MOL2NET, International Conference Series on Multidisciplinary Sciences

Screening of the Binding Trajectories of Inhibitors via Tunnels using Novel Software CaverDock

Pinto, G. [a,b], *Vavra, O.* [a], *Kokkonen, P.*[a,b], *Filipovic, J.* [c], *Jurcik, A.*[d], *Kozlikova, B.*[d], *Bednar, D.*[a,b], *Damborsky, J.*[a,b]

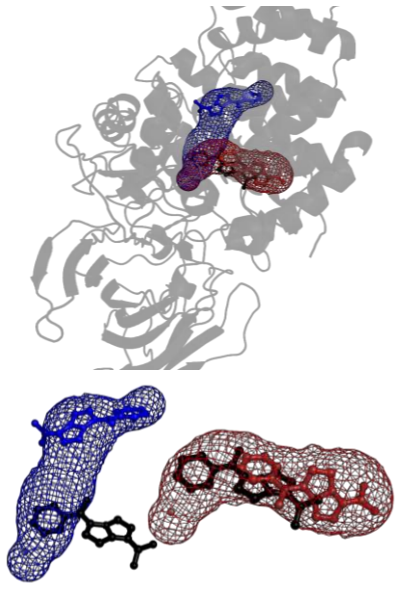
a Loschmidt Laboratories, Department of Experimental Biology and RECETOX, Faculty of Science, Masaryk University, Kamenice 5/A13, 625 00 Brno, Czech Republic

b International Clinical Research Center, St. Anne's University Hospital Brno, Pekarska 53, 656 91 Brno, Czech Republic

c Institute of Computer Science, Masaryk University, Botanicka 554/68a, 602 00 Brno, Czech Republic

d Human Computer Interaction Laboratory, Faculty of Informatics, Masaryk University, Botanicka 68a, 602 00 Brno, Czech Republic

Graphical Abstract



Abstract.

Protein tunnels and gates are attractive targets for drug design [1]. The drug molecules blocking the access of natural substrate or release of products are very efficient modulators of biological activity. Tunnels are important for the transport of ligands, solvent, and ions, and can be found in many proteins. We have developed a user-friendly graphical interface for a study of protein tunnels and channels Caver Analyst 2.0 [2]. Caver Analyst, part of the Caver suit [3], can be used to identify tunnels in both static structures as well as molecular dynamics trajectories. Studying tunnels in protein assemblies from molecular dynamics simulations offers possibilities to observe transient tunnels and their changes in time. Study of the transport of ligands through the protein tunnels can be carried out using the software CaverDock [4-6]. CaverDock is a fast, robust and accurate tool, which allows the screening of binding and unbinding processes for pharmacologically interesting compounds. It is based on a modified AutoDock Vina algorithm [6]. CaverDock is fast enough to be used in virtual screening studies. It is possible to choose how to treat the residues along the tunnel, this means that both rigid and flexible runs are

	available on this tool. The user can also define how many flexible residues to use. *The software Caver 3.0 and CaverAnalyst 2.0 are available free of charge at the website http://www.caver.cz/, while the software CaverDock 1.0 is available at the website https://loschmidt.chemi.muni.cz/caverdock/.*

References

1. Marques, S.M., et al. 2016: Enzyme Tunnels and Gates as Relevant Targets in Drug Design. Medicinal Research Reviews 37: 1095-1139.

2. Adam Jurcik, David Bednar, Jan Byska, Sergio M. Marques, Katarina Furmanova, Lukas Daniel, Piia Kokkonen, Jan Brezovsky, Ondrej Strnad, Jan Stourac, Antonin Pavelka, Martin Manak, Jiri Damborsky, Barbora Kozlikova. 2018: Caver Analyst 2.0: Analysis and Visualization of Channels and Tunnels in Protein Structures and Molecular Dynamics Trajectories. Bioinformatics,34(20), 2018, 3586–3588.

3. Chovancova, E. et al. (2012) PLOS Computational Biology 8: e1002708

4. Vavra, O., et al. 2018: CaverDock: A New Tool for Analysis of Ligand Binding and Unbinding Based on Molecular Docking. Bioinformatics (under review).

5. Filipovic, J., et al. 2018: A Novel Method for Analysis of Ligand Binding and Unbinding Based on Molecular Docking. IEEE/ACM Transactions on Computational Biology (under review).

6. Trott, O. and Olson, A.J., 2010: AutoDock Vina: Improving the Speed and Accuracy of Docking with a New Scoring Function, Efficient Optimization and Multithreading. Journal of Computational Chemistry 31: 455-461.