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Numerical Modeling of Transport Properties of Reactive Oxygen and Nitrogen Species in Biological Membrane under Electric Field

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In recent years, plasma medicine has been rapidly developing as a new research field due to the establishment of stable formation technology of low-temperature atmospheric pressure plasma [1]. However, the biological reaction processes induced by plasma irradiation are not fully understood with respect to their physicochemical behavior. In this study, the transport properties of reactive oxygen and nitrogen species (RONS) in cell membranes under electric field were investigated using molecular dynamics (MD).

In this analysis, we constructed a lipid membrane model containing a variety of RONS. The lipid bilayer is composed of POPC (1-palmitoly-2-oleoyl-sn-glycero-3-phosphocholine), a phospholipid that forms a typical biological cell membrane. The calculation conditions are as follows. The pressure was 1 atm, the temperature was 303 K, the time step was 2 fs, and the total simulation time was 5 ns. The applied electric field is from 0.1 to 0.5 V/nm and the number of windows is 37.

The trajectories of each molecule were obtained from classical MD simulations. An umbrella sampling method was used to apply an artificial bias potential to obtain data in the region of high energy levels, which are often lacking [2]. AMBER18 was used for the present MD simulation of biomolecules.

Figure 1 shows that the position-dependent diffusion coefficients of OH, HO_2, and H_2O_2 are lower inside the membrane and higher in the water layer. There was no significant difference in these diffusion coefficients. On the other hand, O showed higher diffusion coefficients in the inner part of the membrane compared to RONS as described above. This result can be qualitatively explained by the polarity of RONS. In other words, non-polar molecules diffuse more easily inside the membrane than polar molecules.

The membrane permeability of H_2O_2, which is larger than that of O atoms and OH molecules, was smaller than that of O atoms and OH molecules. This reason must be that the membrane permeability depends on the size of the molecule. The present membrane permeability coefficient at 0.3 V/nm was four times larger than that without electric field. As shown in Figure 2, the electric field slightly reduces the energy bias against RONS molecules in the membrane, which can be said to facilitate permeation.

The formation of water channels at an electric field strength of 0.5 V/nm indicates that hydrophilic RONS are efficiently transported through the lipid bilayer of POPC. The differences in membrane permeability were observed depending on the retention area of RONS. In particular, most of the ONOOH penetrated the present membrane within 1.0 ns after channel formation.

References
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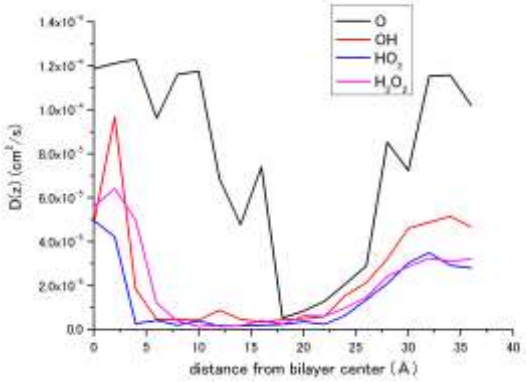

Figure 1. Position-dependent diffusion coefficients of various RONS.

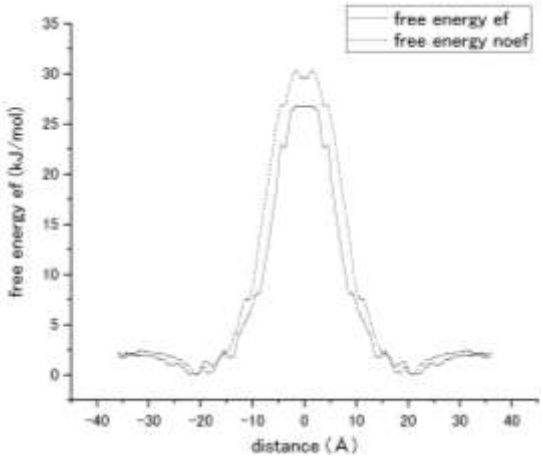

Figure 2. Free energy of H_2O_2 in POPC membrane with and without electric field.