Electronic Supplementary Material (ESI) for Nanoscale.

Supplementary Information for

MD simulation study of direct permeation of nanoparticle across cell membrane under external electric field

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Contents:

1. Detailed molecular compositions of simulation systems

Table S1 Molecular composition of LB-1

Number of total lipid molecules	2,304	[-]
Number of DPPC molecules	2,304	[-]
Number of DPPC molecules	0	[-]
Number of CG-water sites	123,834	[-]
Number of CG-sodium ion sites in outer compartment	710	[-]
Number of CG-sodium ion sites in inner compartment	710	[-]
Number of CG-chloride ion sites in outer compartment	830	[-]
Number of CG-chloride ion sites in inner compartment	710	[-]
Number of NP	1	[-]

Table S2 Molecular composition of LB-2

Number of total lipid molecules	2,304	[-]
Number of DPPC molecules	1,936	[-]
Number of DPPC molecules	368	[-]
Number of CG-water sites	123,466	[-]
Number of CG-sodium ion sites in outer compartment	710	[-]
Number of CG-sodium ion sites in inner compartment	1,078	[-]
Number of CG-chloride ion sites in outer compartment	830	[-]
Number of CG-chloride ion sites in inner compartment	710	[-]
Number of NP	1	[-]

Table S3 Molecular composition of LB-3

Number of total lipid molecules	2,304	[-]
Number of DPPC molecules	1,936	[-]
Number of DPPC molecules	368	[-]
Number of CG-water sites	123,466	[-]
Number of CG-sodium ion sites in outer compartment	894	[-]
Number of CG-sodium ion sites in inner compartment	894	[-]
Number of CG-chloride ion sites in outer compartment	830	[-]
Number of CG-chloride ion sites in inner compartment	710	[-]
Number of NP	1	[-]

2. Membrane breakdown potential V_c

We have preliminary determined the membrane breakdown potential V_c, which corresponds to the minimum membrane potential causing defect and poration in the membrane. To determine the membrane breakdown potential V_c in each simulation system, MD simulations without the NP were performed under several intensities of the external electric field. Figure S1 shows cross-sectional area of transmembrane pore as a function of applied membrane potential at each simulation system. The cross-sectional area of transmembrane pore increased over the zero at the critical potential. This critical potential was defined as the membrane breakdown potential V_c.

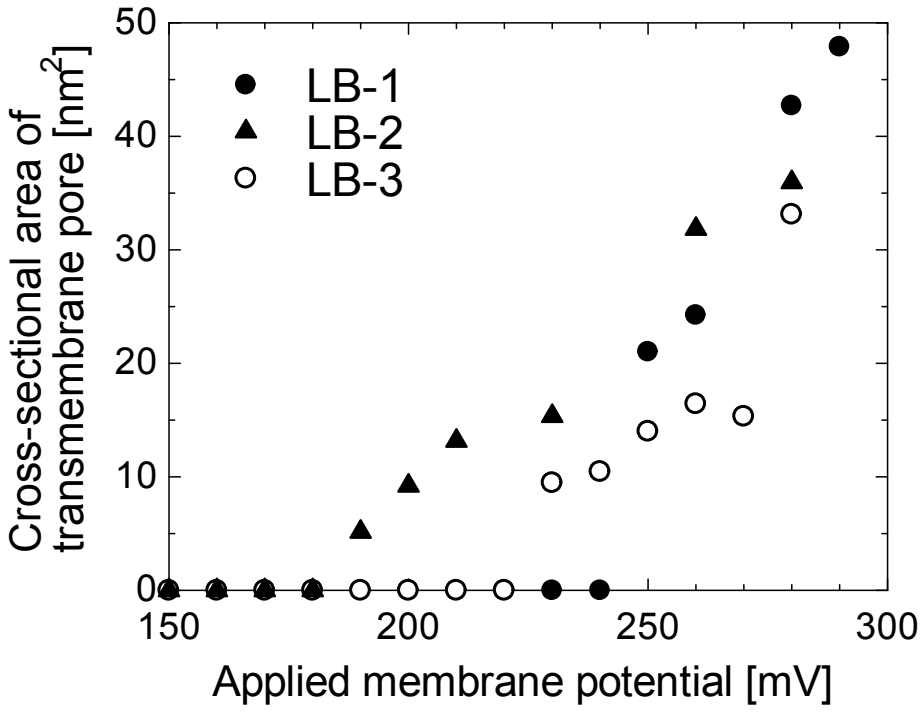

Figure S1. Cross-sectional area of transmembrane pore as a function of applied membrane potential in each simulation system.

