Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Material to

Entropy drives the insertion of Ibuprofen into model membranes

Natalia Rojas-Valencia,[†] Isaias Lans,[‡,¶] Marcela Manrique-Moreno,[†] C. Z. Hadad,[*,†] and Albeiro Restrepo[*,†]

Instituto de Química, Universidad de Antioquia UdeA, Calle 70 No. 52–21, Medellín, Colombia, Grupo de Bioquímica Teórica, Universidad Industrial de Santander, Cra 26, Calle 9, Bucaramanga, Colombia., and Max Planck Tandem Group, Universidad de Antioquia UdeA, Calle 70 No. 52–21, Medellín, Colombia

E-mail: cacier.hadad@udea.edu.co; albeiro.restrepo@udea.edu.co

[*]To whom correspondence should be addressed
[†]Instituto de Química, UdeA, Medellín, Colombia
[‡]Universidad Industrial de Santander, UIS, Bucaramanga, Colombia
[¶]Max Planck tandem group, UdeA, Medellín, Colombia

Validation of the binary membrane/water system

Area per lipid

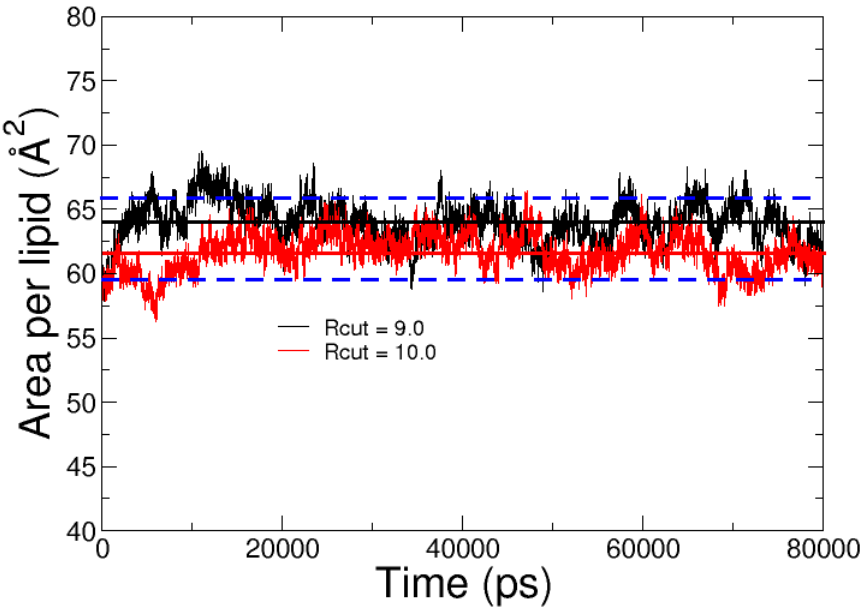

Figure 1: Red and black lines represent the averages obtained with 9.0 and 10.0 Å respectively. Blue lines show the experimental values. [1–3]

Order parameters

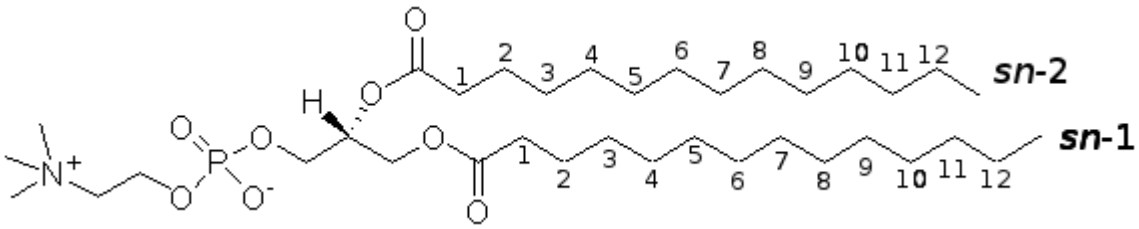

Figure 2: A DMPC molecule is shown. Only labeled atoms are considered for the calculation of order parameters in the lipid bilayer (see Figure 3).

