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SUPPORTING INFORMATION FOR "How a few help all: Cooperative crossing of lipid membranes by COSAN anions"†

David C. Malaspina, Francesc Teixidor, Clara Viñas,* and Jordi Faraudo*

Methods

Our Molecular Dynamics Simulations were performed with NAMD[1] and analyzed using VMD[2] software.

The force field employed for the membrane lipids was CHARMM36[3]. The water model used for the simulations was TIP3P, as employed for CHARMM force field. For [*o*-COSAN]$^-$ ions we used a previous parameterization from DFT calculations compatible with CHARMM developed in Ref[4]. In all the simulations we use the cis rotamer for the [*o*-COSAN]$^-$ ion since it is the most stable rotamer in water[4].

The employed simulation parameters were standard in NAMD. The equations of motion were integrated every 2 fs and electrostatic interactions updated every 4 fs. All bonds between heavy atoms and hydrogen atoms were maintained rigid. Short range electrostatic and Lennard-Jones interactions were computed with a cutoff of 1.2 nm (LJ switching distance of 1.0 nm). For long range electrostatic Particle Mesh Ewald (PME) algorithm was used taking a grid spacing of 1.0 Å. Full periodic boundary conditions in all directions were employed.

The temperature was controlled with a Langevin thermostat using a damping coefficient of 1 ps^{-1}. In order to maintain a relaxed structure of the membrane we employed a flexible cell with semi-isotropic pressure control, specifying a zero surface tension. We used the Nosé-Hoover Langevin piston imposing p=1 atm in the z direction, with a piston oscillation period of 100 fs and a piston decay time of 50 fs.

We built two different systems to study the translocation of [*o*-COSAN]$^-$ ions. The first system consists of a single [*o*-COSAN]$^-$, its Na^+ counterion and a bilayer membrane in water. The second system contains a self-assembled micelle with 15 [*o*-COSAN]$^-$ as obtained in previous simulations[4], with their Na^+ counterions put into contact with the same bilayer membrane.

The membrane lipid bilayer was built from previous simulations[5] and contains dipalmitoylphosphatidylcholine (DPPC) as the main lipid and cholesterol (CHOL) in proportion 5-DPPC:3-CHOL. The membrane contains 230 DPPC molecules and 138 CHOL molecules, the initial dimension of the membrane was 8.4 nm in x-axis and 8.7 nm y-axis. The membrane was previously equilibrated without [*o*-COSAN]$^-$ ions and later [*o*-COSAN]$^-$ ions were added in the water phase. The system with a single [*o*-COSAN]$^-$ molecule had 28,943 water molecules and a total of 126,987 atoms, while the system with 15 [*o*-COSAN]$^-$ molecules had of 126,656 atoms (28,618 water molecules). The production time for the system with a single [*o*-COSAN]$^-$ system was 300 ns while production time for the case with 15 [*o*-COSAN]$^-$ was 513 ns.

The free energy calculation for 1 [*o*-COSAN]$^-$ across the lipid membrane was performed using Adaptive Biasing Force (ABS) method implemented in NAMD[6,7].

Intrinsic density profiles of Co atoms shown in the main paper were calculated with our own code developed in Fortran language. This intrinsic density profile method allow to avoid artifacts due to the membrane flexibility found in the standard calculation of density profiles. Our implementation is analogous to previous ones for other softmatter systems such as in[8]. We select as a reference the P atoms of DPPC membrane lipids. The algorithm identifies, at a given time, the P atom closest to each Co atom for each [*o*-COSAN] and the distance in the z direction was calculated. Using these intrinsic distances, we calculate the density profile of Co atoms, averaged over different time windows. The algorithm also differentiate the upper leaflet from the lower leaflet and the final density profile is the sum of both profiles.

Notes and references

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Institut de Ciencia de Materials de Barcelona, ICMAB-CSIC, Campus de la UAB, E-08193, Bellaterra, Spain; E-mail: clara@icmab.es, jfaraudo@icmab.es

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