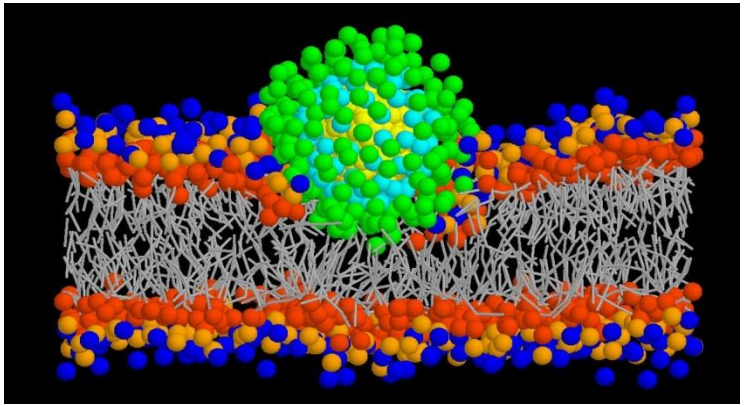
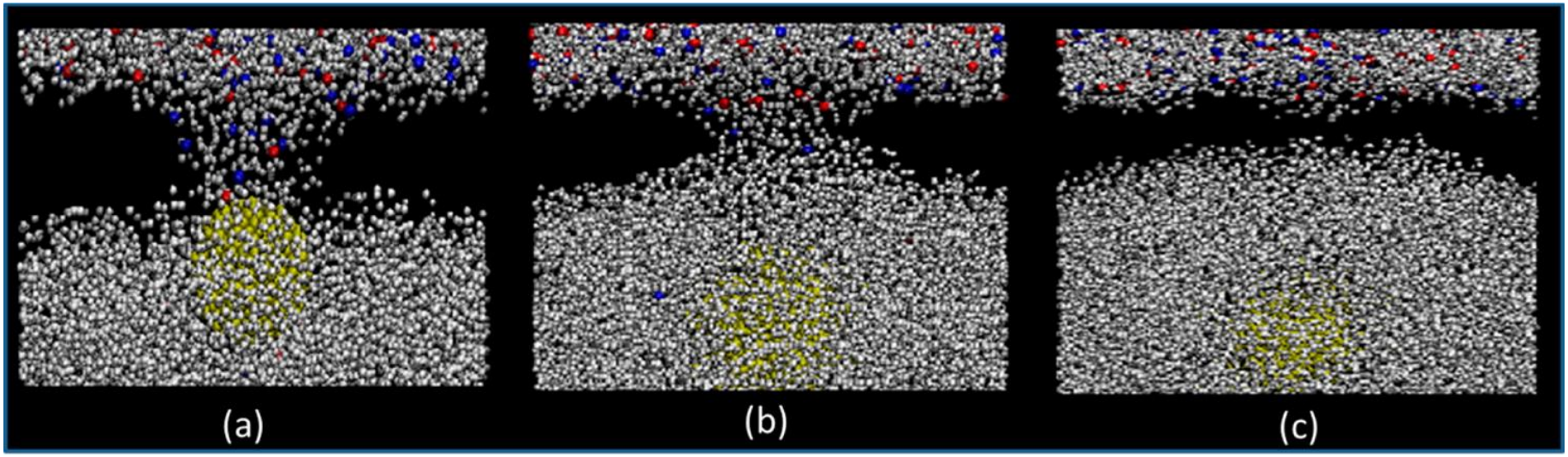
Surface-functionalized nanoparticle permeation triggers lipid displacement and water and ion leakage





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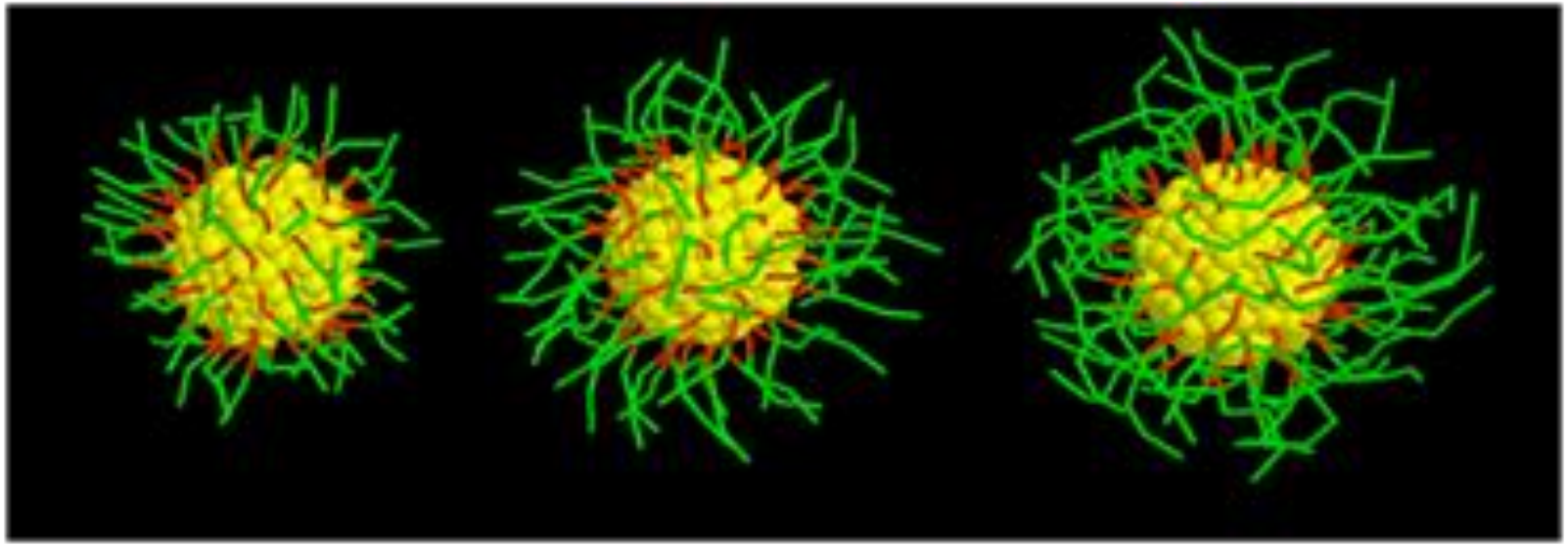
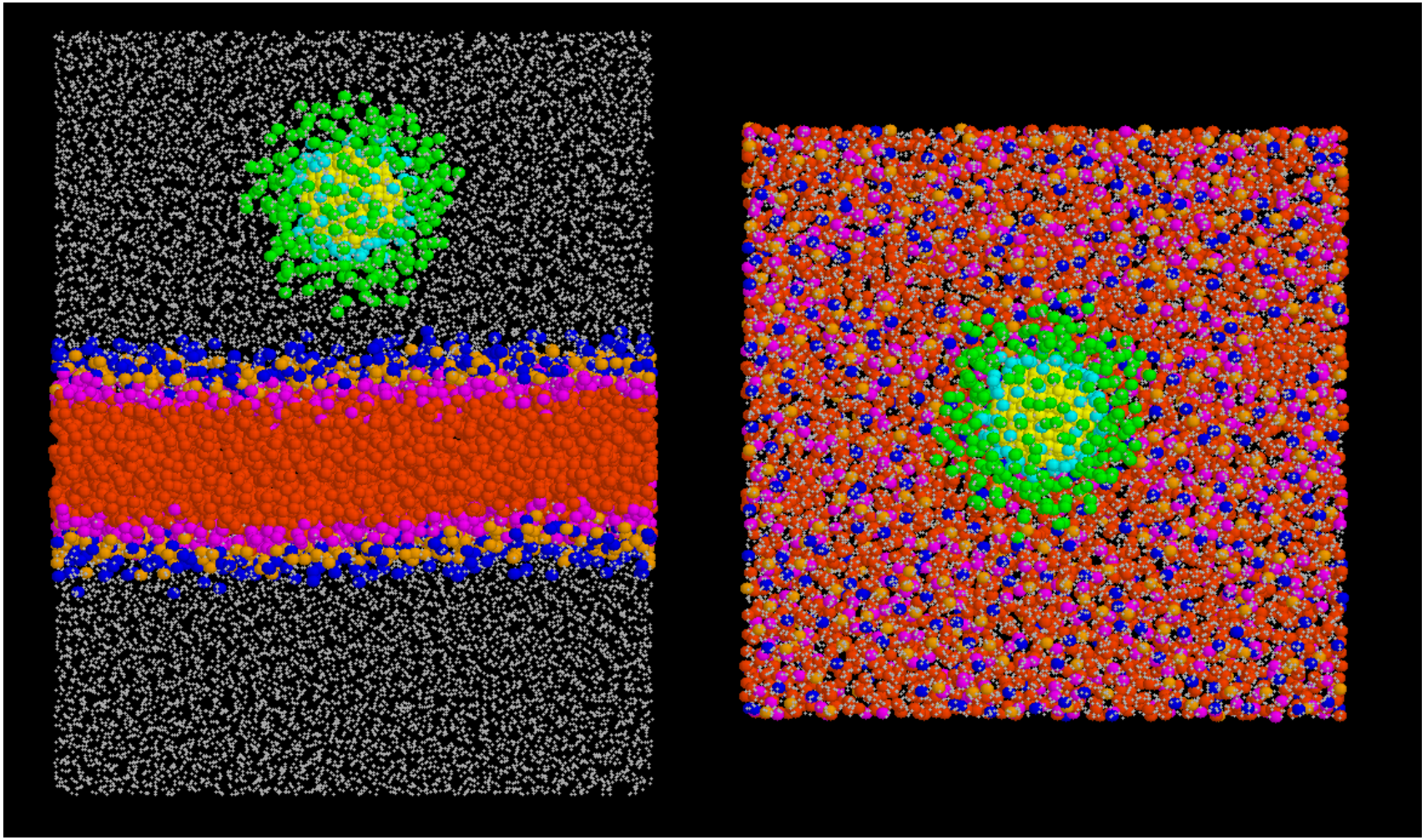
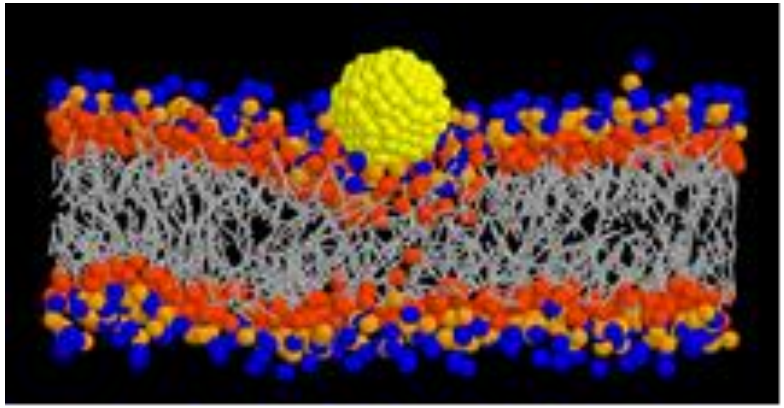
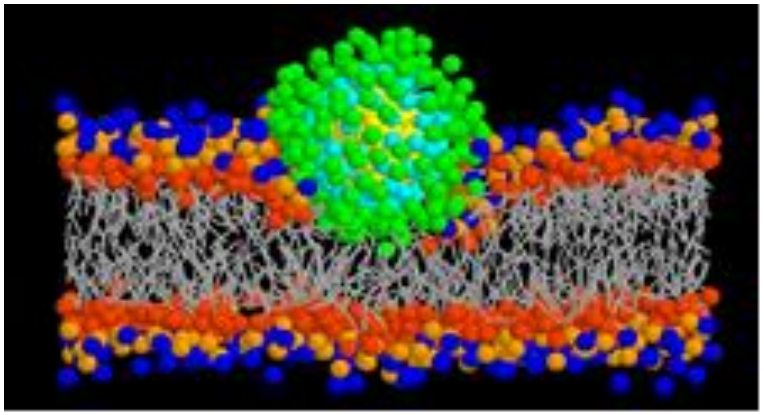


