Molecular dynamic simulation of the transmembrane pore growth under effect of the electric field

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Effect of the plasma upon tissue characteristics has a complex character. First of all one should mention generation of the radicals, ions, excited species, UV emission. Besides of that plasma contains the high intensity electric field stimulating the phenomenon of electroporation (EP) which manifests itself in the growth of pores in a cell membrane under the action of the external electrical field. Therefore the electrical field can be considered as an effective tools promoting the penetration of drugs, genes etc. inside a cell. The main problem arising at the theoretical description of the pore evolution in the presence of the external electrical field relates to evaluation of the time dependent pore size distribution function (PSDF). Two main approaches have been elaborated for solution of this problem. One of those is based on the Einstein-Smoluchowski equation in accordance with which the pore evolution proceeds as a stochastic process and a pore is represented by a few energy parameters [1]. These parameters are chosen usually by an empirical way. The second approach which is based on molecular dynamic (MD) simulation of the pore evolution [2] appears to be more justified. Disadvantages of this approach relate to very high computing time cost. For these reasons the interconnection between the parameters of the electrical field applied to a cell of a specific nature and the size of pores in its membrane remains to be empirical.

In order to overcome the above-mentioned disadvantages of the existing approaches, we apply MD for recovering kinetic coefficients used in the Einstein-Smoluchowski equation for PSDF. All molecular dynamics simulations were performed using GROMACS ver. 4.5.4 program package. OPLS united-atom parameters were used for lipid molecules, while the simple point charge model was used for water.. Two different bilayers of the membrane were considered: POPC membrane with 128 molecules of the lipid, 6606 water molecules and POPE membrane with 340 lipid molecules and 6729 water molecules. After preliminary 1 ns thermalization an external electrostatic field of the magnitude 0.3-0.5 V/nm was applied, so the pore creation process has been observed during next 3 ns. After its completion, the field was turned off, and the pore started to shrink. Then it reached quasi-equilibrium state of minimum radius, and remained stable to the end of the simulation (~2 ns). 10-15 equidistant snapshots from the latter piece of the trajectory were extracted and served as the staring points for all further computations. These simulations permitted us to find non-empirical values of the pores energy parameters which after that are compared with empirical values. Sensitivity of the obtained results to membrane type and used force potential are analyzed and discussed.

References

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