Influence of Ligand Distribution on Uptake Efficiency
Supplementary information

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LIGAND-FREE PATCHES

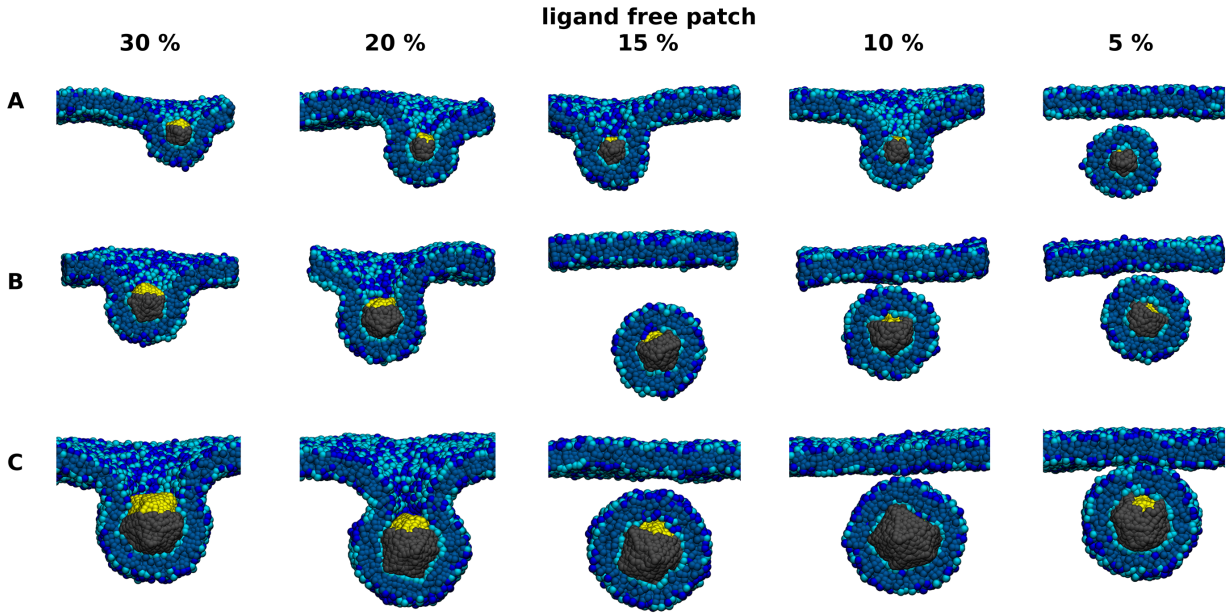

FIG. S1: Finals snapshots of our simulations of membranes interacting with nanoparticles with ligand free patches of several sizes.. Three different sizes of particles with diameters: (A) 5, (B) 8, and (C) 12 nm were studied. We observed that the uptake of larger particles is easier than for smaller particles and the ligand-free patch can be as large as 15 % for the successful uptake. For the smallest nanoparticle only 5 % of the area could be ligand-free to observer spontaneous uptake within timescale of our simulation 30 00 τ. The snapshots display a cut through the membrane at the particle position. Color coding is the same as in previous figures.

ERROR OF UPTAKE TIME

We estimated the error of uptake time to be 500 τ based on few repeated simulation as shown in Control simulations section. However, we expect the length of metastable states to be effected by thermal membrane fluctuations, so we estimated the error of uptake time for simulations with metastable states to be 2 000 τ (see Figure S4).

