Allen-Cahn equation and Mean field model of cell electroporation

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Biographie – Je suis en thèse à l'université de Bordeaux sous la direction de Annabelle Collin et Clair Poignard. J'ai connu le sujet de l'électroporation pendant un stage en M2 sous la direction de Clair Poignard. Ce sujet a des liens très forts avec la médicine (traitement du cancer) et avec l'industrie de produits alimentaires. En particulier, à échelle cellulaire le phénomène de l'electroporation est important dans le domaine des organisme génétiquement modifiés (OGM).

Resumé :

One of the main characteristics of a cell membrane is that it's a semi-permeable layer, that is, it can allow only certain molecules to pass through it. This semi-permeability is crucial in a lot of regulatory processes that take place in the cell. For example, a cell can regulate the concentration of certains ions inside it by letting in more or less ions from its environment through its membrane.

The membrane of a cell is mostly made up of a lipid-bilayer, as a result when it is under the influence of an electric field it behaves like a dielectric. In contrast, the inside of the cell behaves mostly like an electrolyte. When an electric field is applied to a cell, there is an accumulation of charge at the membrane and so a transmembrane voltage (TMV) appears. When this voltage goes above a certain threshold the permeability of the cell membrane dramatically increases and so molecules that before couldn't enter the cell now are able to. This phenomenon is called electroporation as it's due to tiny pores appearing on the cell membrane which allow the passage of molecules through it.

A number of models have been proposed to understand and describe this phenomenon [3]. Among them, one of the most used in the literature was proposed by W. Krassowska and C. Neu [2]. In it, they model the state of the cell membrane through a pore density function N, meaning that $N(t,x)$ is the number of pores per unit of membrane area at a point x on the membrane and at a time t.

Even though this model does fit experimental data (at least qualitatively), there are still some aspects it can be improved upon. Among them is its dependance in a lot of parameters, some of which are hard to give a physical sense to and some of which are hard to measure in practice. In fact some of the constants needed for this model are only known within an order of magnitude in any given cell.

We propose a different approach to modeling this phenomenon. We model the state of a cell membrane by means of an order parameter which measures the amount of water inside the membrane: $\phi : \Gamma \to [-1,1]$, where $\Gamma \subset \mathbb{R}^3$ is a closed surface representing the cell membrane. The evolution of this order parameter is then given by the L^2 derivative of the following energy functional :

$$F[\phi] = \underbrace{\frac{D}{2}\int_\Gamma |\nabla\phi|^2}_{\text{Membrane diffusion}} \quad \overbrace{+\int_\Gamma W(\phi)}^{\text{Potential Energy of Membrane}} \quad - \quad \underbrace{\frac{1}{2}\int_\Gamma C_m(\phi)\big([U]_{|\Gamma}\big)^2}_{\text{TMV influence on the membrane}} \tag{1}$$

where $W : \mathbb{R} \to \mathbb{R}$ is a double-well potential. In the simplest case, when $W(x) = \frac{1}{4}(x^2 - 1)^2$ we obtain the so called Allen-Cahn equation but with an extra term due to the electric field's influence on the membrane:

$$\begin{cases} \partial_t \phi - D\triangle_\Gamma \phi = -\phi(\phi^2 - 1) + \frac{C_m'(\phi)}{2} \underbrace{[U]_{|\Gamma}^2}_{\text{TMV}} \\ \phi(0, \cdot) = \phi_0. \end{cases} \tag{2}$$

The whole system describing the phenomenon is then given by (2) coupled with a Poisson equation on the electric potential U (like in krassowska's model):

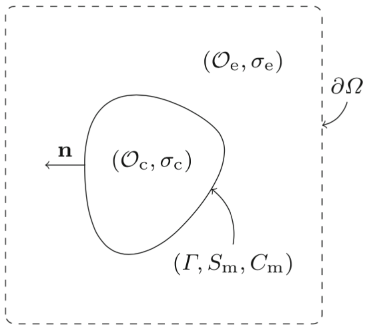

Figure 1: Cell diagram: $\mathcal{O}_c$ and $\mathcal{O}_e$ are the cell interior and the exterior environment. $\Gamma = \partial\mathcal{O}_c$ is the cell membrane. σ_c and σ_e are the conductivities of the interior and exterior of the cell. And finally, S_m and C_m is the membrane conductivity and capacitance. Diagram from [1]

$$\begin{cases} \triangle U = 0, \text{ in } \mathcal{O}_c \cup \mathcal{O}_e, \\ U(0, \cdot) = 0, \text{ in } \mathcal{O}_e \cup \mathcal{O}_c \\ U(t, x) = g(t, x), \text{ on } \partial\Omega \\ \sigma_c \partial_n U_{|\Gamma-} = \sigma_e \partial_n U_{|\Gamma+}, \text{ conservation of charge across the membrane} \\ \sigma_c \partial_n U_{|\Gamma-} = C_m(\phi)\partial_t [U]_\Gamma + S_m(\phi)[U]_\Gamma, \text{ modeling of current through } \Gamma. \end{cases} \tag{3}$$

We show well posedness for the coupled system of (2) and (3) in a suitable Sobolev space and show some numerical simulations of this model. We also discuss future ways in which we plan to complexify this model to include other aspects of the electroporation phenomenon.

Références

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