Supplementary Material (ESI) for Soft Matter

SUPPLEMENTARY INFORMATION

Permeability of drugs and hormones through a lipid bilayer: a dual-resolution molecular dynamics study

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Inertial features of permeant molecules

The atomic-level permeant molecules simulated in this study are modelled as rigid bodies. Accordingly, they are characterised by their principal moments of inertia; these quantities, along with the total permeant masses, are listed in Table 1. The procedure adopted to obtain the principal moments of inertia has been reported elsewhere.[1]

Simulation data

Examples of the time evolution of the constraint force acting on permeants during the z-constraint simulations are displayed in Fig. 1. It can be seen that there are evident substantial fluctuations; however, thanks to the extent of the sampling time, we believe that overall the data are statistically reliable.

Permeability predictor numerical results

Table 2 reports the numerical results of our permeability predictor $P_{\Delta G}$ (defined by eqn (9) in the main body of this paper); these data are also presented as column diagrams in Figures 2-6. The corresponding permeability rankings are reported in Tables 1-4 in the main body of this paper.

Table 1: Permeant inertial features.[a]

	mass	I_{x}	I_{y}	I_{z}
alprenolol	249	9.29	26.92	25.61
atenolol	266	28.44	34.49	9.50
pindolol	248	29.69	29.02	7.31
progesterone	314	7.68	41.11	38.35
testosterone	288	6.95	32.09	29.39

[a] Masses are expressed in units of amu. Principal inertias (I_{x}, I_{y}, I_{z}) are expressed in units of amu $\cdot$ nm^2.

