Transport Characteristics of Reactive Oxygen Species in Cell Membranes with Molecular Dynamics - Superposition Effect of Electric Field -

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Reactive oxygen species generated by plasma irradiation have various medical effects to cell membranes. Efficient transport of reactive oxygen species into cells are essential for those appropriate regulations. Therefore, we focused on the electric field superposition effect during plasma irradiation. In present work, transport behavior of reactive oxygen species under electric field application was simulated using classical molecular dynamics. The threshold of channel formation was 0.4 V/nm, which corresponded to the general breakdown of biological membranes. The z-direction diffusion coefficient of reactive oxygen species greatly increased. The number of hydroperoxy raidcals penetrated into the channel was larger than that of hydrogen peroxide since hydroperoxy radicals accumulate at the interface between water and lipid.

1. Introduction

Recently, some stabilization techniques of atmospheric pressure non-equilibrium plasma have been established. Therefore, plasma medical science is rapidly developing as a new research field. In the field, it has been found that reactive oxygen species (ROS) generated by above plasma are important factors of various medical effects. However, polarized ROS have no significant membrane permeability [1]. We focused on the superposition effect of applied electric field during plasma irradiation. The similar process to electroporation would form water channels in cell membranes and promote the transport of ROS. In the present work, the deformation of cell membrane by electric field application was modeled with classical molecular dynamics. The influence of electric field on the diffusion coefficient of ROS was also discussed.

2. Analytical Method

In the present analysis, dipalmitoylphosphatidyl-choline (DPPC) was selected as typical phospholipid of cell membranes. The analytical membrane model was constructed with 128 DPPC and 3655 water molecules. We adopted force fields of GROMOS43A1-S3 [2] for lipid and SPC for water, respectively. 30 molecules of hydrogen peroxide (H_2O_2), hydroperoxy radical (HO_2) or singlet oxygen ($^1O_2$) were also involved in the membrane model. At first, we equilibrated the pressure, density and temperature of system as to be 1.05 bar, 1000 kg/m^3, and 323 K using Parrinello-Rahman and Nose-Hoover methods. Then, we performed MD simulations of 20 ns using a general software GROMACS 5.1.2. The strength of electric field was varied from 0.1 to 0.5 V/nm. The time step was set to 2.0 fs.

3. Results and Discussion

With respect to the electric filed strength, it was found that the threshold of channel formation was 0.4 V/nm. This value almost corresponded to the general breakdown of cell membranes. For example, Fig. 1 shows the transport dynamics of H_2O_2 at 0.5 V/nm. In this case, the channel formation time was 6.15 ns. As is shown in table 1, the z-direction diffusion coefficient averaged during 1 ns was 230 μm^2/s after channel formation. In comparison with the diffusion coefficient at non-electric field, it is clear that the membrane permeability of H_2O_2 was improved by the assistance of channel. On the other hand, HO_2 easily accumulated at the interface between water and lipid [1]. Consequently, most of HO_2 around membrane surface effectively flowed into the channel.

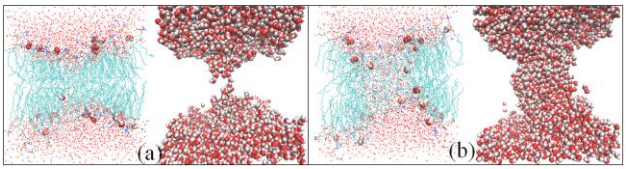

Fig. 1. Transport dynamics of H_2O_2 at 0.5 V/nm of electric field. The transient time is (a) 6.15 ns and (b) 6.75 ns. The right window of each figure represents only water molecules with VDW display style.

Table 1. Dependence of diffusion coefficient of ROS on electric field

Insert	0.5 V/nm [μm^2/s]	Non-electric field [μm^2/s]
H_2O_2	230	1.8
HO_2	279	6.2

4. References

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