Supplemental Online Information for:

Towards the Identification of the Allosteric Phe-binding Site in Phenylalanine Hydroxylase

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Phe docking procedure

Complexes were generated using conformations of the minimum energy structures of dimeric enzymes extracted from the MD simulations on the unbound forms. To obtain the minimum energy structure of each unbound PAH forms, the potential energy of all structures, produced during MD simulations, was calculated using the g_energy program in GROMACS. This program extracts the energy components from the energy files. Subsequently, the minimum energy structure was extracted from the files obtained from g_energy using a home-made script.

The protonation of the unbound enzyme structures was carried out with the 3D Protonation MOE's tool. The default parameters of the MOE-Dock program were used. The docking placement was carried out using the triangle matcher methodology where the poses are generated by aligning ligand triplets of atoms on triplets of alpha sphere of receptor in a systematic fashion. A dock database was generated containing 30 poses of the receptor and of the ligand ranked according to the energy. London dG scoring function was applied to estimate the free binding energy of the ligand from each pose. The generated poses were subjected to refinement with a force field method and rescoring using the GBVI/WSA dG scoring function. The residues forming the Phe-binding site in the complexes were defined with MOE to be those residues with atoms within 4.5 Å of the ligand.

FIGURE S1

Figure S1: Root mean square fluctuation of the C^α atoms during the simulations of the unbound PAH forms. Colour code: wt-hPAH in black, wt-rPAH in red, G46S in green.