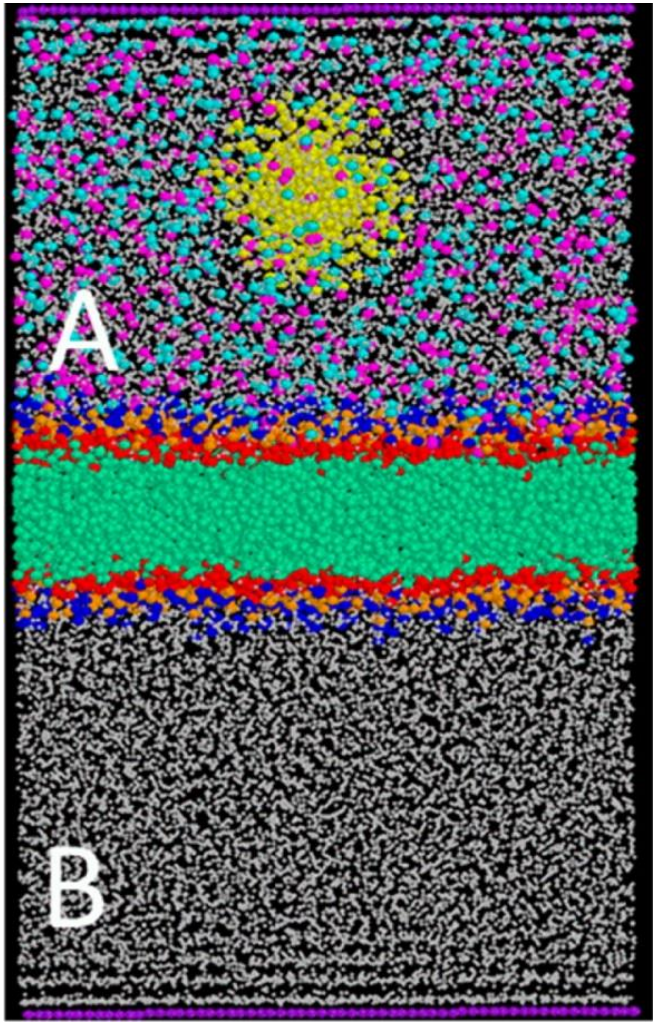
The structure of the ligand-coated gold nanoparticles.
The residues are replaced by R=(CH2)n to form nanoparticles;
shown here are structures for n=4, 8, 12 from left to right



Side and top view of the simulation system for investigating the transport of a nanoparticle across the DPPC lipid membrane. (Yellow dots represents the gold core, cyan the surface sulfur atoms, green the hydrophobic chains, blue the choline group, orange the phosphate group, magenta the glycerol group, red orange the acyl chain tail group, white dots are water molecules).







Lipid bilayer membrane simulation system used for examining nanoparticle permeation from the top compartment (A) to the bottom compartment (B) across the lipid bilayer membrane (blue = choline, orange = phosphate, red = glycerol, green = lipid tails, white = water, light blue = chloride, magenta = sodium, gold = nanoparticle core with ligands, purple = impermeable walls).

