## C3

# Molecular dynamics simulations of membrane electroporation

***Mounir Tarek***
*CNRS- Université de Lorrains, Nancy France*
*Europeen Laboratory EBAM*

Duration of the experiments: 90 min
Max. number of participants: 18
Location: Computer room (P18-A2)
Level: Basic

**PREREQUISITES**
No specific knowledge is required for this laboratory practice.

**The aim** of this laboratory practice is to get familiar with the tools for molecular dynamics, possibilities to set on models and graphical presentation of atomistic models.

**THEORETICAL BACKGROUND**
The application of strong electric fields to cells or tissues permeabilizes the cell membrane and produces aqueous-filled pores in the lipid bilayer (along with other chemical and structural changes of the membrane) [1]. Electroporation is witnessed when the lipid membrane is subject to transmembrane voltage (TMV) of the order of few hundred millivolts, which is induced during exposure to an electrical pulse. Such TMV is sufficient to produce an electric field within the membrane of the order of ~ $10^8$ V/m. The electroporation process is believed to involve (1) charging of the membrane due to ion flow, (2) rearrangement of the molecular structure of the membrane, (3) formation of pores, which perforate the membrane and are filled by water molecules (so-called aqueous, or hydrophilic, pores), (4) an increase in ionic and molecular transport through these pores, and, under appropriate conditions, membrane integrity recovery when the external field stress is removed [2,3].
**Molecular Dynamics** (**MD**) simulations belong to a set of computational methods in which the dynamical behaviour of an ensemble of atoms or molecules, interacting via approximations of physical pair potentials, is determined from the resolution of the equation of motions [4]. MD simulations enable ones to investigate the molecular processes affecting the atomic level organization of membranes when these are submitted to voltage gradient of magnitude similar to those applied during electropulsation [5,6].

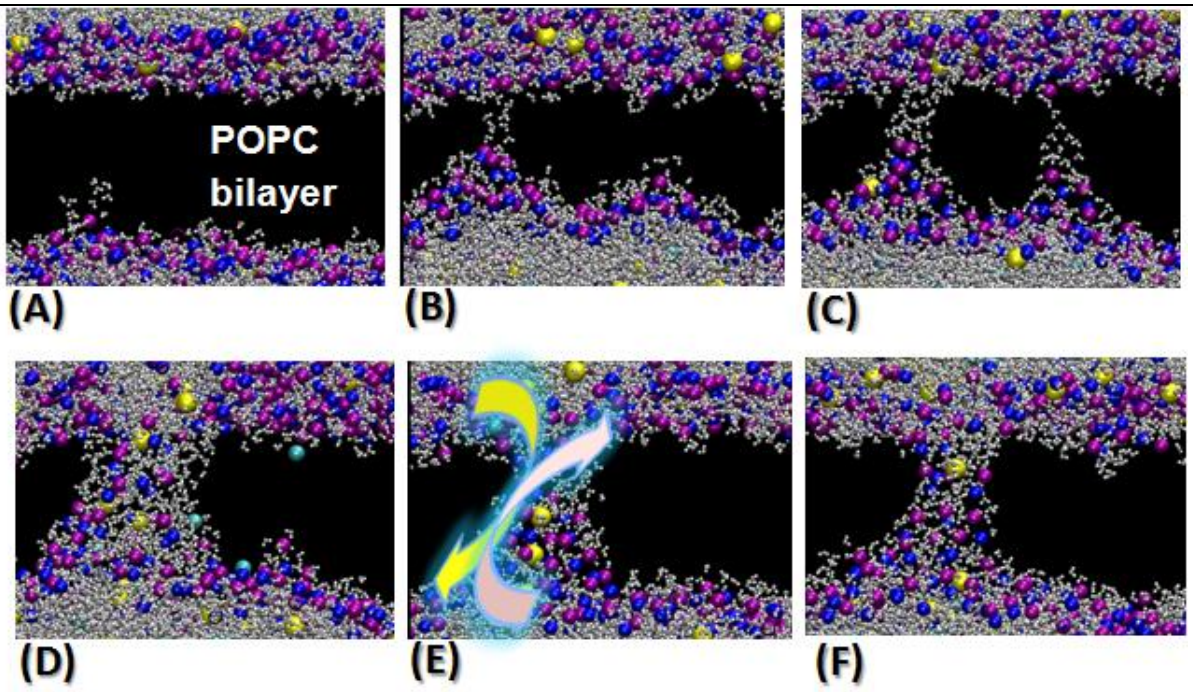


**Figure 1:** Configurations from the MD simulation for a large POPC bilayer subject to a transverse electric field. (A) Bilayer at equilibrium. (B-C) Formation of water wires at the initial stage of the electroporation process. (D-F) Formation at a later stage of large water pores that conduct ions (yellow and cyan spheres) across the membrane and that are stabilized by lipid head-group (magenta and blue spheres) [3].

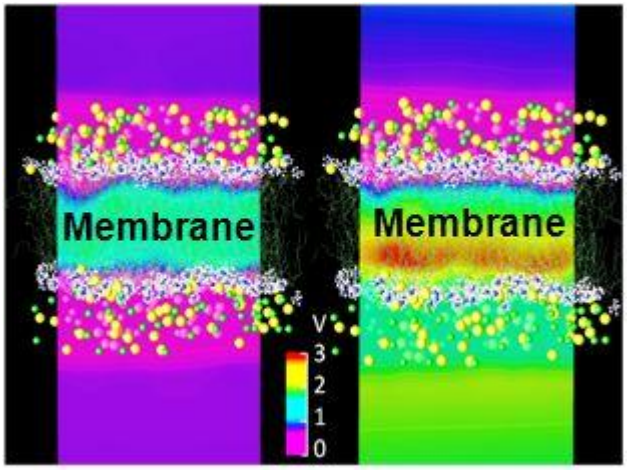


**Figure 2:** Electrostatic potential maps generated from the MD simulations of a POPC lipid bilayer (acyl chains, green; head groups, white) surrounded by electrolyte baths at 1 M NaCl (Na+ yellow, Cl- green, water not shown) terminated by an air/water interface. Left: net charge imbalance $Q = 0$ e (TMV=0 mV). Right: $Q = 6$ e (TMV=2 V).

## EXPERIMENT

Due to the limited time and large resources needed to generate MD trajectories of membranes, the latter will be provided to the students. The simulations concern pure planar phospholipid bilayers (membrane constituents) and water described at the atomic level. A set of long trajectories spanning a few nanoseconds generated with or without a TMV induced by unbalanced ionic concentrations in the extracellular and intracellular will be provided. The students will (1) determine the distribution of the electric potential and electric field in model membrane bilayers (2) measure the membrane capacitance, (3) visualize at the

molecular level the formation of membrane pores under the influence of a transmembrane voltage, and (4) measure the intrinsic conductance of such pores.

**REFERENCES:**


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**NOTES & RESULTS**