Supporting Information for

pH-Responsive Dendrimers Interacting with Lipid Membranes

Wen-de Tian[†] and Yu-qiang Ma[‡†*]

Supporting Figures

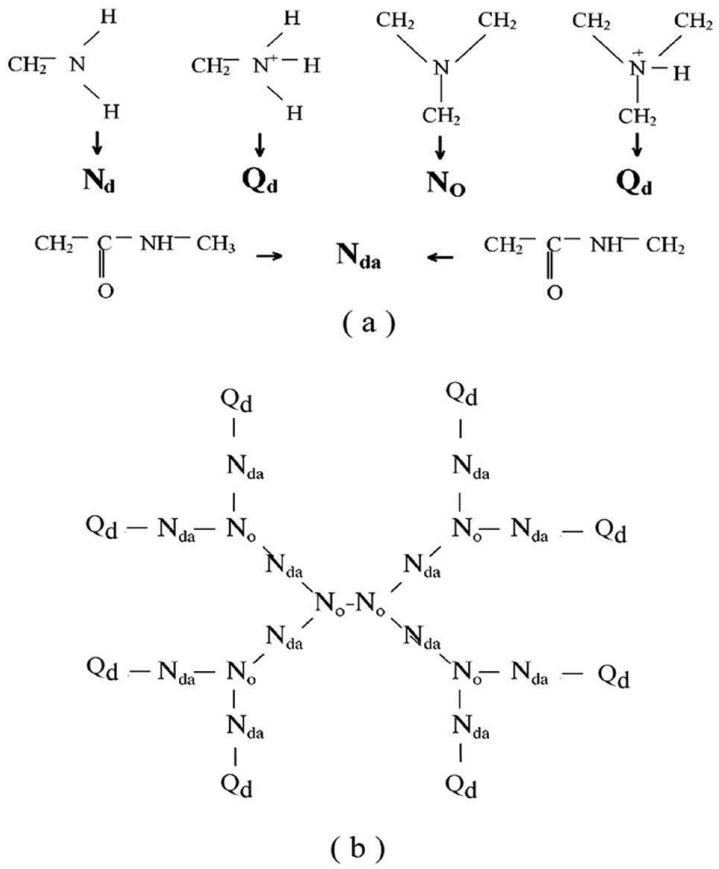

Figure S 1: (a) Mapping of dendrimer chemical moieties into coarse-grained beads. The dendrimer is composed of four different types of chemical moiety, each represented by a single bead type. N_0 stands for a neutrally charged group; Q_d represents a charged group with hydrogen-bond donors; N_{da} indicates a neutrally charged group with a hydrogen-bond donor and an acceptor. (b) Schematic illustration of the topology of the G1 PAMAM dendrimer with protonated terminals. The interior portion consists of N_0 and N_{da} moieties, respectively, for nodes and branches, and the surface consists of Q_d groups. Higher generations can be described by extending this topology. The CG G3 and G4 dendrimers hereby consist of 122 and 250 CG beads in the framework of the MARTINI CG force field, respectively. The harmonic bonding and angle potentials are used to connect these beads.

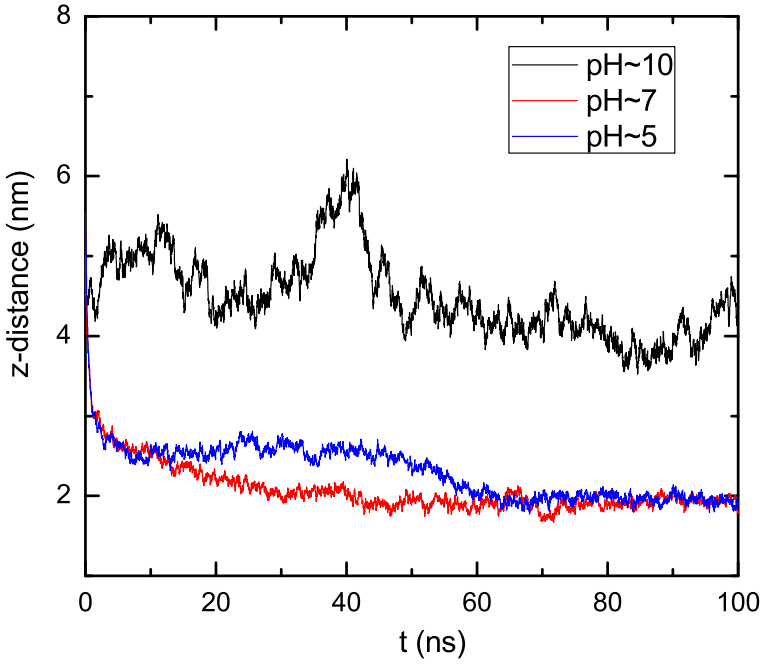

Figure S 2: The center-of-mass separation distance in the z direction(z-distance) between the dendrimer and the lipid bilayer as a function of simulation time. It is about 4.0 nm at pH $\sim$ 10, and 2.0 nm at pH $\sim$ 7 and 5. The effective interaction between the dendrimer and lipid bilayer seems not strong enough to suppress the thermal fluctuation in the case of pH $\sim$ 10. Figure 4 in the main text shows the membrane excludes the neutral dendrimer under this condition.