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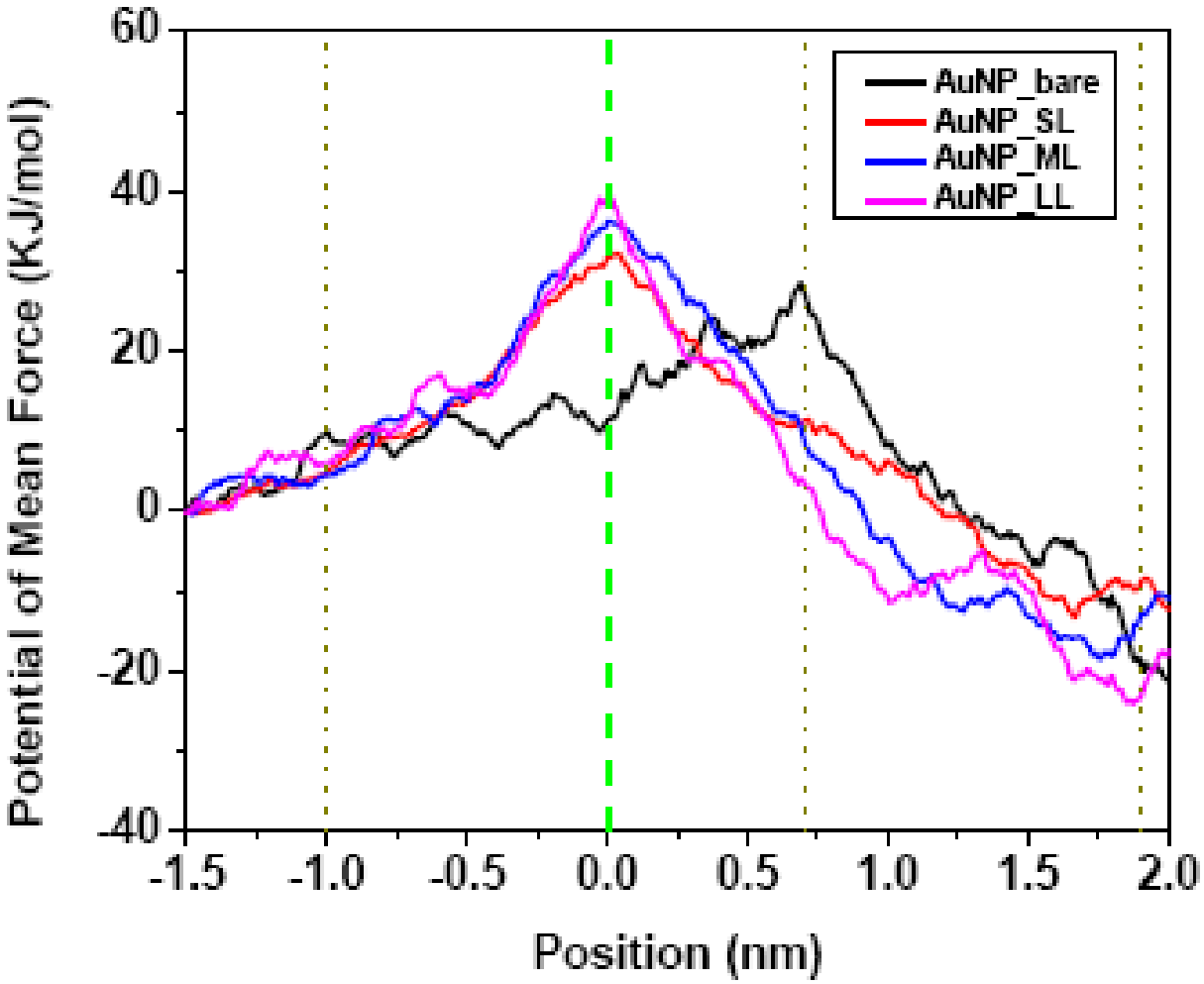
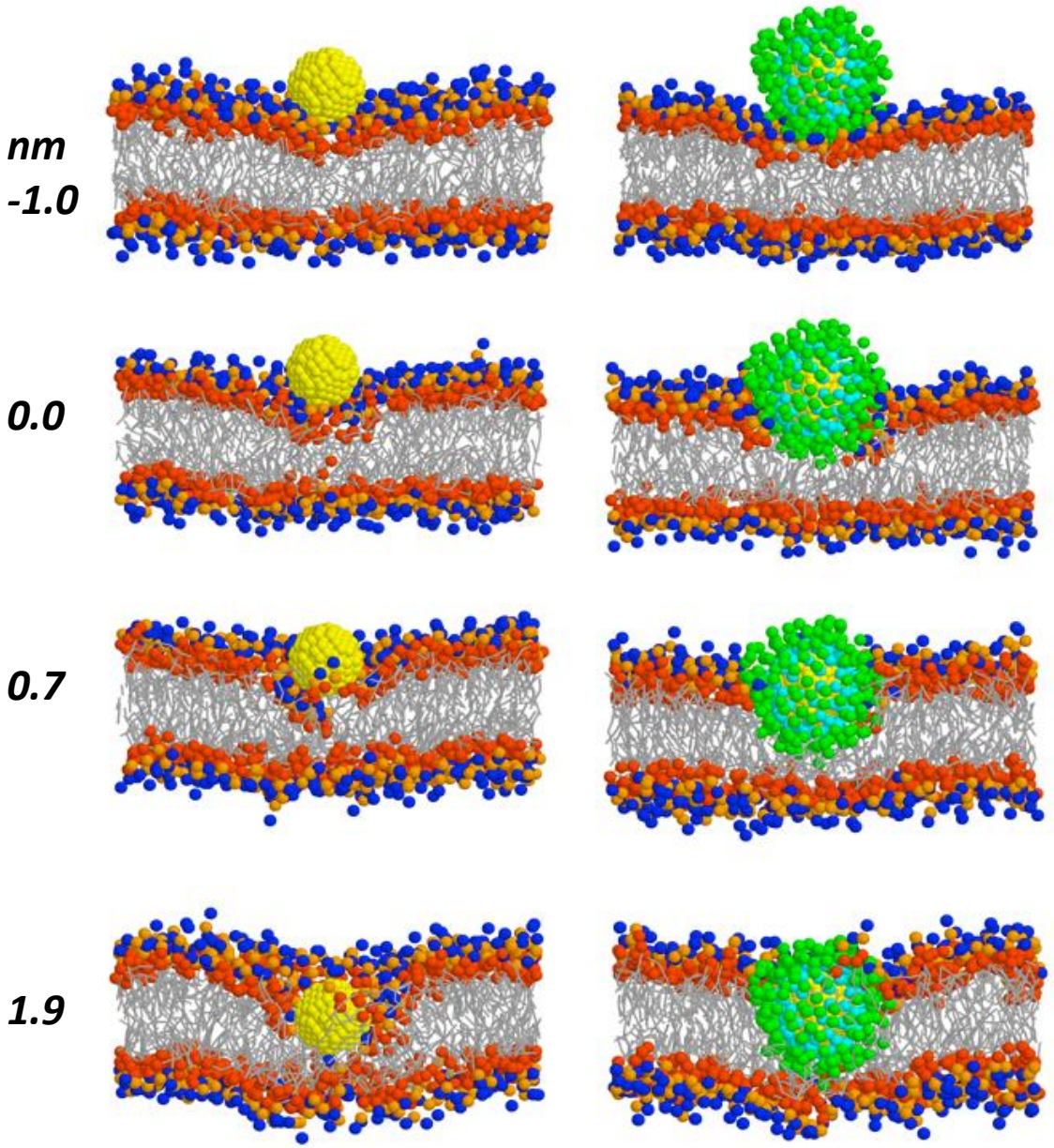


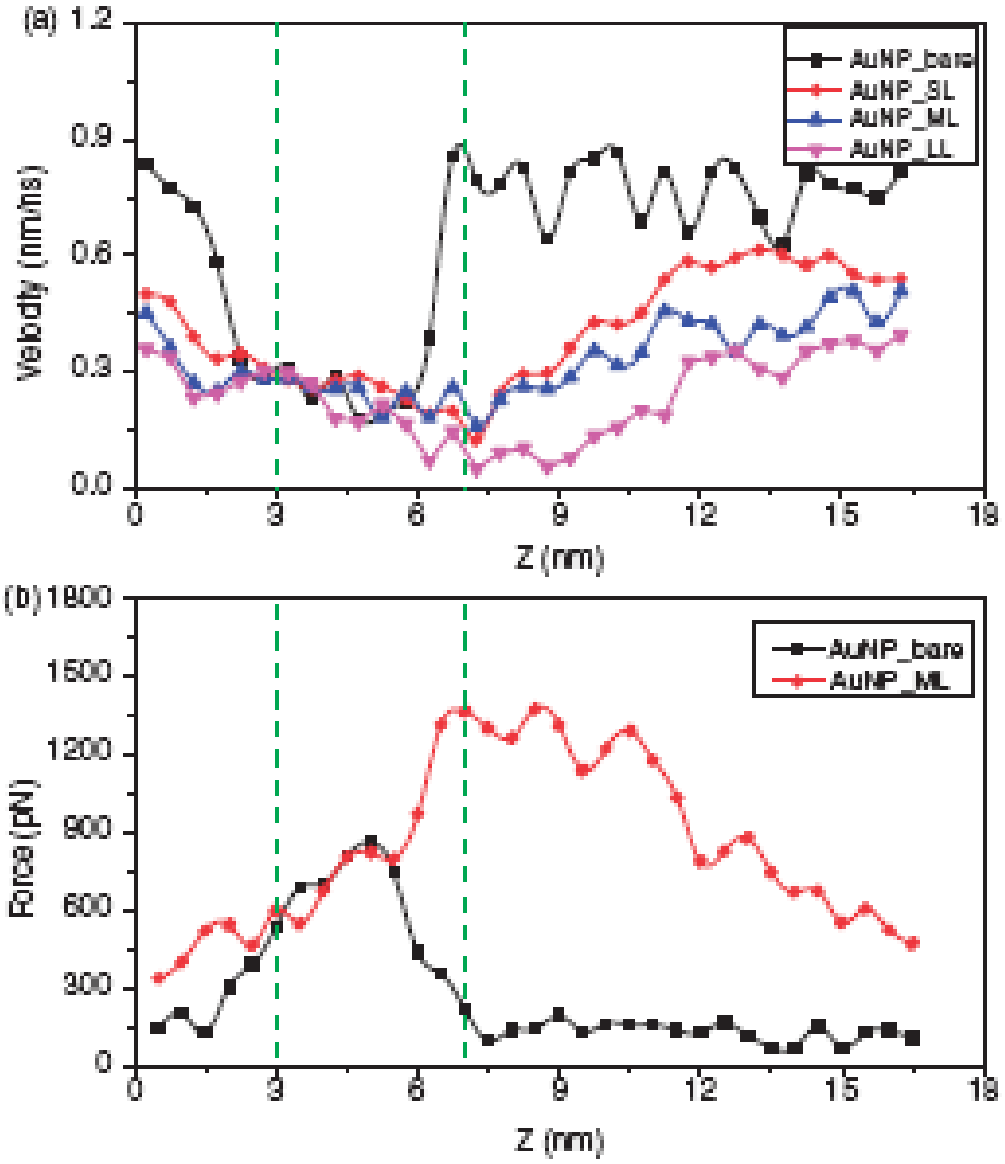
Potential of mean force profile for the permeation of nanoparticles through the first layer of the membrane bilayer. (The x-axis refers to the position of the center-of-mass of the nanoparticle, the green dashed line indicates the interface between water phase and lipid phase and the dotted lines indicate the positions corresponding to the snapshots shown in following slide.



