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

Multiple binding modes of ibuprofen in human serum albumin identified by absolute binding free energy calculations

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Supplementary Information

The most relevant structure, topology and configuration files used to perform molecular docking, molecular dynamics simulations and alchemical free energy calculations are given as Electronic Supplementary Information material. All these files are included into a single compressed file with *.tar.gz* extension.

Structures and input parameters for molecular docking simulations

The structure of albumin used for molecular docking, which includes only polar hydrogen atoms, is given in AutoDock Vina format (file *AutoDock-Vina_albumin.pdbqt*); the structure of charged ibuprofen is also provided (file *AutoDock-Vina_charged-IBP.pdbqt*). Furthermore, an example of configuration script for performing molecular docking is given (file *AutoDock-Vina_albumin.pdbqt*). More accurate searches are performed by increasing the thoroughness of the search (parameter 'exhaustiveness'), setting as coordinate of the center the specific regions corresponding to each potential binding sites (parameters 'center_x', 'center_y' and 'center_z'), and reducing the size of the search space (parameters 'size_x', 'size_y' and 'size_z').

Structures, topology and input parameters for free energy simulations

The structure files of ibuprofen complexed with albumin in all the putative biding sites explored through alchemical binding free energy simulations are given. The name of each file includes indication of the protonation state (either *charged* or *neutral*), the location (either *DS1*, *DS2*, *FA1*, *FA2*, *FA5*, *FA6*, PC_{down} or PC_{up}), and the binding mode (*mode1* or, when additionally present, *mode2*, *mode3* and *mode4*) ranked from the most to the less favorable one in terms of the binding free energy that was later found in the calculations.

The topology for the complex of albumin and charged ibuprofen in GROMACS format is also provided (file *Gromacs_topol_complex_charged-IBP.top*); the corresponding topology for the complex of albumin and neutral ibuprofen is similar, except for the parameters of the ligand.

A sample file with input simulation parameters for performing free energy calculation is also included (file *Gromacs_grompp_0.mdp*). The other files needed (*Gromacs_grompp_1.mdp*, *Gromacs_grompp_2.mdp*, .., *Gromacs_grompp_23.mdp*) are similar, except for the line 'init_lambda_state = 0' (which will be, respectively, 'init_lambda_state = 1', 'init_lambda_state = 2', .., 'init_lambda_state = 23').