

At any moment, living systems contain several thousands of small organic molecules both endogenous and exogenous, the metabolome. To exert their function, the hosts of molecules need to arrive at their sites of action mostly represented by protein surfaces or internal cavities. The transport of the metabolome is mainly governed by protein tunnels and channels. They secure the transport of ligands between different regions, connecting inner protein cavities with its surface, two or more different cavities, or even different cellular environments such as in the membrane proteins. The presence of very sophisticated transport regulation markedly contributes to symbiotic co-existence of individual chemical species within a single compartment or whole cell without the presence of overly disruptive interferences. In enzymes, the tunnels connect buried functional sites to the bulk solvent enabling access of substrates and release of products but also many additional functions essential for the proper function of proteins exposed to the interference of individual species present in the metabolome of the living cell are provided by tunnels.

Despite their importance, transport tunnels are often omitted from investigations on protein function due to their transient nature that significantly complicates their identification and analysis in a protein structure. To surmount this obstacle, tunnels have to be analyzed by using very sophisticated molecular dynamics simulations, which are computationally very demanding and their execution requires considerable expertise and knowledge of studied protein. In this project we will develop methodology to perform such analysis effectively and automatically thus enabling access to the rigorous study of the transport component of protein function for much larger part of the scientific community. Hand-in-hand, we will also apply the developed methods to investigate proteins relevant to human health as well as those utilized in various biotechnologies. This will provide more complete understanding of mechanisms of actions performed by various proteins in the cell. Ultimately knowledge of tunnels can contribute to the engineering of better proteins for application in various biotechnologies. Similarly, targeting the tunnels of enzymes involved in various pathologies could open up alternative avenues towards development of novel inhibitors/drugs.