

Electronic Supplementary Information

Simulation of Amino Acid Diffusion Across Water/Hydrophobic Interfaces.

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Computational method

Combined QM/MM simulations

Molecular dynamics simulations have been carried out using the combined QM/MM approach¹ previously described. In this approach,² we use electrostatic embedding, that is, the Hamiltonian of the QM molecule includes the electrostatic interaction with the charges of the solvent MM molecules. The Hamiltonian of the solute-solvent system is:

$$H = H_{QM} + H_{MM} + H_{QM/MM}$$

H_{QM} contains interactions in the quantum subsystem (solute) while H_{MM} contains the interactions in the classical subsystem (solvent). $H_{QM/MM}$ contains solute-solvent interactions, including electrostatic (electron-charge and nucleus-charge) and van der Waals (Lennard-Jones potential):

$$H_{QM/MM} = H_{QM/MM}^{elect} + H_{QM/MM}^{vdw}$$

The solute's wave function is computed at each step of the simulation using the electronic Hamiltonian:

$$(H_{QM} + H_{QM/MM})|\psi\rangle = E|\psi\rangle$$

The forces acting on nuclei (QM and MM) are evaluated analytically. Indeed, one needs the energy derivatives with respect to the QM or MM atom position for the QM/MM electrostatic part, which are equivalent to the derivatives of the Coulomb interaction in a standard QM calculation (nucleus-electron and nucleus-nucleus), plus those of the van der Waals part, which are obtained straightforward. The equations of motions are then solved to obtain the new QM and MM atom positions.

Simulation box

The simulation box has been described in the main text of the manuscript. Figure S1 illustrates the density profiles which are comparable to those previously reported for the same interface.³

Force-field

Glycine is described at the quantum mechanical B3LYP/6-31G* level. Solvent molecules were described using a classical force-field proposed before for the H₂O/CCl₄ interface.³ Specifically, for water we employ the flexible SPC force-field.⁴ For the calculation of QM/MM non-electrostatic interactions, the van der Waals parameters for the QM atoms (Glycine) were taken from the OPLS force field⁵ available in the Tinker code.⁶

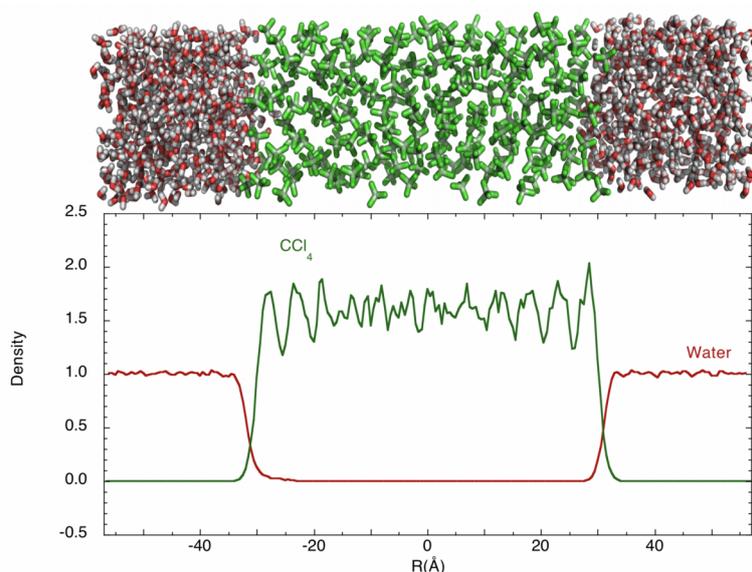


Figure S1. Average densities for the solution in the QM/MM MD simulations.

Simulations

NVT simulations were carried out at T=298K using the Nosé-Hoover thermostat.⁷ A cutoff of 12 Å was used for the interactions of both QM and MM systems with their environment. The time step was 0.5 fs. The systems were first equilibrated in bulk solution (minimum equilibration time was 25 ps). After equilibration in either bulk water (zwitterion) or organic solution (neutral forms), the system was pushed into the opposite phase using a bias potential:

$$E = \frac{1}{2}k(r - r_o)^2$$

where r represents the distance between the center of mass of the Gly and the center of mass of the organic solvent. A value of $k=50$ kcal/mol/Å² was shown to give suitable results for this constraint. Distances were varied by steps of 1 Å. At each distance the system was relaxed for 5 ps (corresponding to results shown in the manuscript), but to check the validity of the computational scheme, longer simulations (25 ps/Å) were also carried out at important points of the reaction coordinate. In particular, for points around the region where proton transfer was observed along the 5 ps/Å simulation. Specifically, we considered the following points: $R = -2, 1, 6, 8, 10, 12$ Å. Nevertheless, any noticeable effect of increasing the simulation time was obtained and therefore the latter results are not developed in the manuscript.

Computer codes

The simulations were done using Gaussian 03⁸ for the QM calculations, Tinker⁶ for the MD simulations and the program developed by us.⁹

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