DFT insights into the chemistry and biochemistry of metals

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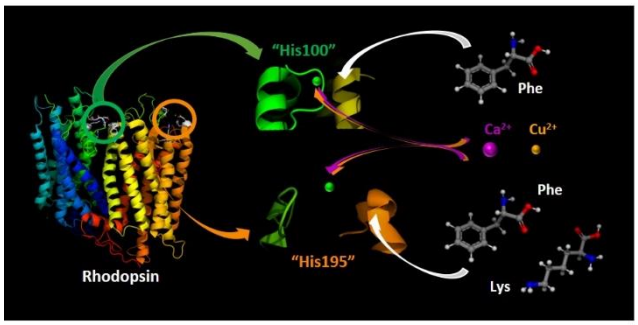

Figure 1: Zinc and its critical role in *Retinitis pigmentosa* disease [1].

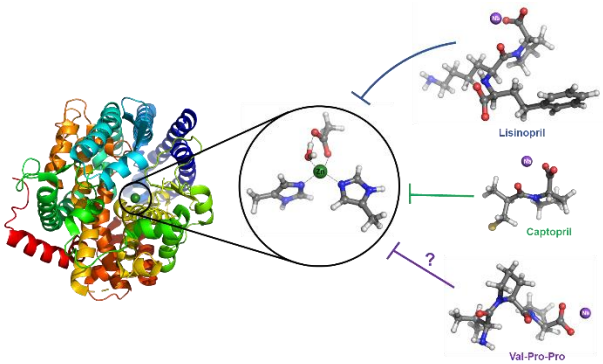

Figure 2: Molecular insights into the interaction of Angiotensin I-converting enzyme inhibitors (Lisinopril, Captopril, Val-Pro-Pro) and HEXXH motif [2].

❖ Description of the problem

In modern chemistry, Density Functional Theory (DFT) calculations play an essential role in elucidating manifold chemical and physical properties of chemical compounds. In our group, DFT calculations are used to probe the electronic structures of metal complexes with simple ligands – water molecules and organic species that mimic the solvent environment and biomolecular targets, for example amino acids and peptides. We are focused on the biologically essential metals and metals that have competing roles in biological systems. Zinc is one such example: the second most abundant transition-metal cation in the human body after iron, considered as a vital constituent of proteins, including enzymes.

❖ Use of HPC Infrastructure

Ab initio and DFT calculations are very trustworthy in reproducing structures of biological systems and revealing the thermodynamic interactions between the building components of the studied systems. The main limiting factor, however, is the number of basis functions that can be computed. A widespread methodology is the use of simplified models for the amino acid residues. Even using these models, we usually need computational time of the order of 4-8 weeks for one such study when using a single multi CPU workstation. Using the HPC infrastructure (Avitohol supercomputer) allows many more tasks to be performed simultaneously and faster. The supercomputer used is located in the HPC center of IICT-BAS [3] and it is maintained by the National Center for High-Performance and Distributed Computing (NCHDC), subject to the National Roadmap for Research Infrastructures (NRRI) [4]. The results were obtained using up to 64 HP Cluster Platform SL250S GEN8 servers, each with 2 Intel Xeon E2650 v2 CPUs and 2 Intel Xeon Phi 7120P coprocessors.

❖ Results and Future Work

By using Avitohol supercomputer we succeeded in obtaining data on the enigmatic function of the zinc cation in two studied centers (His100 and His195) of the key protein rhodopsin and on the of binding of Val-Pro-Pro (a milk-derived tripeptide with assumed mild inhibitory activity against ACE) and two pharmaceutical drugs (Captopril and Lisinopril) to the HEXXH metal-binding motif of ACE. The team is going to start a new task, namely, study of silver binding to biomolecular targets and the origin of the antibacterial activity of silver.

1.https://doi.org/10.1021/acs.inorgchem.0c02664
2. https://doi.org/10.1016/j.bpc.2021.106626
3. http://www.iict.bas.bg/avitohol/
4. http://nchdc.acad.bg/