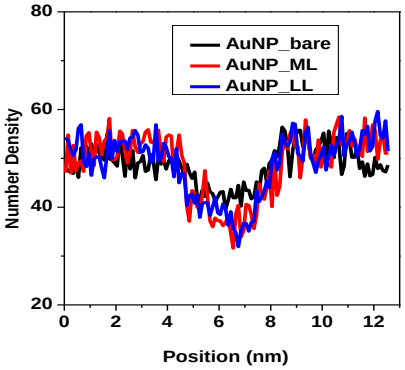
Snapshots for the permeation of bare and ligand-coated nanoparticles (AuNP_ML) through the first layer of lipid membrane.

Using the same driving force (600 pN), we obtain velocity profiles of the gold nanoparticles (z component).

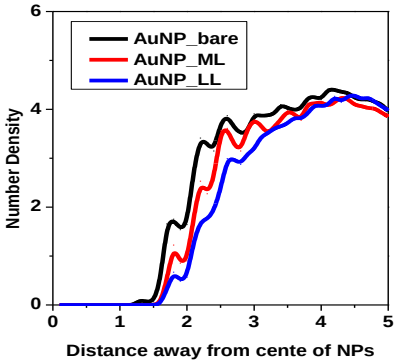
Using a fixed velocity (0.41ms–1), we obtain the force profile



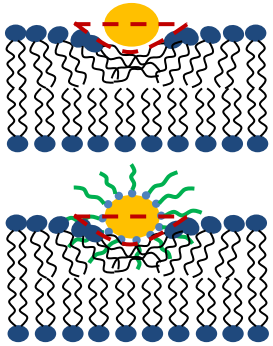
Velocity and force profiles for nanoparticle permeation. The green dashed line indicates the equilibrium position of the phosphate head groups. Note the differences between bare and ligand-coated NPs.



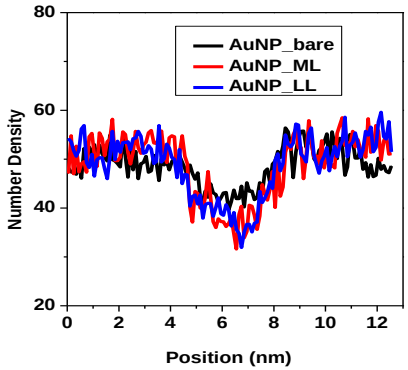
(a)



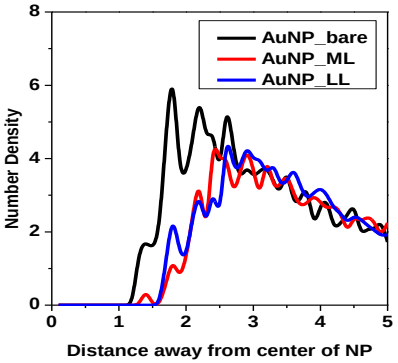
(b)



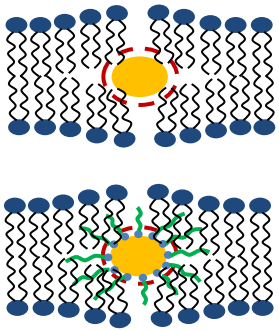
(c)



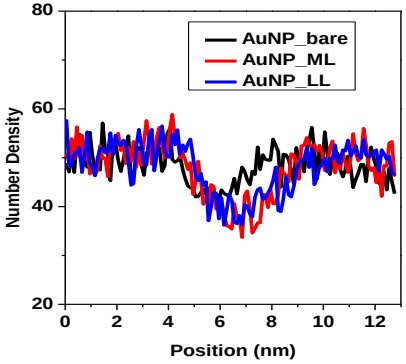
(d)



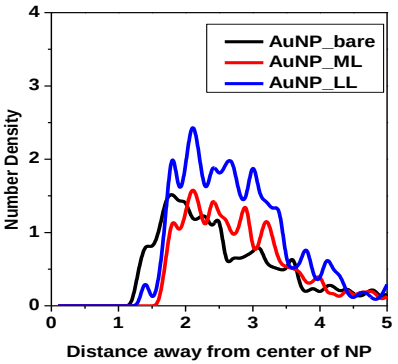
(e)



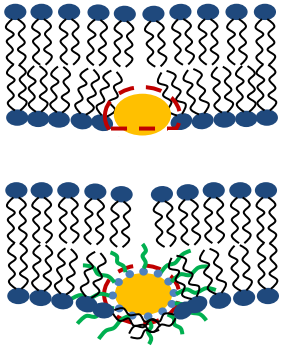
(f)



(g)



(h)



(i)

Illustrations and x-plane lipid membrane density profile and radial density profiles for those lipid molecules in front of the nanoparticles (AuNP_bare, AuNP_ML and AuNP_LL nanoparticles are shown here).

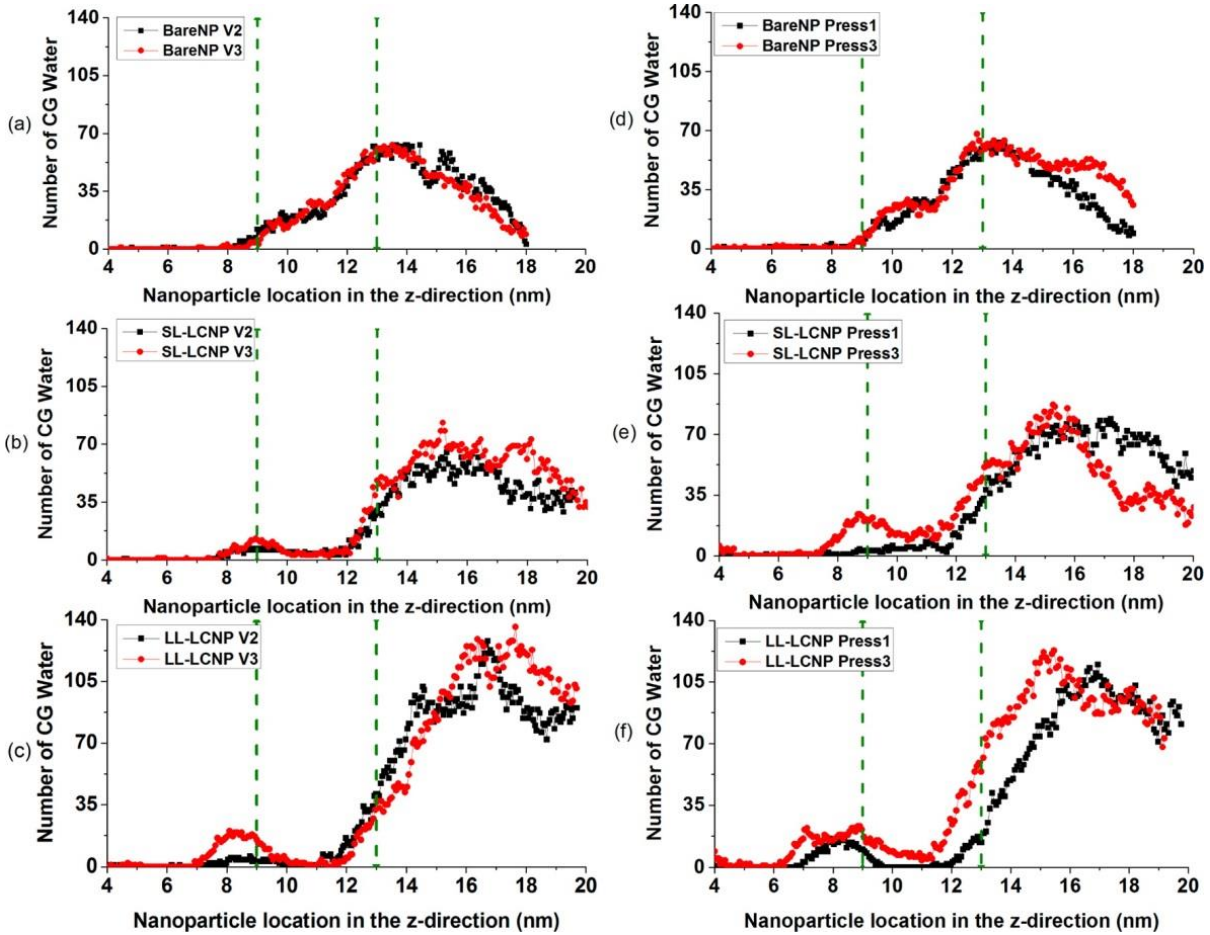
(a-c) Nanoparticles in the entry region;

(d-f) Nanoparticles inside the membrane;

(g-i) Nanoparticles in the exit region.