TRAJECTORY SNAPSHOTS

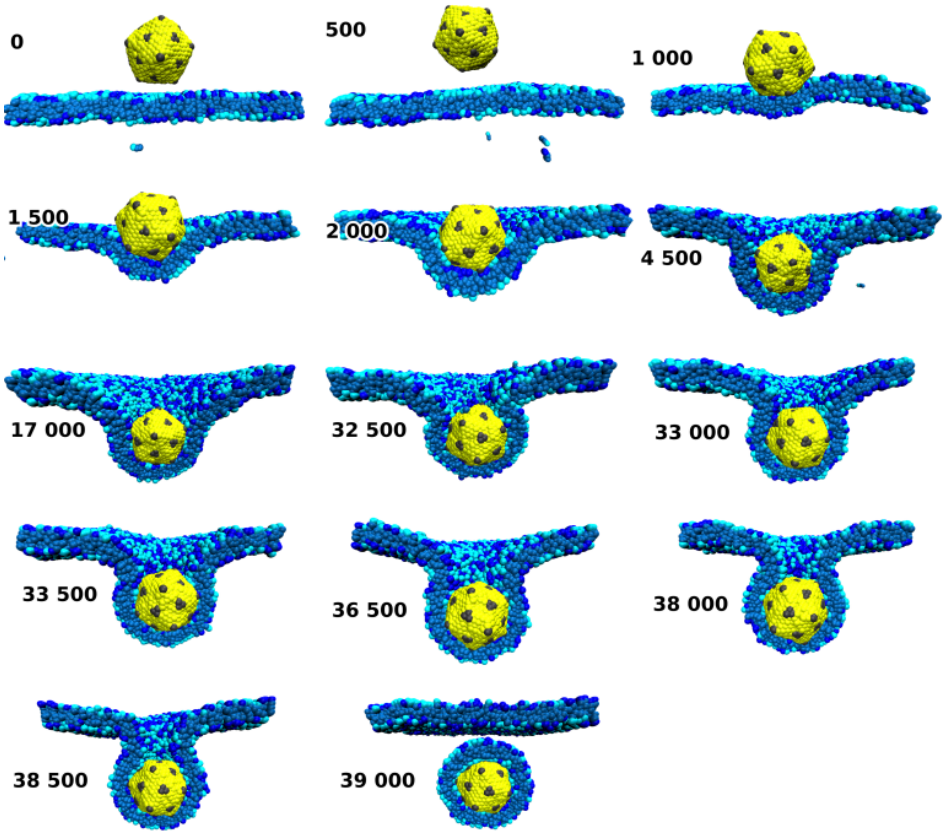

FIG. S2: Representative snapshots of MD trajectory of the nanoparticle with V1F3E0 pattern, where membrane is interacting with the nanoparticle and undergoes a long metastable state (5 000 - 33 500 τ). During the metastable state the nanoparticle was rotating and the membrane fluctuating until more ligands and receptors got into the contact and the uptake progressed further. The snapshots display a cut through the membrane at the particle position. Phospholipid molecules are shown blue (hydrophilic parts – dark blue, membrane receptors – light blue, and hydrophobic part – mid blue). Yellow and black beads represent hydrophilic parts and ligands respectively.

CONTROL SIMULATIONS

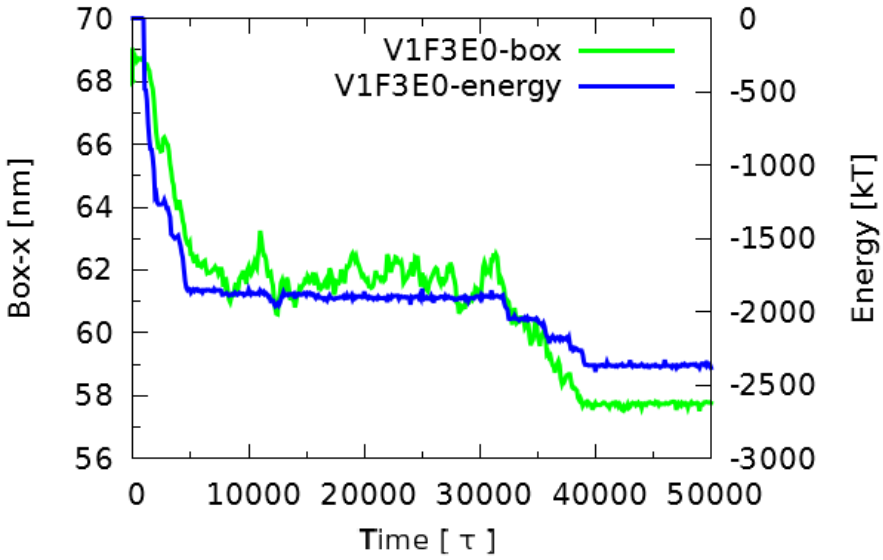

FIG. S3: The time dependence of box size and ligand-receptor interaction energy for nanoparticle V1F3E0. There was one metastable state for period 5 000 – 34 500 τ as evident from both the box size and the interaction energy profiles.

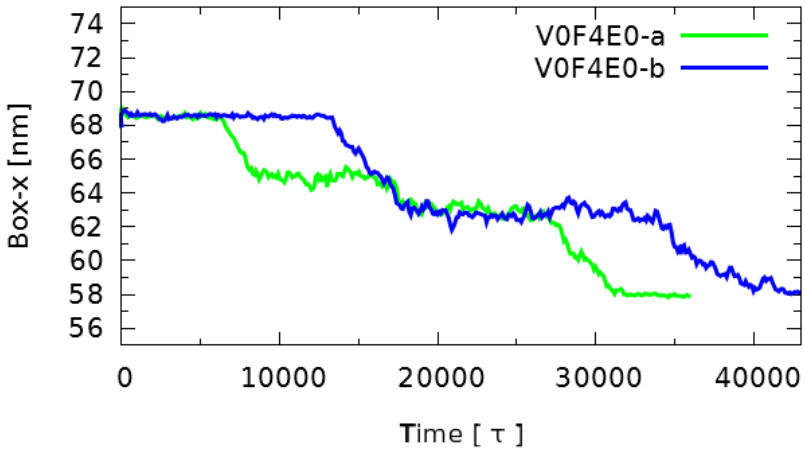

FIG. S4: The time dependence of box size for the nanoparticle V0S4E0 from two independent runs (a and b). Because of two random initial conditions there were two different times before the nanoparticle started to be wrapped by membrane (about 6 000 τ for simulation-a and 13 000 τ for simulation-b). The overall length of metastable states and the uptake remained roughly the same (MS being 18 000 τ and the uptake time 25 000 τ).

