Figure 1S. Protein-ligand interaction energies (in kcal/mol) before and after minimization with AMMOS2 for the best docking pose with different number of water molecules in the binding pocket for thrombin, HIV-1 protease, estrogen receptor, ribonuclease, carboxypeptidase, metalloproteinase. C0 notes the energy of the docked complex before minimization, C1 to C5 correspond to the five cases of protein flexibility. The PDB ID of the proteins are noted.

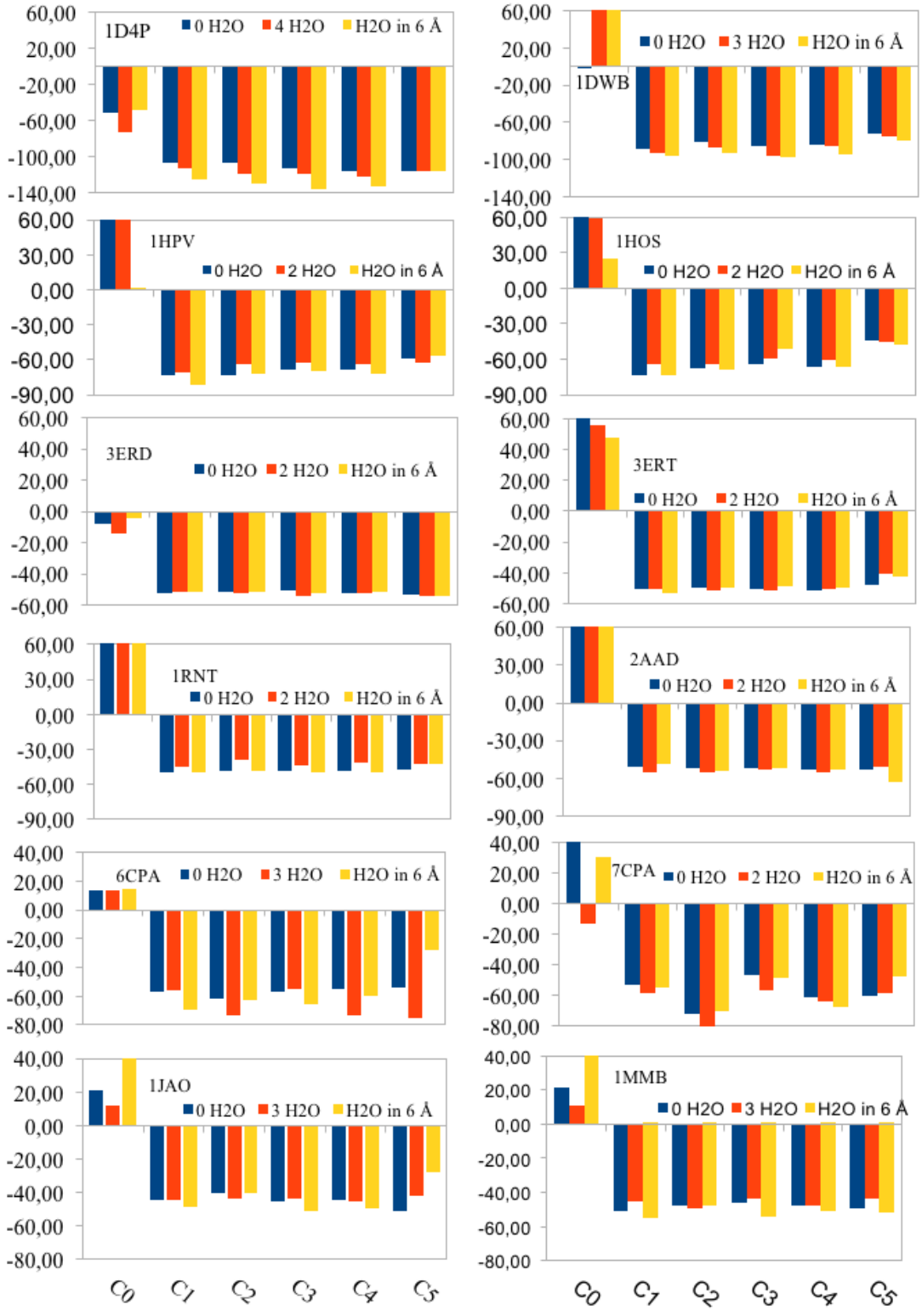


Figure 2S. Protein-ligand interaction energies (in kcal/mol) calculated with the AMMOS2 server after docking with AutoDock4.2 (in blue), after minimization with Chimera (in orange) and after minimization with AMMOS2 (in grey) including all water molecules present in the X-ray structures within a distance of 6 Å of the co-crystallized ligand. A. Protein flexibility Case 1; B. Protein flexibility Case 3.

Chimera minimization included 1000 steps of steepest descent optimization and water molecules and metal ions were considered as a part of the receptor. Chimera required about 10 minutes for 1 ligand and full protein flexibility minimization for a protein of typical length (350 residues).