3. The NP behaviors without the external electric field

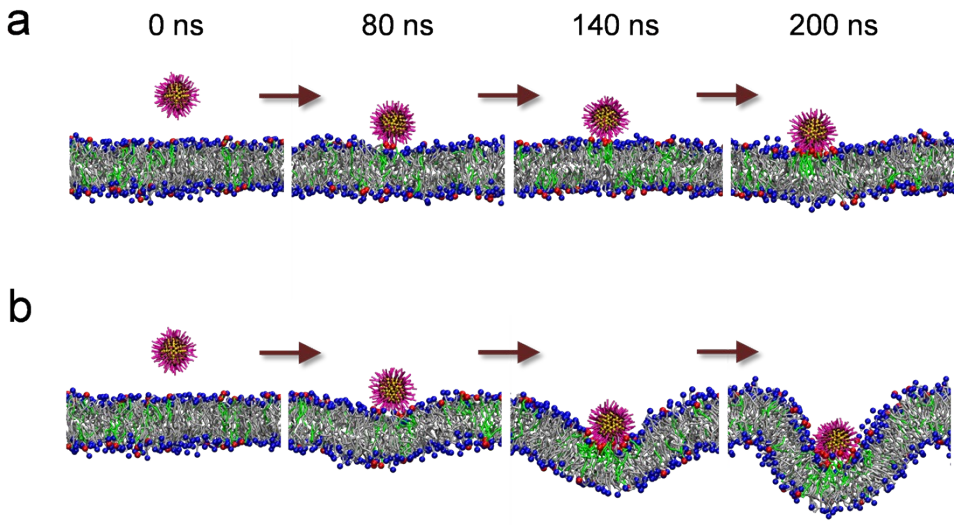

Figure S2. Snapshots of cross-sectional side views of typical NP behaviors without the external electric field (V^* = 0.0) in (a) unbiased and (b) biased (pull) simulations. The simulation system was the LB-3. Waters and ions were not shown for clarity.

