MS10-P4 Molecular modelling studies of protein-ligand interactions on haloalkane dehalogenases

Michal Kutý[1,2,3], Pavel Malcher[3], Ivana Kuta Smatanova[1,2]

1. Faculty of Science, University of South Bohemia in Ceske Budejovice, Branisovska 31, 370 05 Ceske Budejovice, Czech Republic
2. Institute of Nanobiology and Structural Biology, Academy of Sciences of the Czech Republic, 142 20 Prague, Czech Republic
3. Fac Fisheries & Protect Waters, Univ South Bohemia Ceske Budejovice, Zátiší 728/II, 389 25 Vodnany, Czech Republic

email: kutym@seznam.cz

Haloalkane dehalogenases (EC 3.8.1.5) are enzymes belong to the α/β-hydrolase superfamily [1] of enzymes that catalyze the hydrolytic cleavage of carbon-halogen bonds in halogenated hydrocarbons to yield the corresponding alcohol, a proton and a halide [2]. Therefore, haloalkane dehalogenases (HLDs) catalyze reactions of great environmental and biotechnological ignificance. This work is focused on the protein-ligand interactions in a recently constructed stable and solvent-resistant haloalkane dehalogenase DhaA from *Rhodococcus rhodochrous* NCIMB 13064 and its variants with mutations in the residues that form the access tunnel connecting the enzyme's buried active site to the surrounding solvent. In the previous study [3] crystallographic analysis followed by classical molecular dyanmics revealed that enhanced catalytic activity of mutant DhaA106 is due to an increase in the diameter of the access tunnel and the mobility of the adjacent secondary structure elements. In this work we study the interactions and different binding sites between a protein and a ligand by using molecular dynamics method GROMACS [4] and **PELE** [5,6] (an acronym **P**rotein **E**nergy **L**andscape **E**xploration) that combines a Monte Carlo stochastic approach with protein structure prediction and is capable of accurately reproducing long time scale processes.

This research is supported by the GACR (P207/12/0775).

References:

1. Ollis, D. L., Cheah, E., Cygler, M., Dijkstra, B., Frolow, F., Franken, S. M., Harel, M., Remington, S. J., Silman, I., Schrag, J., Sussman, J. L.,Verschueren, K. H. G. & Goldman, A. (1992), *Protein Eng.* 5 , 197–211.

2. Damborský J., Rorije E., Jesenská A., Nagata Y., Klopman G., Peijnenburg W. J. (2001), *Environ. Toxicol. Chem.*, 20, 2681–2689.

3. Liskova V., Bednar D., Prudnikova T., Rezacova P., Koudelakova T., Sebestova E., Kuta Smatanova I., Brezovsky J., Chaloupkova R., Damborsky J. (2015), Balancing the stability-activity trade-off by fine-tuning dehalogenase access tunnels. *ChemCatChem* 7, 648 –659.

4. Van Der Spoel D, Lindahl E, Hess B, Groenhof G, Mark AE, Berendsen HJ (2005). "GROMACS: fast, flexible, and free". *J Comput Chem* 26 (16): 1701–18.

5. PELE: Protein energy landscape exploration. A novel Monte Carlo based technique (2005), *J. Chem. Theo. Comput.*, 1(6):1304-1311.

6. PELE web server: atomistic study of biomolecular systems at your fingertips (2013), *Nucleic Acids Research, 41(W1):W322-W328.*

Keywords: haloalkane dehalogenases, structure, molecular modeling, PELE, Gromacs