Supporting Information of

Nanotoxicity of Boron Nitride Nanosheet to Bacterial Membranes

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SI-1. MSD calculation.

Mean square displacement (MSD) was calculated by "gmx msd", a built-in tool of GROMACS. We simplified the case by represent each lipid with its phosphorus atom. And only the lateral (in x-y plane) displacement was considered. The time between reference points was set to be 10ps.

The diffusion constant was calculated by least squares fitting a straight line ($D*t + c$) through the MSD(t) from 10 ns to 60 ns data. error estimate was calculated as the difference of the diffusion coefficients obtained from fits over the two halves of the fit interval.

SI-2. Mass density profiles calculation.

2D number-density maps were obtained using GROMACS built-in tools "gmx densmap" with a grid size of 0.02 nm in the x-y plane, averaged over the last 20 ns data from the simulations. Only heavy atoms were counted in this calculation. For bilayer with BNNS systems, the translational and rotational motion of BNNS along x-y plane were removed before this analysis.

SI-3. Order parameter analysis.

Order parameter is a sensitive measure of structural orientation or dynamics of lipids in a bilayer. From simulations, when averaging by fast axial rotation is assumed, lipid order parameter characterizes the orientational mobility of the C–D bond and is defined as

$$S_{CD} = \left\langle \frac{3\cos^2\theta - 1}{2} \right\rangle \qquad (2)$$

where θ is the angle between the C–D bond vector and a reference axis. In our case it is the z axis which is perpendicular to the membrane plane. Order parameter per atom for carbon tails is calculated with "gmx order", a built-in tools of GROMACS.[1]

1. Chau, P.-L.; Hardwick, A., A new order parameter for tetrahedral configurations. *Mol. Phys.* **1998,** *93* (3), 511-518.

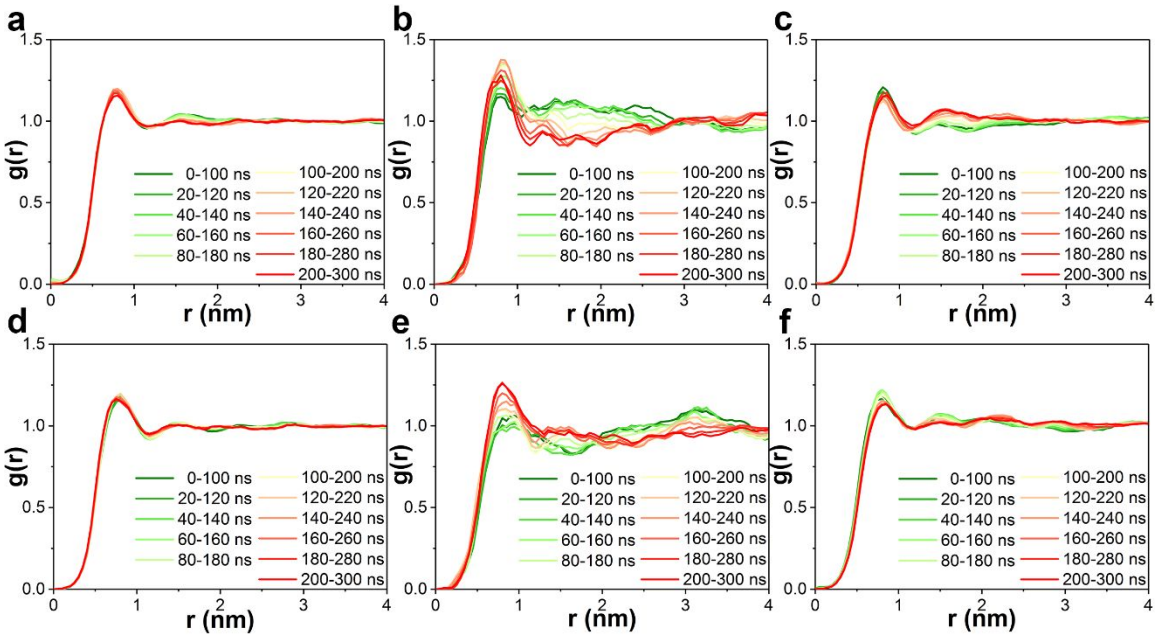

Figure S1. Time evolution of lipids RDF in the Inner_GramN systems. (a-c) RDF of POPE-POPE, POPG-POPG and POPE-POPG in the upper layer. (d-f) RDF of POPE-POPE, POPG-POPG and POPE-POPG in the lower layer. g(r) is averaged in 100 ns sliding blocks from 0 ns (green) – 300 ns (red).