Y-plane lipid membrane density profiles show the same trend as x-plane's, which is not shown here. The dashed red line in (c), (f) and (i) shows the effective size of pore created in the lipid membrane.

Water permeation



Number of CG water molecules found in the hydrophobic membrane interior with **2.0 nm** diameter NPs under the following conditions: (a–c) Effect of nanoparticle velocity and **ligand length**: press1, no concentration gradient. (d–f) Effect of pressure differential and **ligand length**: no concentration gradient, V3 (0.7 m/s). The green dotted lines represent the equilibrated position of the phosphate groups in the DPPC lipid bilayer membrane.

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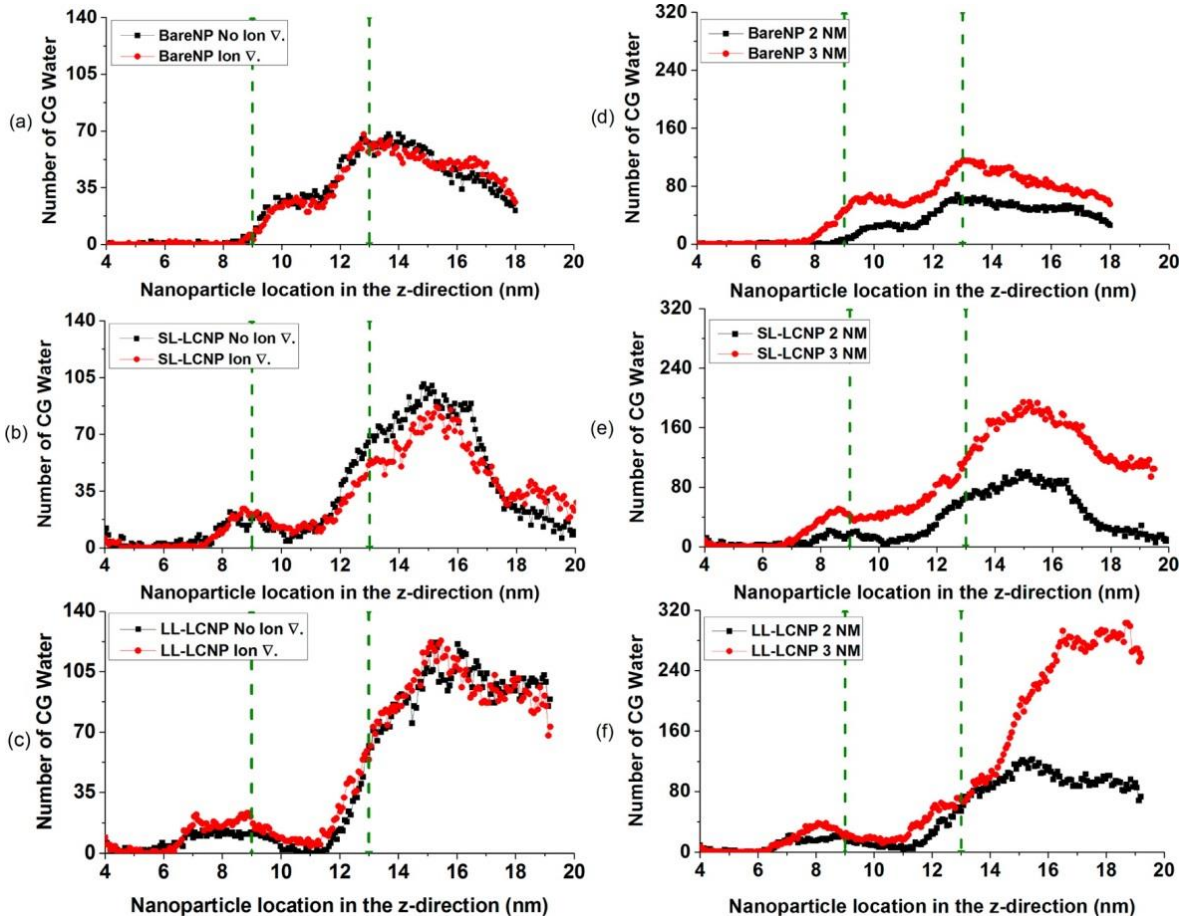

Number of CG water molecules found in the hydrophobic membrane interior for **3.0 nm** nanoparticle under the following conditions: press3, V3(0.7 m/s). (a–c) Effect of ion concentration gradient and **ligand length**, obtained from 2.0 nm diameter nanoparticles. (d–f) Effect of nanoparticle size and **ligand length** with ion concentration gradient. The green dotted lines represent the equilibrated position of the phosphate groups in the DPPC lipid bilayer membrane.

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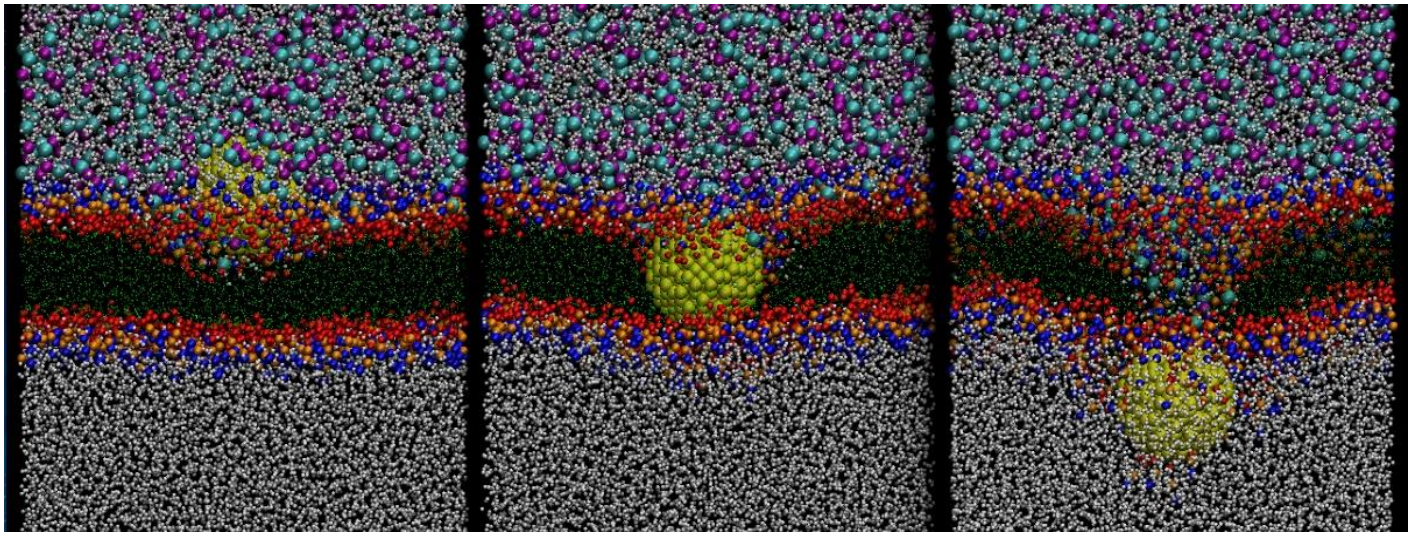
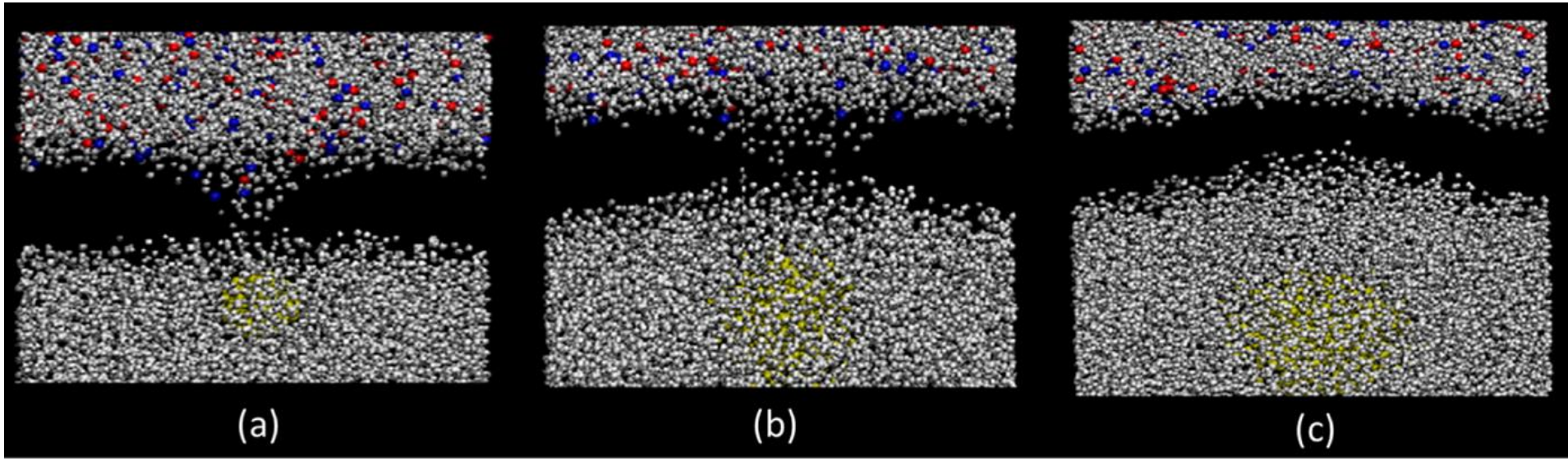