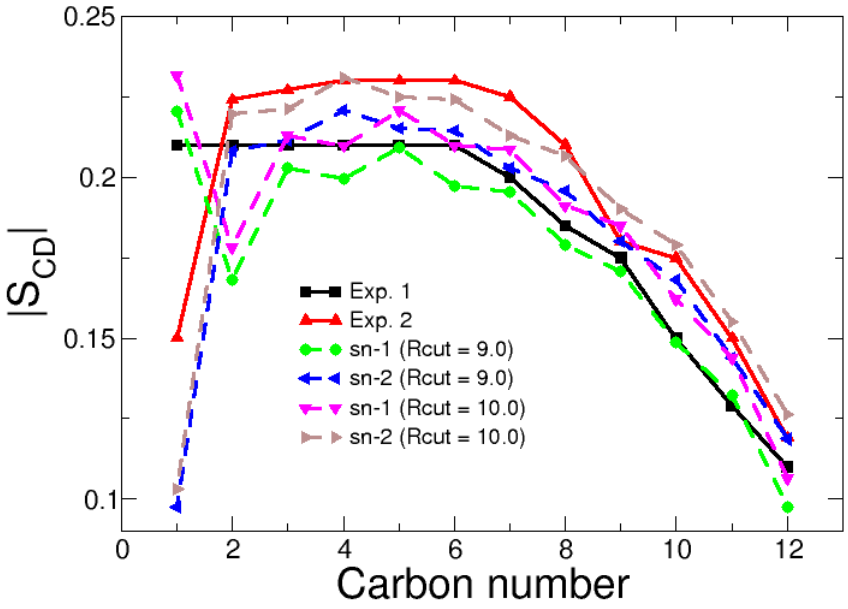

Figure 3: Order parameters for the hydrocarbon chains. Experimental[4,5] as well as calculated (cutoff radii in Å) values are shown.

Thickness of the lipid bilayer

From the distance of the two peaks in the density of phosphorous atoms distribution on each layer shown in Figure 4, 35.8 and 35.63 Å were obtained for 9.0 and 10.0 Å cutoff radii respectively as thickness of the lipid bilayer. The experimental values fall in the 33.2–36.7 range.[3,6–8]

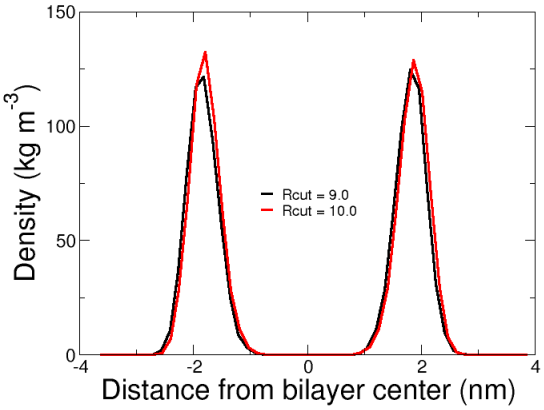

Figure 4: Distribution of phosphorous atoms in the lipid bilayer.