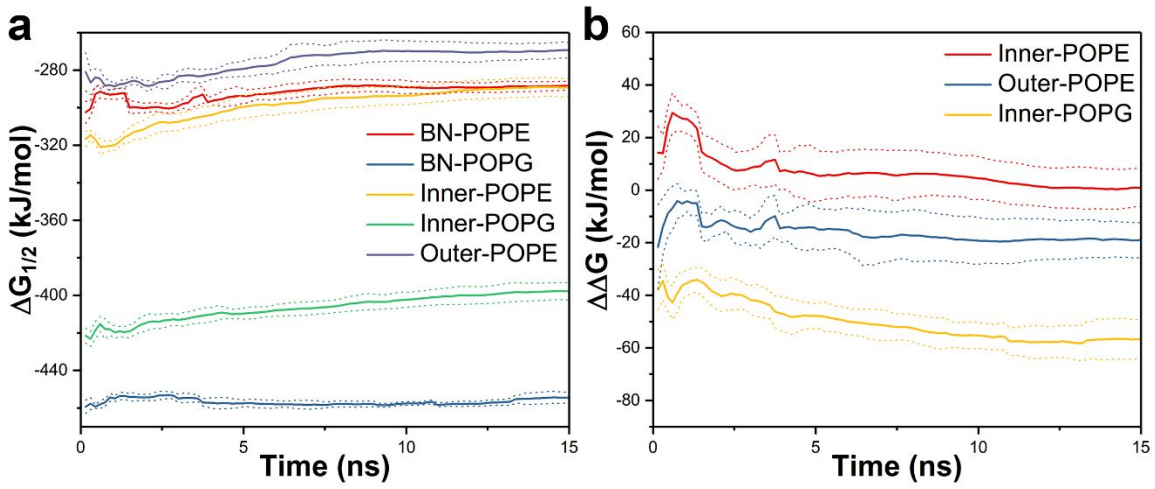

Figure S2. Convergence of the FEP calculations. (a) Free energy estimate versus simulated time for lipid molecules recoupling to calculated systems ($\Delta G_{1/2}$). (b) Free energy estimate versus simulated time for transferring a lipid from membrane to BNNS surface ($\Delta\Delta G$). A single BAR free energy estimate was carried out from 0 ns to the simulated time. The 5-15 ns data were used for final FEP estimations in Figure 5.

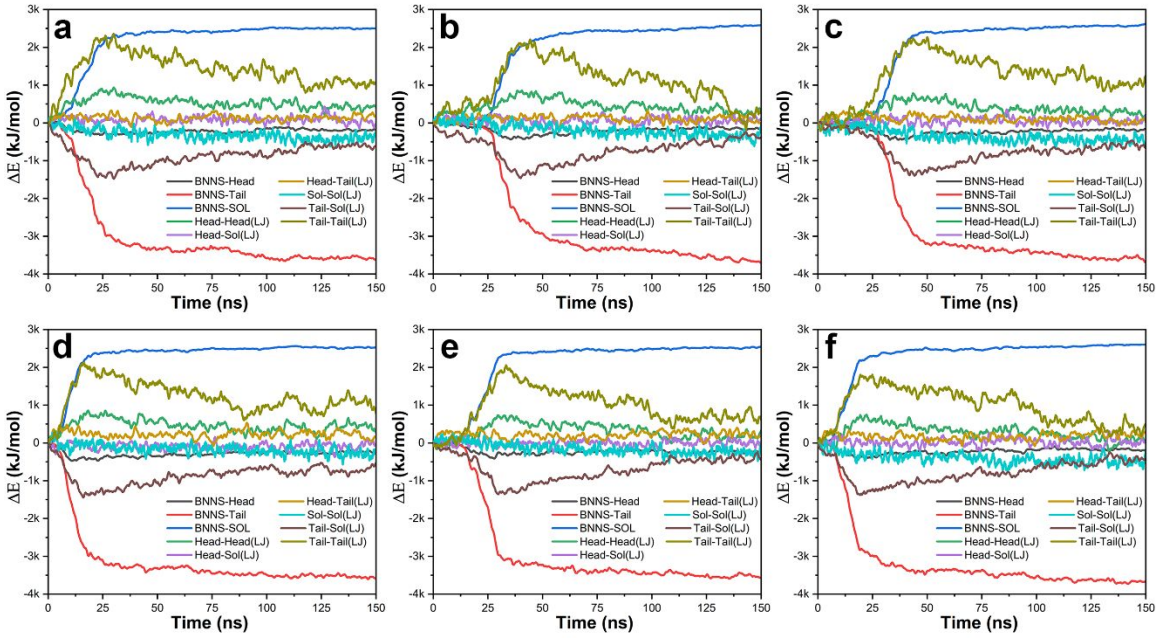

Figure S3. Time evolution of interaction energy in the Outer_GramN and Inner_GramN systems. Figure a-f show the results of Outer_1, Outer_2, Outer_3, Inner_1, Inner_2, Inner_3 systems, respectively.