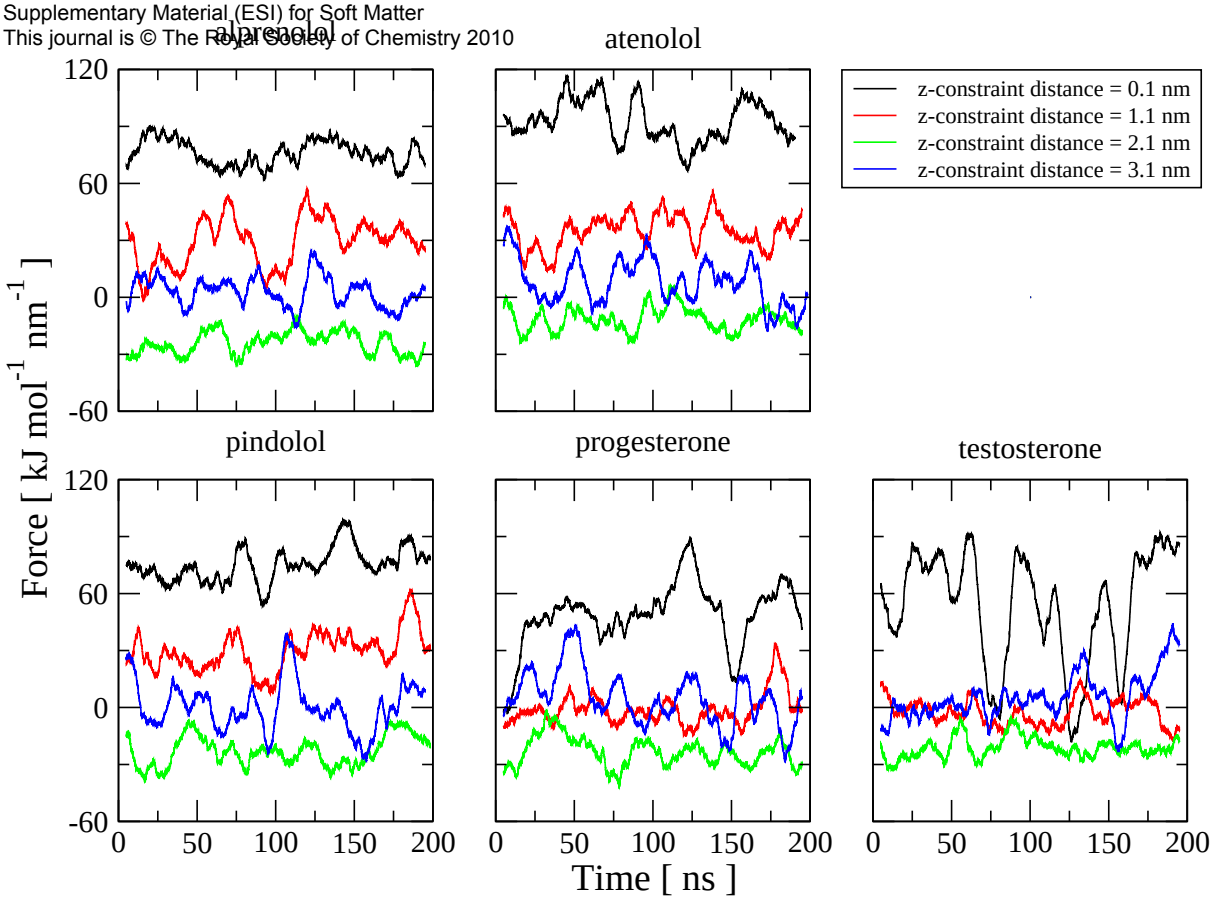

Fig. 1: Constraint forces. Time evolution of constraint forces for each of the permeant studied, for selected z-constraint distances. The selected distances (from the bilayer center) are reported in the legend. For clarity, the data are represented as moving averages over 10 ns time windows (the plotted constraint force at x ns thus corresponds to the average over the time interval from $(x-5)$ ns to $(x+5)$ ns).

Table 2: Permeability predictor numerical results.

	atenolol	pindolol	progesterone	alprenolol	testosterone
$P_{\Delta G}^{\text{data from this work}}$	0.0334 ± 0.0003	0.0431 ± 0.0011	0.0565 ± 0.0006	0.0569 ± 0.0011	0.0705 ± 0.0019
	water	acetamide	acetic acid	methylamine	
$P_{\Delta G}^{\text{data from ref. 1}}$	0.0893 ± 0.0018	0.1075 ± 0.0040	0.1142 ± 0.0093	0.3226 ± 0.0037	
$P_{\Delta G}^{\text{data from ref. 2}}$	0.1173 ± 0.0049	0.1106 ± 0.0057	0.1674 ± 0.0185	0.2990 ± 0.0234	
	urea	glycerol	water		
$P_{\Delta G}^{\text{data from ref. 3}}$	0.0681 ± 0.0019	0.0900 ± 0.0032	0.0902 ± 0.0033		
	arabinose	xylose	ribose		
$P_{\Delta G}^{\text{data from ref. 4}}$	0.0525 ± 0.0007	0.0530 ± 0.0009	0.0575 ± 0.0012		

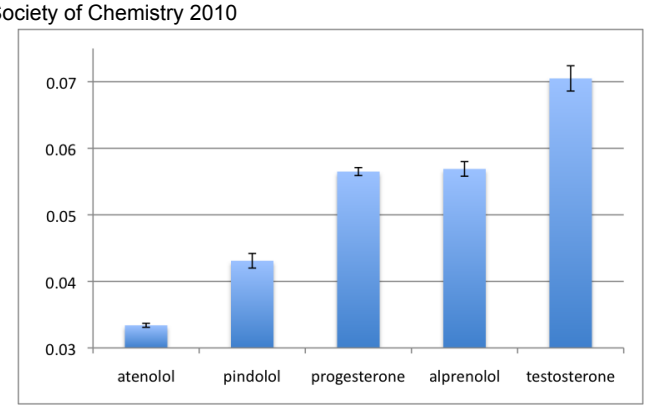

Fig. 2: Values of the permeability predictor $P_{\Delta G}$ applied to the free energy data reported in the main body of this paper.

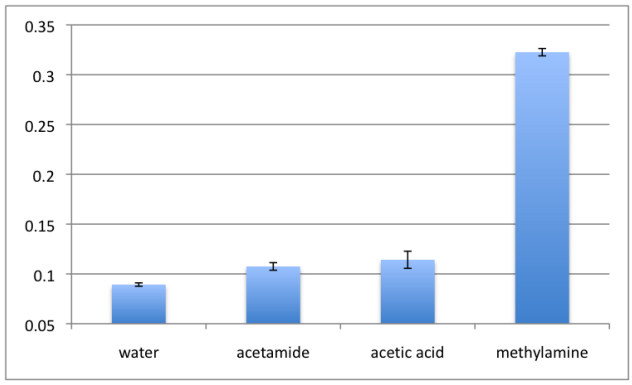

Fig. 3: Values of the permeability predictor $P_{\Delta G}$ applied to the free energy data of Orsi et al.[1]

