Protonation and orientation: a computational approach to cocaine diffusion through a model membrane.

Supporting information

Wadtey Oung, Nora Kremer, Safa ben Amara, Ali Zaidi, Thorsten Koslowski

Figure 1. Umbrella sampling histograms for moving a neutral cocaine molecule from the center of a lipid DMPC bilayer (z = 0) towards the aqueous phase.



Figure 2. Umbrella sampling histograms for moving a cocaine cation from the center of a lipid DMPC bilayer (z = 0) towards the aqueous phase.



Figure 3. Raw data originating from the weighted histogram analysis method on the distributions shown in figure 1 and 2. Neutral (\times symbol, black) and protonated (• symbol, red) free energies as a function of the distance from the center of a lipid bilayer. On the energy scale, the plots have been calibrated using eq. 2 of the main article. The dashed line separates the regime with an excess of the cationic species (right of the line) from that dominated by neutral molecules (left of the line). The red arrow indicates the shift of the protonated free energy curve with a decreasing pH value.



Figure 4. Representative snapshots of the umbrella sampling simulations of the cocaine cation permeation. a) z > 2.5 Å, b) z < 2.5 Å. The cocaine cation is shown as a black stick model, water molecules as red stick models, lipid head groups in sky blue. For clarity, lipid side chains are not shown.





Figure 5. Determination of the neutral cocaine molecule diffusion coefficient within the lipid DMPC bilayer in a double logarithmic representation. The line corresponds to a least squares regression analysis.

