Molecular dynamics simulations of membrane electroporation C3

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Duration of the experiments: 90 min
Max. number of participants: 18
Location: Computer Laboratory (CIT)
Level: Basic

PREREQUISITES

No specific knowledge is required for this laboratory practice.

THEORETICAL BACKGROUND

The application of high electric fields to cells or tissues permeabilizes the cell membrane and is thought to produce aqueous-filled pores in the lipid bilayer. Electroporation is witnessed when the lipid membrane is subject to transmembrane voltages (TMV) of the order of few hundred millivolts, which results from the application of electrical pulses on a microsecond to millisecond time scale which are sufficient to produce a transient trans-membrane potential and an electrical field across the membrane of the order of ~ 10^8 V/m. This 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.

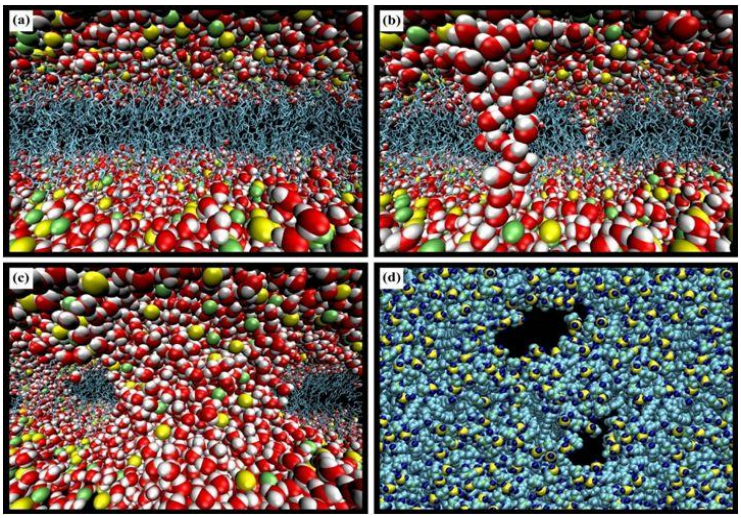

Figure. 1 Configurations from the MD simulation for a large DMPC bilayer drawn in perspective. (a) Bilayer at equilibrium. (b) Formation of water wires at the initial stage of the electroporation process when the bilayer is subject to a transverse electric field. (c) and (d) Formation at a later stage of large water pores stabilized by lipid headgroups. (M. Tarek. *Biophys. J.* 2005)

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. 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. The aim of this practical exercise is to characterize from MD simulations trajectories the electrostatic properties of membranes subject to a transmembrane potential (0 to 2 V).

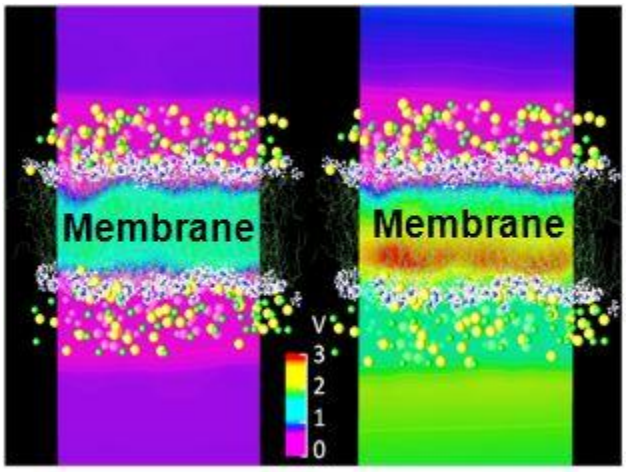

Figure 2 Electrostatic potential maps generated from the MD simulations of a POPC lipid bilayer (acyl chains, green; head groups, white) surrounded by electrolyte baths at _1 M NaCl (Na+ yellow, Cl- green, water not shown) terminated by an air/water interface. Left: net charge imbalance Q = 0 e (TMV=0 mV). Right: Q = 6 e (TMV=2 V)

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

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 few nanoseconds generated with or without a transmembrane voltage induced by unbalanced ionic concentrations in the extracellular and intracellular will be provided. The students will (1) determine the distribution of 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 measure the intrinsic conductance of such pores.

FURTHER READING:

1. Tarek, M. Membrane Electroporation: A Molecular Dynamics Study *Biophys. J.* 88: 4045-4053, 2005.
2. Dehez, F.; Tarek, M.; and Chipot, C. Energetics of Ion Transport in a Peptide Nanotube *J. Phys. Chem. B* 111: 10633-10635, 2007
3. Tarek, M. review January 2009 ADD

NOTES & RESULTS