ALL SIMULATIONS - BOX SIZE

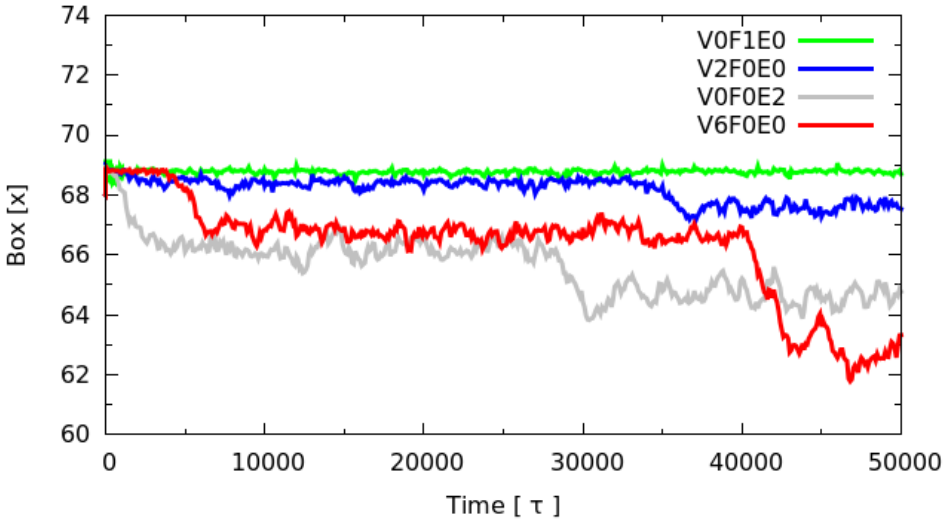

FIG. S5: The time dependence of box size and ligand-receptor interaction energy for nanoparticles with no uptake within the whole range of simulation (50 000 τ).

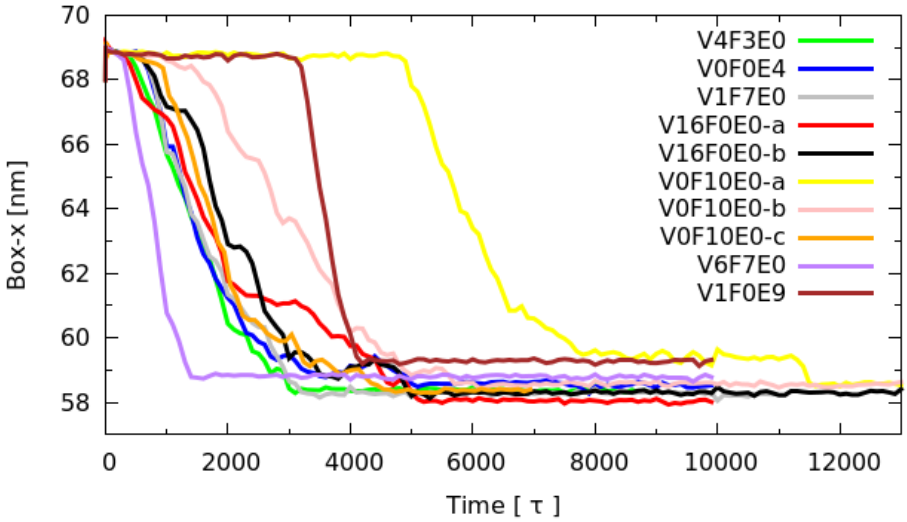

FIG. S6: The time dependence of box size and ligand-receptor interaction energy for nanoparticles with spontaneous straight uptake without metastable states.

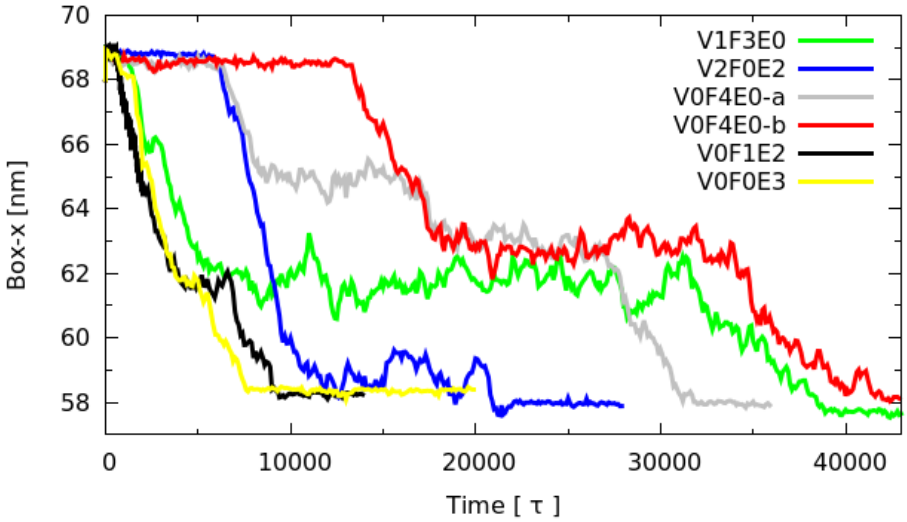

FIG. S7: The time dependence of box size and ligand-receptor interaction energy for nanoparticles with uptake with metastable states.