4. Permeation of ions caused by the NP permeation

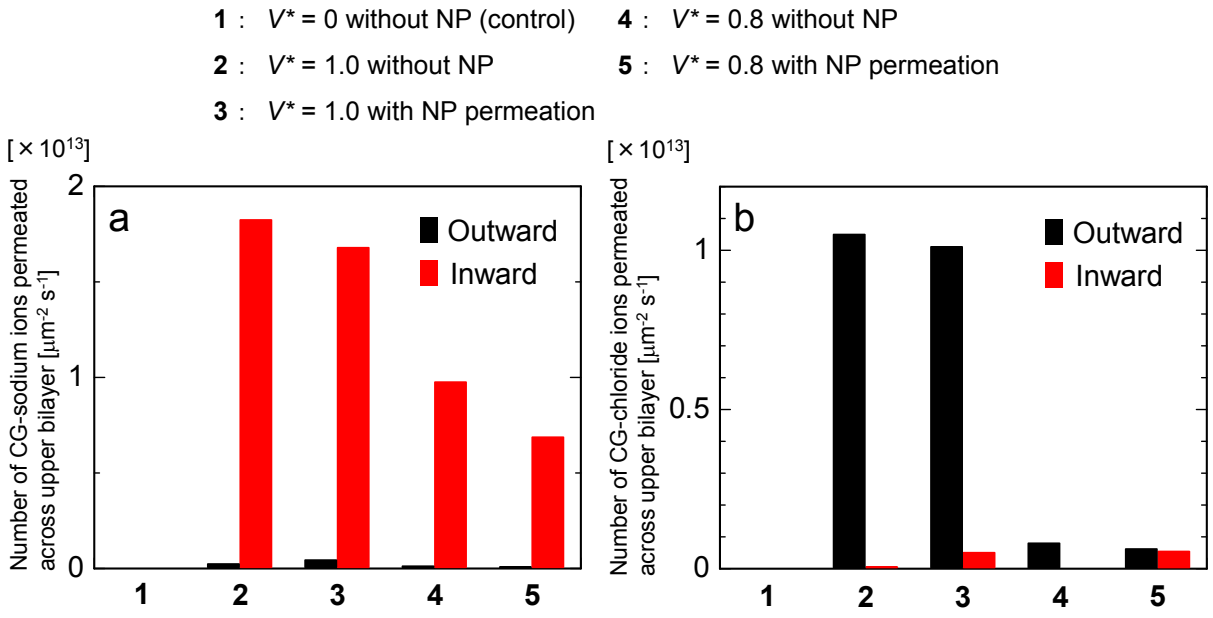

Figure S3. Number of coarse-grained (a) sodium and (b) chloride ions permeated across upper lipid bilayer at several conditions.

5. Examples of four modes of the NP behaviors

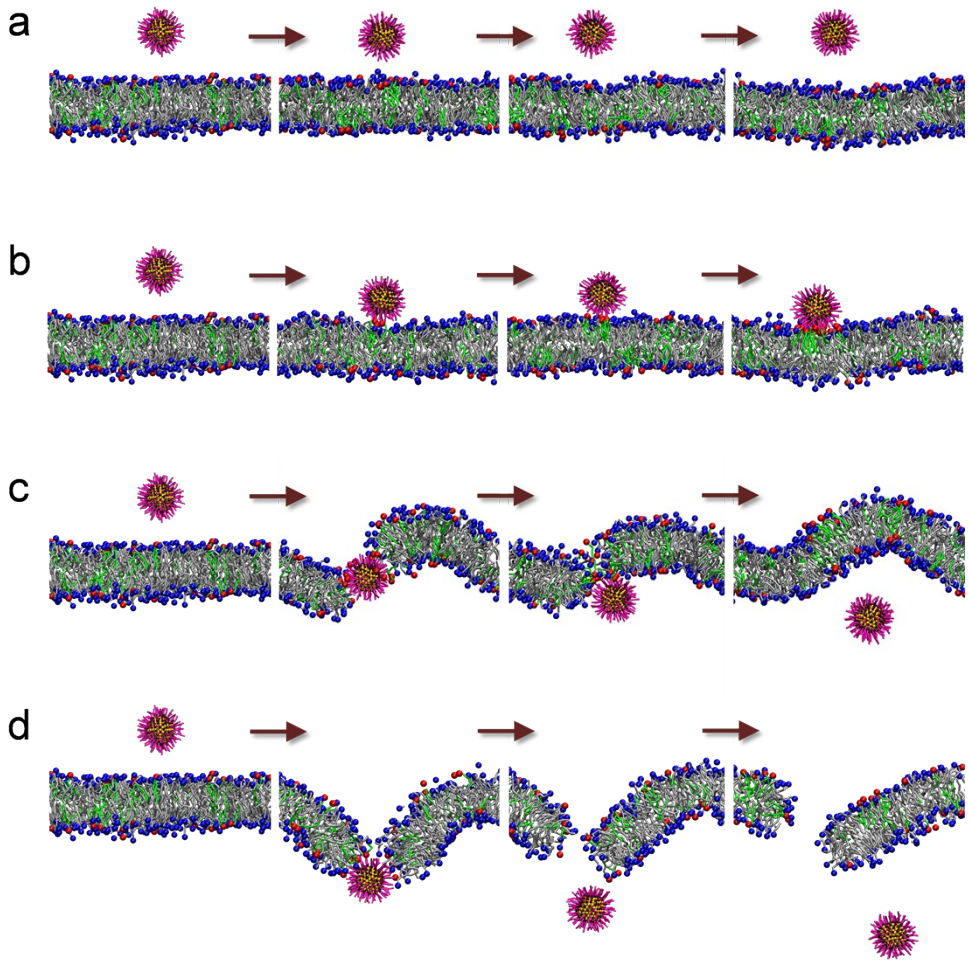

Figure S4. Examples of four modes of the NP behaviors: (a) no adhesion (diffusion in the outer solvent compartment); (b) adhesion on surface of the outer leaflet; (c) direct permeation with self-resealing of the membrane; (d) direct permeation with the persistent transmembrane poration. Waters and ions were not shown for clarity.