Typical snapshots for the water and ion translocation mediated by a 3.0 nm bare nanoparticle permeating the membrane.

Formation of water pore

for 2.0 nm nanoparticle , bare, short ligands, long ligands

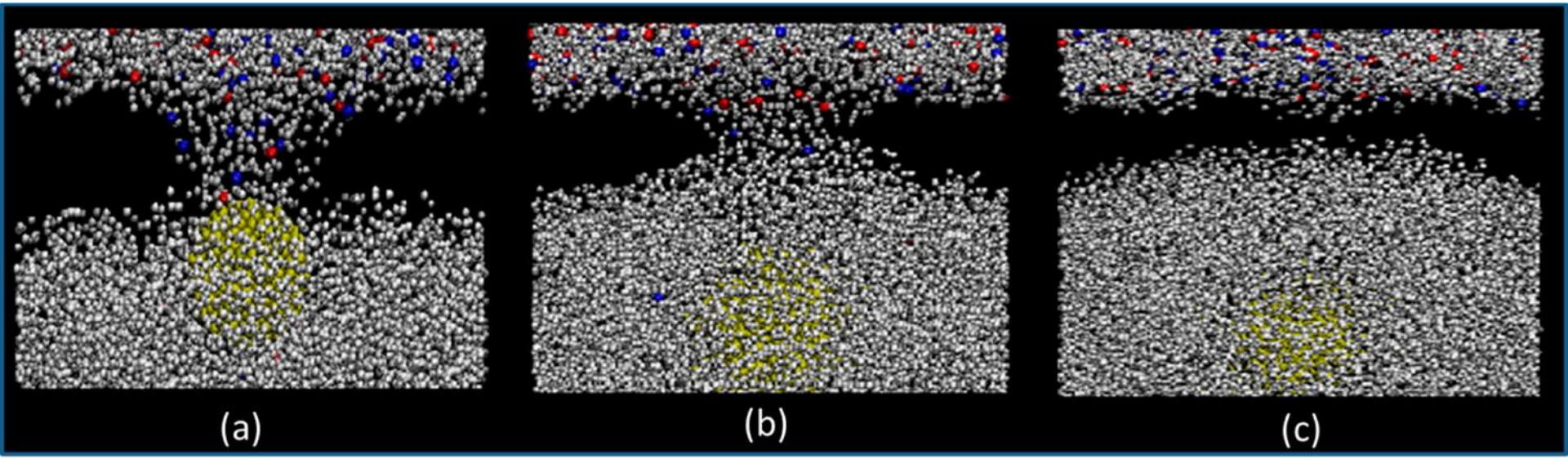


(a) bare NP, (b) SL-LCNP, and (c) LL-LCNP at maximum water leakage observed.

Snapshots of ion concentration gradient simulation system for 2.0 nm diameter
The water molecules are shown in white; the nanoparticle and ligands, in yellow; and the sodium and chloride ions, in blue and red, respectively.

