## Solvent Dynamics and Thermodynamics at the Crystal-Solution Interface of Ibuprofen -Supplementary material

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## **Bulk Solvent Analysis**

In this section we report the radial pair distribution function for all solvents used in the study (Figure 1) as obtained from simulations, as well as a comparison of the model density to the experimental density for each solvent (Tab. 2).

## Solution Structure for the Case of Cyclohexanone

As discussed in the main body of this paper, surface-solvent interactions induce long range structuring of the solvent phase for a few cases. Here we take the case of cyclohexanone in



Figure 1: Radial Pair Distribution Function of the centres of mass of solvent molecules in the bulk liquid.

Table 2: The table reports the experimental solvent density at ambient conditions alongside the values obtained from MD simulations of the bulk solvent. The percentage error of the MD result with respect to the experimental reference is listed in the last column.

solvent	density $[kg m^3]$		
	experimental	MD	% error
water	1000	985	1.5
1-butanol	810	814	0.5
toluene	867	849	2
cyclohexanone	948	935	1.4
cyclohexane	779	766	1.7
acetonitrile	786	719	8.5
trichloromethane	1489	1406	5.6
ethyl acetate	902	930	3.1
methanol	792	804	1.5
ethanol	789	786	0.4

the {002}, {100} and {011} crystal faces to show that the structure is indeed induced by the presence of a crystal surface, and that the strength of this effect varies depending on the crystal face. Figure2 shows the free energy profile for a cyclohexanone molecule in the presence of a crystal surface (yellow) and in the bulk solvent (blue) overlapped. The red line represents the difference between the two at the points of the peaks. From the plots we can deduce that by far the most thermodynamically stable adsorbed state of a cyclohexanone



Figure 2: **Blue**: free energy profile of a cyclohexanone molecule in bulk solution as a function of distance from a reference molecule **Yellow**: free energy profile of a cyclohexanone molecule in the presence of a crystal surface **Red**: difference between the two FE profiles

molecule is at the  $\{002\}$  crystal face with a barrier difference of 8 kJ/mol from the bulk solution. The next biggest difference is between the  $\{100\}$  POLAR face and the solution of 4 kJ/mol. We also note that the range of the layering varies between different surface cases. In the presence of the  $\{100\}$  POLAR surface the layering effect propagates well beyond 5 nm from the crystal surface, while the layering induced in the presence of the  $\{002\}$  face is much shorter and it dies off around 3 nm. Comparatively, the  $\{100\}$  APOLAR and  $\{011\}$  surfaces induce a much more negligible layering effect. Nevertheless, this analysis confirms that the structuring of the solvent is indeed a consequence of the presence of a crystal surface, and the strength of the effect varies depending on the specific surface-solvent interactions.

## Exchange rate vs. Barrier Height

As mentioned, for all surface-solvent combinations we extract information on the residence time of a solvent molecule in the adsorbed state, as well as the height of the barrier  $\Delta G^*$ between the adsorbed state and the subsequent states (Please refer to the Methods in the main text). In principle, the residence time of a solvent molecule at the crystal surface is inversely proportional to the rate of removal of a solvent molecule from the adsorbed at the crystal surface state. In turn, the rate is correlated to the height of the free energy barrier  $\Delta G^*$  by a linear relationship with  $e^{-\frac{\Delta G^*}{k_B T}}$ . Figure 3 shows a plot of rate of removal versus the exponential expression for each of the ibuprofen crystal surfaces in the study. The data points for the cases involving the  $\{100\}, \{002\}$  and  $\{011\}$  surfaces appear linearly distributed, as expected. The data points involving the  $\{110\}$  face, however, show a nonlinear relationship. This finding suggests that for this case the height of the barrier  $\Delta G^*$ has not been accurately estimated from the calculation of the free energy profile. The  $\{110\}$ surface is rough in almost all solvent cases which results more dynamic and complex surfacesolvent interactions. Such interactions are perhaps inaccurately represented in the collective variable space of the distance from the crystal surface causing a possible state overlap and a free energy barrier height that is underestimated.



Figure 3: Plot of rate of removal of a solvent molecule from the adsorbed state at the crystal surface vs. the exponential of the barrier height.