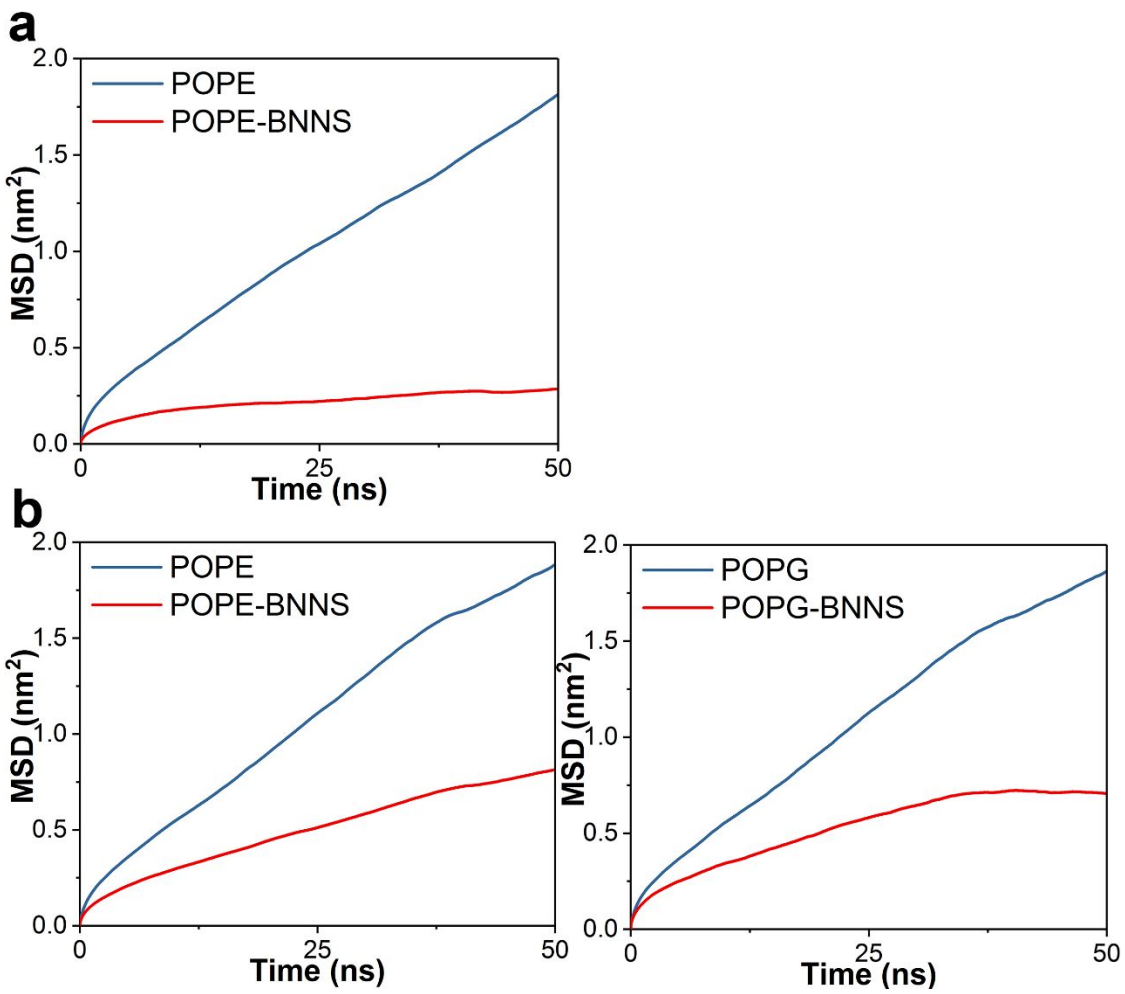

Figure S4. Mean square displacement of lipid molecules in (a) Outer_GramN and (b) Inner_GramN system with/without BNNS.