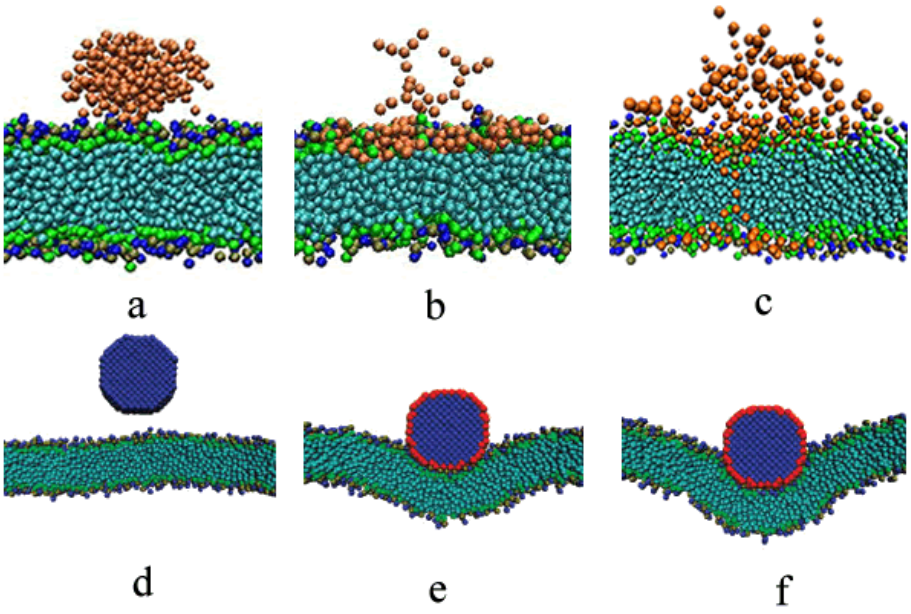

Figure S 3: The comparison of the charged flexible dendrimers and the rigid nanoparticles interacting with the lipid membranes. (a)-(c) show representative snapshots in equilibrated states of the charged G4 dendrimers interacting with the lipid membranes with the decrease of pH, and a hole appears without the bend of the membrane as the surface charge density of nanoparticle increases. (d)-(f) were adapted with permission from Ref. 3 (Copyright (2010) American Chemical Society), where the membrane starts to bend with the increase in the surface charge densities of rigid nanoparticle. Red points denote charged monomers on the surface of nanoparticles in (e) and (f). From the comparison of final conformations, we conclude that the hole formation on the membrane is not owing to the rigidity of nanoparticles, and thus cautions should be taken by theorists when modeling the dendrimer as a hard particle interacting with membranes.

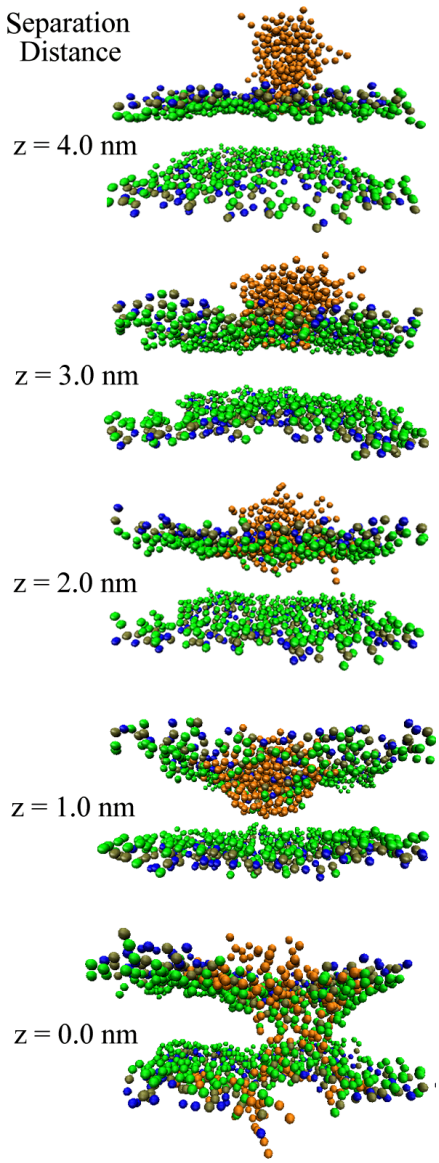

Figure S 4: Snapshots of the G4 dendrimer-membrane complexes under the pH $\sim$ 10 condition along the interaction coordinate at separation distances of 4.0, 3.0, 2.0, 1.0 and 0.0 nm. Near z = 4.0 nm, the dendrimer is near the equilibrium separation, as determined by the potential of mean force(PMF) in the text and Figure S1. With the decrease of distances, the dendrimer induces the deformation of the upside leaflet of the bilayer. At z = 0.0 nm, the dendrimer penetrates through the bilayer.

Supporting Tables

Table S1. Average values of radii of gyration(R_g) of dendrimer in high, neutral, and low pH environments compared with atomistic simulations[a]

System	Lee et al.[1]	Maiti et al.[2]	this work
pH∼10.0	1.48 ± 0.01	1.68 ± 0.01	1.69 ± 0.01
pH∼7.0	2.67 ± 0.02	1.70 ± 0.01	1.81 ± 0.01
pH∼5.0	2.99 ± 0.01	1.90 ± 0.01	2.22 ± 0.01

[a] Lee et al.[1] carried out atomistic simulations of dendrimers without explicit water. The validity of the force field they used was checked through comparing with the system of G2 dendrimers with explicit water molecules. Maiti et al.[2] carried out atomistic simulations of dendrimers in explicit water. Our coarse-grained simulations qualitatively agree with the results from those atomic simulations.

Supporting Videos

Video S1: The process of the dendrimer inserting into the lipid bilayer and leading to the formation of a small pore under the acidic condition.

Video S2: The dynamics of the DPPG lipids when the dendrimer inserting into the membrane, which shows that DPPG lipids on the up leaflet move toward the center-of-mass of the dendrimer.

[1] I. Lee, *Macromolecules*, 2002, **35**, 4510-4520.

[2] P. K. Maiti, *Macromolecules*, 2005, **38**, 979-991.

[3] Y. Li, N. Gu, *J. Phys. Chem. B*, 2010, **114**, 2749.