Formation of water pore

for 3.0 nm nanoparticle , bare, short ligands, long ligands



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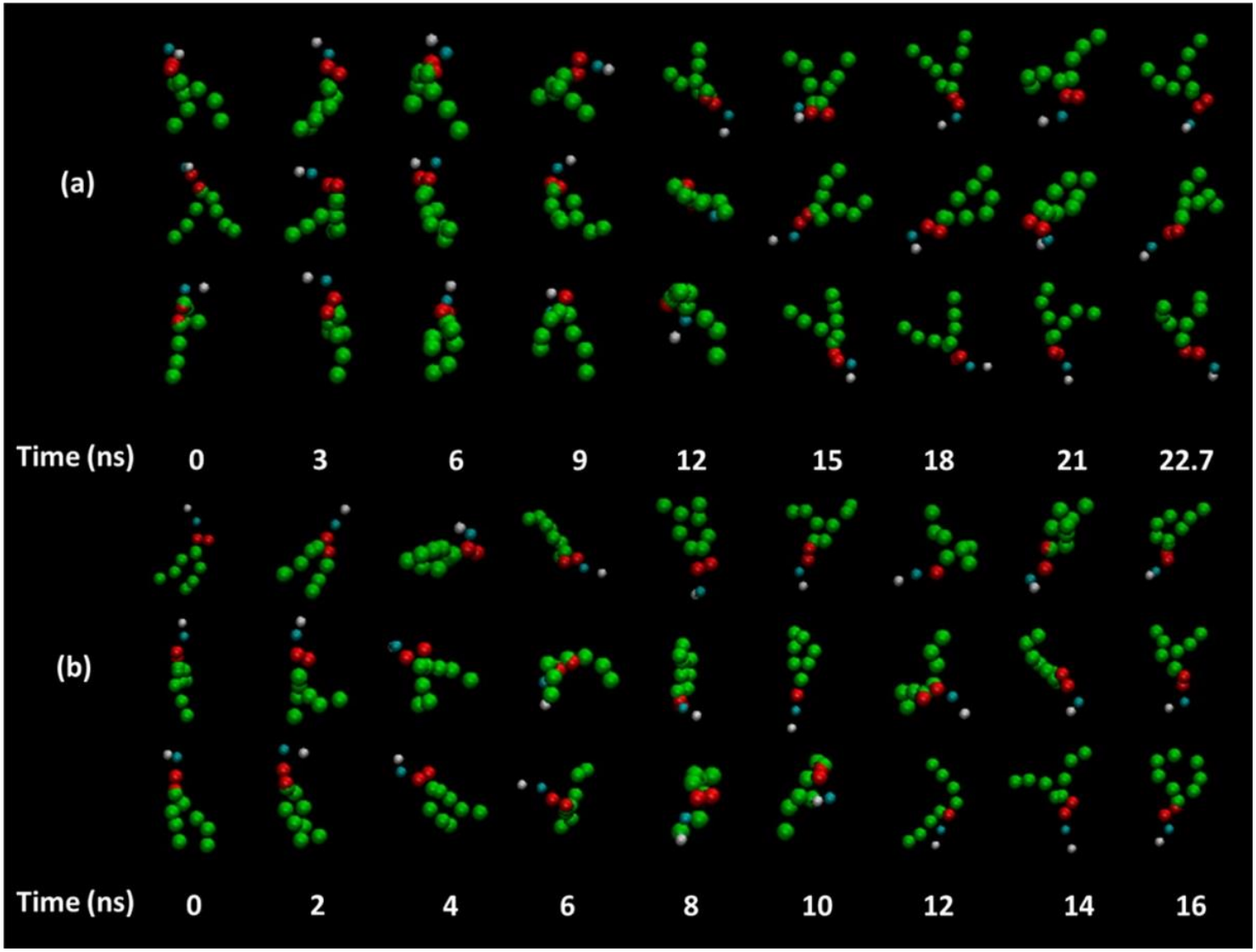
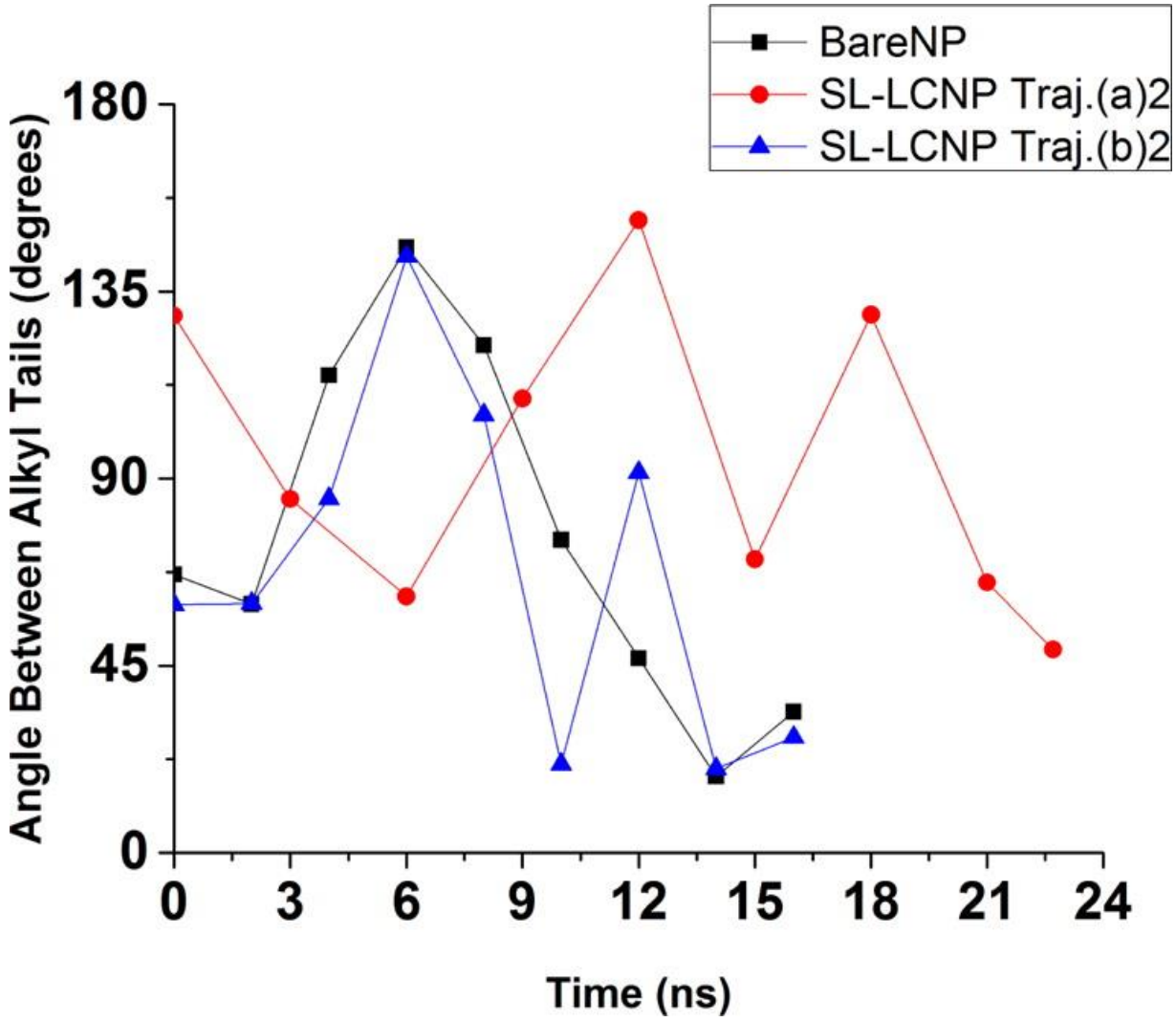
Snapshots of ion concentration gradient simulation system for 3.0 nm diameter
The water molecules are shown in white; the nanoparticle and ligands, in yellow; and the sodium and chloride ions, in blue and red, respectively.

Lipid Flip-flop

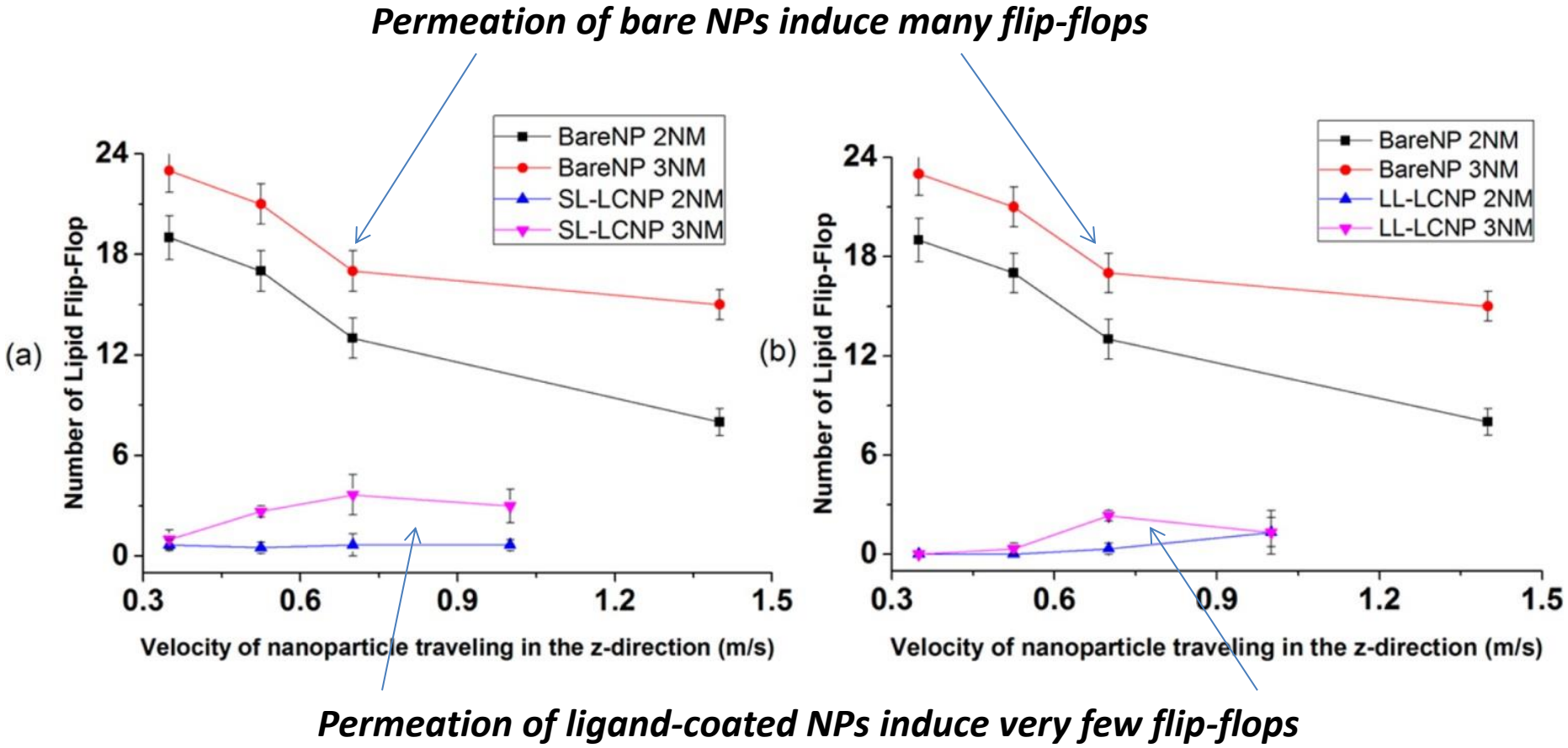


Typical lipid flip-flop event trajectories for a SL-LCNP that are obtained from 3.0 nm diameter NPs, for a press1 system under ion concentration gradient, and nanoparticle velocities of (a) 0.7 and (b) 1.0 m/s.

