertainties, in value or dislocation inside the system, an accurate range analysis is carried out. This approach, representing a peculiar aspect of this work, gives the possibility of evaluating the range of electrical pulses values (amplitude, rise time, duration) to be applied, in order to obtain reversible or irreversible effects on the cellular membrane.