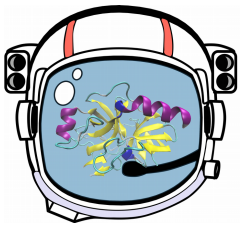

Description for general public
of the research project

Structure and reactivity of proteins in the gas phase – a meeting between advanced mass spectrometry and molecular modelling

Is life in high vacuum possible? No oxygen, no liquid water? The answer seems obvious – no, even if viruses or some spores of simple bacteria are able to survive harsh conditions of outer space. However our initial question can be gradated. Is it possible that structures, or even activity, of proteins – our basic molecular building blocks responsible for chemical reactions decisive for life – are preserved in the gas phase? Recently there is growing amount of experimental data indicating that, even after „unpacking" from the safe water shell, some proteins are able to preserve their structure, or even some residual enzymatic activity. This is an observation as striking as the fact known to scientists for several decades – proteins entrapped in crystal environment usually preserve their structure very well, which allows for routine studies of protein 3D structures by diffraction methods. However, behaviour of proteins in the gas phase is known considerably less than in liquid or crystal – so here is the starting point of our project…

The principal objective of the studies to be carried out in the framework of this project is determination, with the help of computational chemistry (molecular modelling), of the influence on the protein structure (and whenever possible – reactivity) of the two following factors: (a) transfer of a protein to the gas phase with additional ionization (change in electric charges) on the amino acid „blocks" forming the protein – removal of protein from its water shell and ionization of amino acids can result in denaturation of the structure, either total or restricted to deformations on the solvent-exposed surface; (b) attaching fluorescent labels to a protein, which also can change its molecular shape. In the latter case the labels behave as retroreflective „cat's eyes" enabling observation of proteins in laser beam, but additionally so-called Förster resonance effect will be used – when the protein contains two fluorescent labels positioned reasonably close, irradiation of one of the labels makes the energy be transmitted to the second one; so, under certain conditions, „I shine in one cat's eye, and the other one shines back". This is very informative on the protein structure, but… could the fact that labels have been attached modify the delicate structure of the protein? We want to investigate this issue on theoretical framework.

Studies planned in the framework of this project by our team are calculations with the use of molecular modelling methods, primarily molecular dynamics with classical force fields. Molecular dynamics is a method to track history of behaviour of a molecule or molecular assembly in time domain. Atoms are assigned with initial velocities, and further – according to the simple Newtonian equations of motion – time evolution of the system is recorded giving a trajectory („a documentary movie on the life of the molecule"). Stability of protein structure, its dynamical flexibility, or even reactivity can be established by this methodology. The use of classical force fields leads to assumption that chemical bonds bind atoms as if by a system of mechanical springs. Such an approximation is not always satisfactory (for example because such model bonds-"springs" are mathematically ideal, they do not adapt to changes in chemical environment of a given atom), and in such case it is necessary to resort to the quantum chemistry methods, much more advanced and computationally costly. Among techniques employed to speed up the calculations, one of the most novel is the use of hardware accelerators (*GPU-accelerated calculations*). Our calculations will be conducted in the closest contact with the experimental group of the Foreign Partner, Prof. Renato Zenobi (ETH Zürich), who will use the computational results to interpret the experimental data that presently, without computational support, cannot be uniquely assigned. This meeting of two branches of chemistry – advanced mass spectrometry and molecular modeling – will lead to advancing the frontiers of human knowledge and, potentially, will make the border between them a new research field – the structural chemistry of biomolecules in the gas phase.

Motivation to undertake this research topic is easily found in our wish to explore mechanisms of protein activities. Therefore our targets were chosen primarily from a well-known family of enzymes, namely proteases, including trypsin and chymotrypsin. Structural comparisons between proteins in the gas phase, solution and crystal will not give us immediately ability to live in high vacuum, but they will yield answers to many questions regarding mysterious process in which chains of amino acids, relatively simple chemical compounds, organize themselves into proteins – the most complex structures which our science explores at the molecular level, the basic machinery of life.