Lipid flip-flops accompanying permeation of ligand-coated NPs are different from those accompanying bare NPs



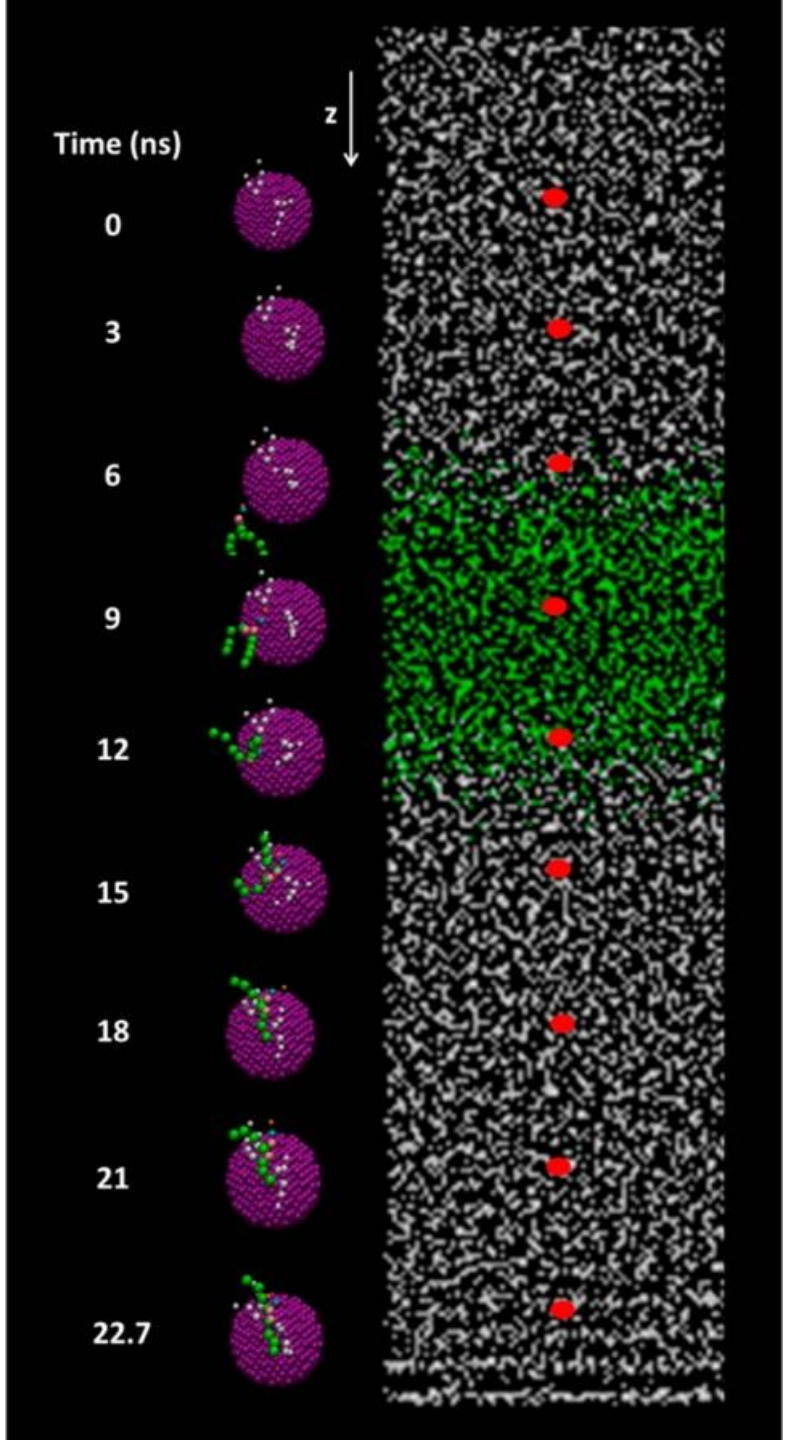
Angle analysis of the alkyl tails of a typical lipid flip-flop (corresponding to the same flip-flop events pictured in the previous slide).



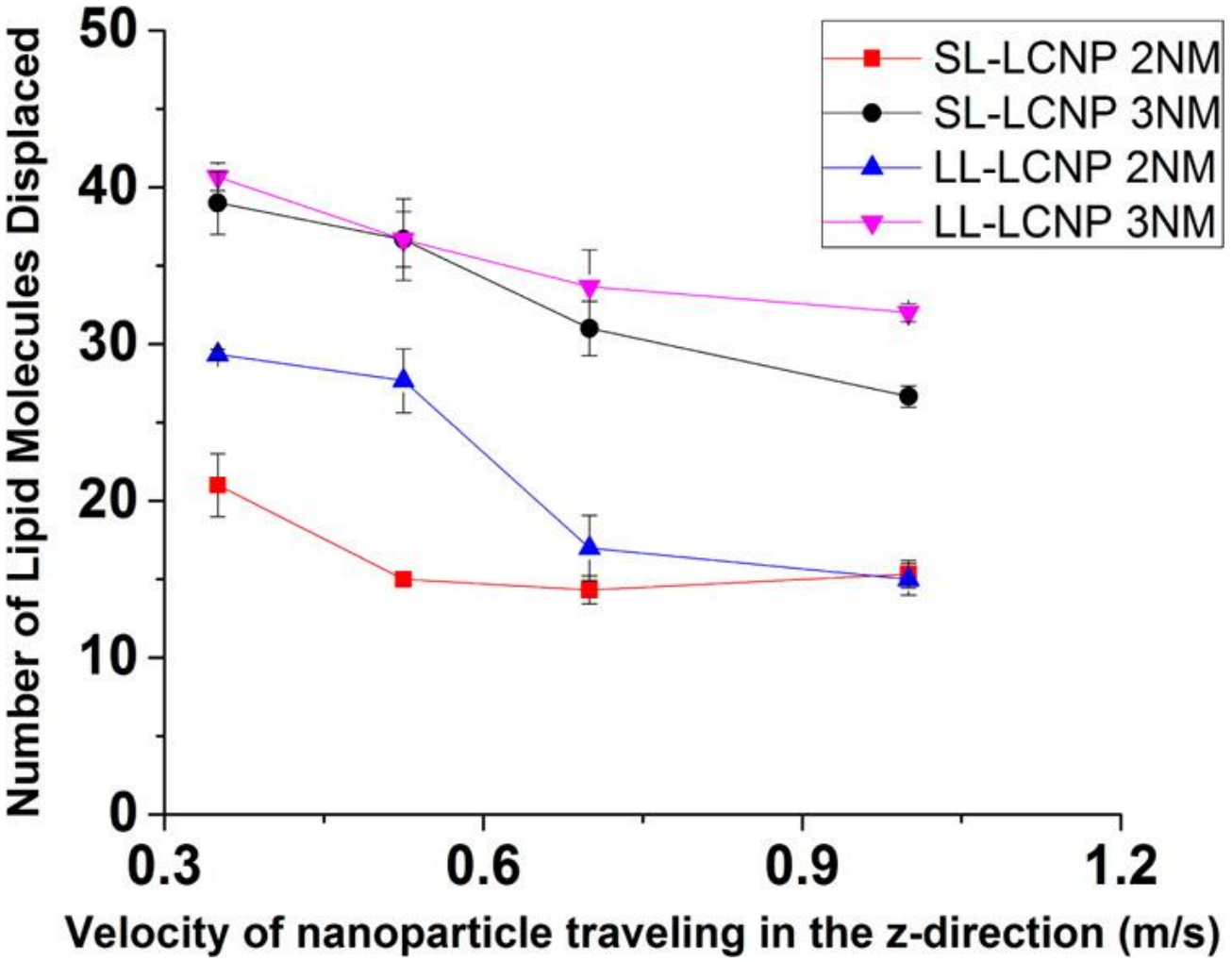
Effect of ligand length and nanoparticle size on the number of lipid molecule **flip-flop** events examined under an ion concentration gradient, press1, varying nanoparticle velocity. The error bars are based on three independent simulations.

Why so few flip-flops?

Lipid entanglement and displacement



Snapshots of the mechanism by which a lipid molecule is dragged to the bulk solution by entanglement with ligands on the nanoparticle (for clarity, the other ligands on the nanoparticle are not shown). The red dots represent the position of the nanoparticle at each snapshot.



Number of **lipid molecules lost** from both bilayer membrane leaflets for a system with ion concentration gradient, as a function of velocity (for the press1 case). The error bars are based on three independent simulations.

Role of surface ligands in nanoparticle permeation through a model membrane: a coarse-grained molecular dynamics simulations study," B. Song, H.-J. Yuan, C. J. Jameson and S. Murad, ***Mol. Phys***. 110, 2181-2195 (2012).

Nanoparticle permeation induces water penetration, ion transport and lipid flip-flop", B. Song, H.-J. Yuan, S. V. Pham, C. J. Jameson, and S. Murad, ***Langmuir***, 28, 16989-17000 (2012).

Surface-functionalized nanoparticle permeation triggers lipid displacement and water and ion leakage", P. A. Oroskar, C. J. Jameson, and S. Murad, ***Langmuir***, 31, 1074-1085 (2015).

Acknowledgments:

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