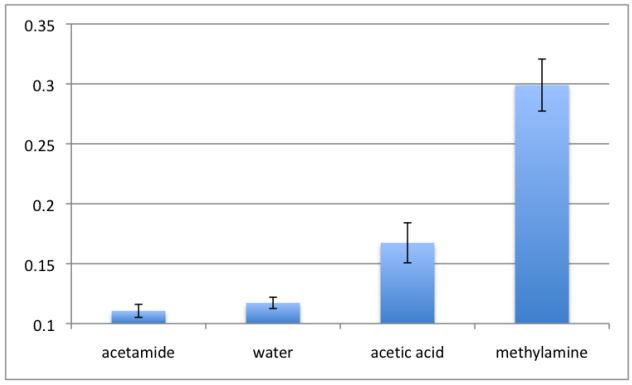

Fig. 4: Values of the permeability predictor $P_{\Delta G}$ applied to the free energy data of Bemporad et al.[2]

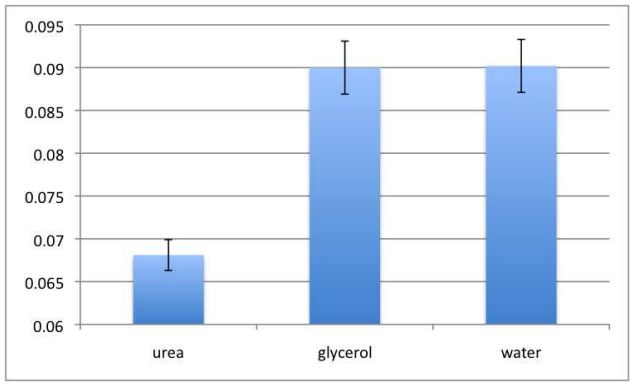

Fig. 5: Values of the permeability predictor $P_{\Delta G}$ applied to the free energy data of Hub and de Groot.[3]

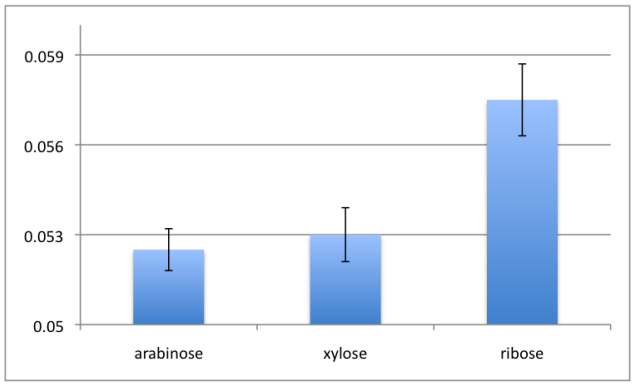

Fig. 6: Values of the permeability predictor $P_{\Delta G}$ applied to the free energy data of Wei and Pohorille.[4]

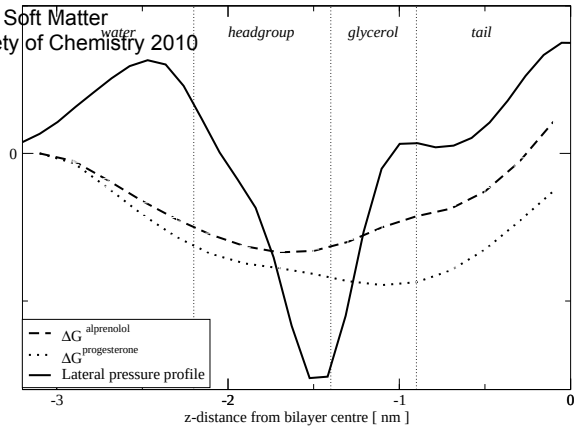

Fig. 7: Qualitative comparison between transfer free energy profiles of selected permeants and the lateral pressure profile across a DMPC bilayer.

Lateral pressure and transfer free energy profiles

Fig. 7 displays the lateral pressure profile of our DMPC bilayer model (reproduced from our previous study[5]) superimposed on two representative transfer free energy profiles (reproduced from Fig. 3 of the main body of this article). The correlation between the pressure trough and the transfer free energy minima is considered in detail in the Discussion section of the main body of this article.

References

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