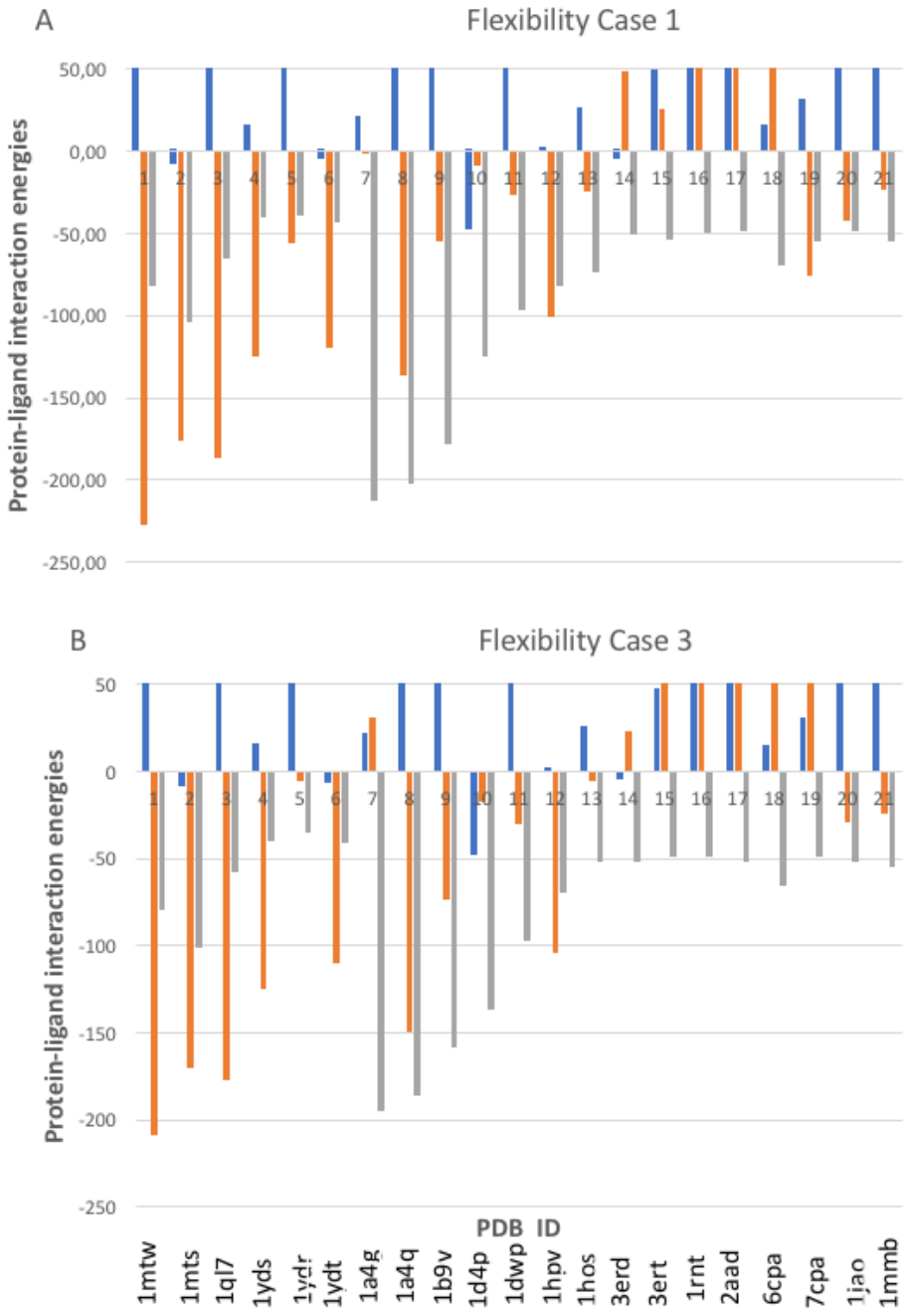
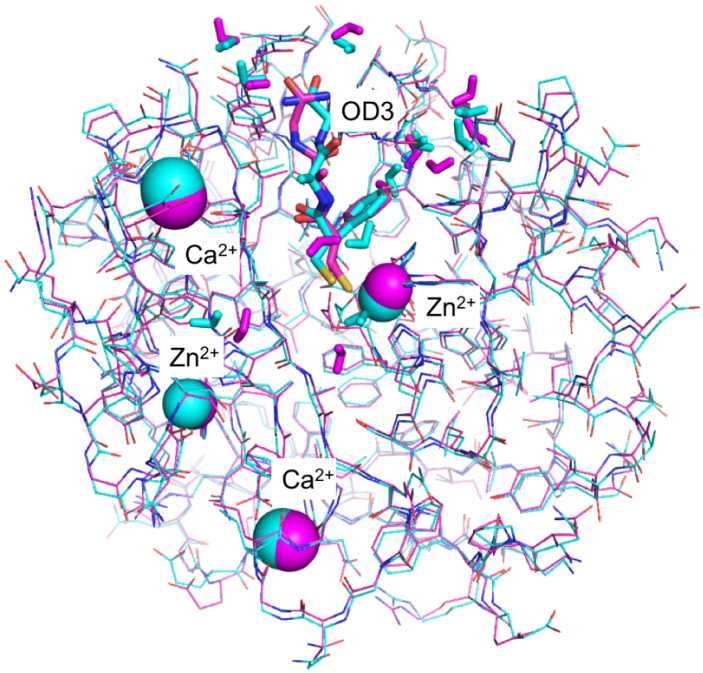


Figure 3S. The X-ray structure of the catalytic domain of the matrix metalloproteinase-8 with bound ligand OD3 (PDB ID: 1JAO) (shown in magenta) is compared to the structure of the complex minimized by full atom protein minimization (Case 1) with AMMOS2 (shown in cyan). The ligand and the water molecules present in the binding pocket are shown in sticks. The two Ca^{2+} and two Zn^{2+} ions are shown as solid spheres.



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