

## Modelling of the electroporation process at the microscopic cell scale.

The electroporation consists of imposing high electric pulses on the cell in order to weaken its plasma membrane. Biologically active molecules that otherwise cannot diffuse through the membrane (*e.g.* hydrophilic compounds such as bleomycin or DNA [Mir1998], [Mir2006]) may then spread through the cell membrane. If the pulses are short enough the membrane is not destroyed and the cell integrates the active molecules without losing its viability ([Weaver96], [Weaver2000], [Chen2006]). Such internalization is a complex phenomenon hidden behind the term electroporation. Well understanding of the phenomenon is essential in order to determine which part of the cell membrane has to be electroporated so that the drug delivery may be optimized.

Inside the collaborative research initiative of INRIA (ARC C3MB) a part of the team MC2 with the Institut Gustave Roussy and the Department of Mathematics of Versailles aims to describe the phenomenon at the cell scale. Particularly, a current model describing the deformation of the cell membrane submitted to short high pulses is in progress for a single biological cell.

The aim of the postdoctorate will consist in studying both numerically and theoretically this new model of the electroporation. After a precise study of the model developed by the ARC C3MB for a single cell, the candidate will extend the model to a finite number of cells.

*In vitro* experiments deal with cell suspensions, such that the distance of two neighboring cells is large compared with the membrane thickness. Introducing this cell-cell distance as a parameter, a precise description of the voltage distribution in the assembly of “non-touching” cells will be performed in order to determine the electropermeabilized regions. We expect to highlight with the help of numerical simulations the experimentally observed differences between electroporation of dilute and dense cell suspensions (Pucihar *et al.* [Pucihar2007]).

Another interesting part of the subject is the modelization of the *in vivo* electroporation. For *in vivo* experiments the “non touching” assumption is no more satisfied. Actually the cells are very close to their neighbor. We expect that the asymptotic behaviour could be significantly different from the *in vitro* case. This could explain the different thresholds of reversible electroporation for *in vitro* and *in vivo* experiments. In the assembly of non-connected “touching” cells the distance between two adjacent cells is no more large compared with the membrane thickness. For the “limit” configuration (membrane thickness tending to zero), this makes appear multiply connected insulating thin layers. Figotin and Kuchment [Kuchment1998] and Rubinstein and Schatzman [Rubinstein2001] have studied the spectrum of Laplacian operators in such media. Based on these papers, we expect the candidate to perform an appropriate asymptotic analysis of the electropermeabilization model. The main difficulties lie in the triple points that appear when the membrane thickness tends to zero. We expect that a modified Kirchoff law argument ([Rubinstein2001]) and an asymptotic analysis based on [Dauge2007] would help to perform the analysis.

Good knowledge in asymptotic analysis in singular domains, and programming skills are required to achieve the goals of the subject.

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