Snapshots of the lipid environment with and without Ibuprofen

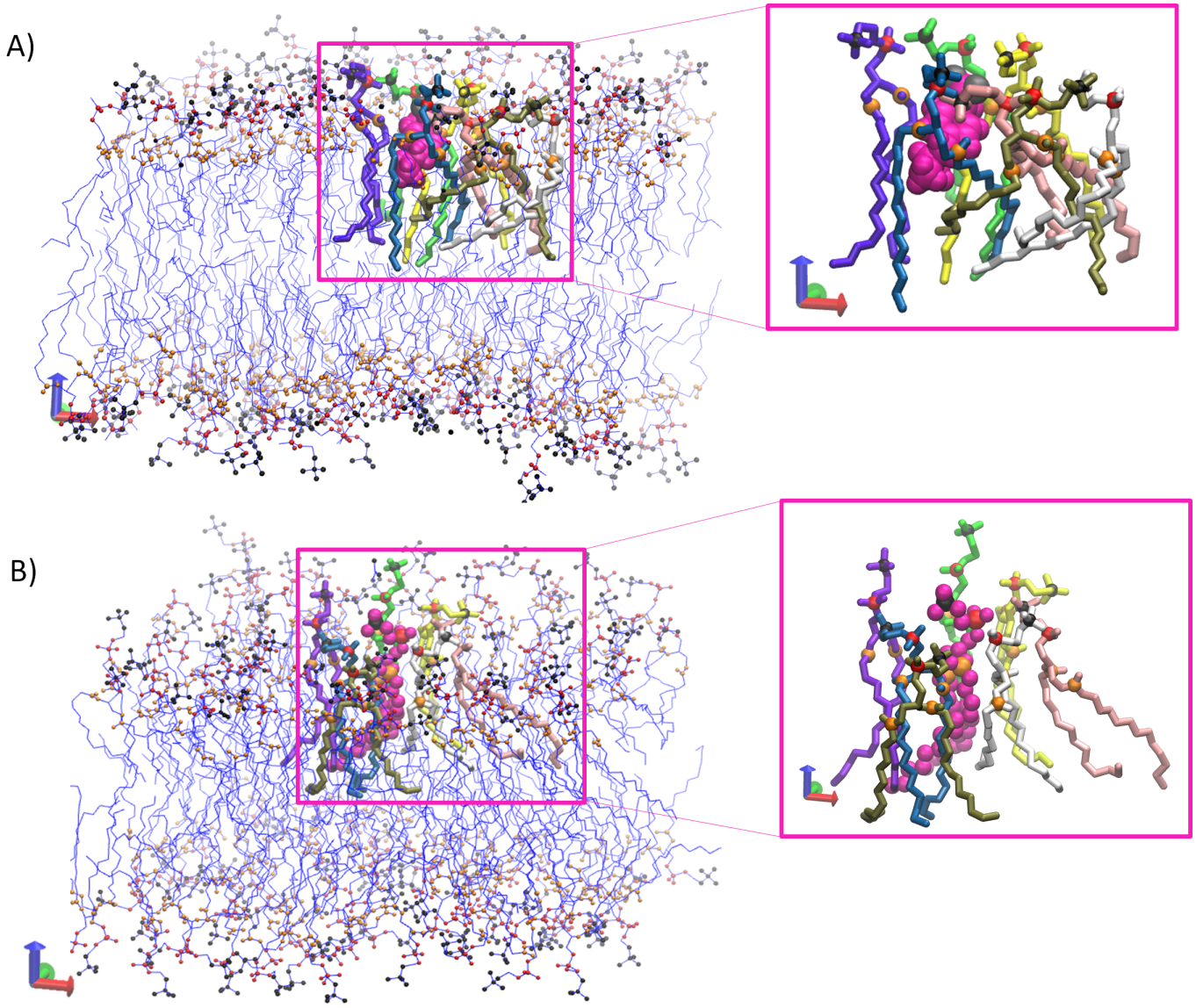

Figure 5: Structural organization of the lipid environment in the presence and absence of Ibuprofen. (A): Ibuprofen is located in the region of the minimum of Gibbs free energy. (B): Ibuprofen is located at the aqueous phase, at ≈ 0.6 nm above the membrane.

References

(1) Koenig, B. W.; Strey, H. H.; Gawrisch, K. Membrane lateral compressibility determined by NMR an X-Ray diffraction: effect of acyl chain polyunsaturation. *Biophys. J.* **1997**, 73, 1954-1966.

(2) Nagle, J. F.; Zhang, R.; Tristram-Nagle, S.; Sun, W.; Petrache, H. I.; Suter, R. M. X-Ray structure determination of fully hydrated L_α phase dipalmitoylphosphatidylcholine bilayers. *Biophys. J.* **1996**, 70, 1419-1431.

(3) Kuăerka, N.; Nieh, M.; Katsaras, J. Fluid phase lipid areas and bilayer thicknesses of commonly used phosphatidylcholines as a function of temperature. *Biochem. Biophys. Acta.* **2011**, 1808, 2761-2771.

(4) Petrache, H. I.; Dodd, S. W.; Brown, M. F. Area per lipid and acyl length distributions in fluid phosphatidylcholines determined by ^{2}H NMR Spectroscopy. *Biophys. J.* **2000**, 79, 3172-3192.

(5) Douliez, J. P.; Leónard, A.; Dufourc, E.J. Restatement of order parameters in biomembranes: calculation of C-C bond order parameters from C-D quadrupolar splittings. *Biophys. J.* **1995**, 68, 1727-1739.

(6) Costigan, S. C.; Booth, P. J.; Templer, R. H. Estimations of lipid bilayer geometry in Âčuid lamellar phases. *Biochem. Biophys. Acta.* **2000**, 1468, 41-54.

(7) Petrache, H. I.; Tristram-Nagle, S.; Nagle, J. F. Fluid phase structure of EPC and DMPC bilayers. *Chem Phys Lipids*. **1998**, 95, 83-94.

(8) Kuăerka, N.; Liu, Y.; Chu, N.; Petrache, H. I.; Tristram-Nagle, S.; Nagle, J. F. Structure of fully hydrated fluid phase DMPC and DLPC lipid bilayers using X−Ray scattering from oriented multilamellar arrays and from Unilamellar Vesicles. *Biophys. J.* **2005**, 88, 2626-2637.