MS21-04 | Quantum Crystallography for Macromolecules: the HAR-ELMO Method

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Hirshfeld Atom Refinement (HAR) is undoubtedly one of the emerging methods of modern Quantum Crystallography [1,2]. Strongly based on tailor-made quantum chemistry calculations, the technique uses only X-ray diffraction data to obtain the positions of hydrogen atoms with precision and accuracy that are usually achieved through neutron diffraction experiments [3].

Since nowadays more and more high-resolution X-ray diffraction data for macromolecules are available, HAR could be exploited also to successfully refine crystallographic structures of proteins. Nevertheless, its extension to large systems is hampered by the fact that the HAR requires a quantum chemical calculation for each iteration of the refinement, with a consequent increase of the computational cost as larger molecules are investigated.

To circumvent the problem, HAR has been coupled with the recently constructed databanks of Extremely Localized Molecular Orbitals [4], which allow fast and reliable reconstructions of wavefunctions and electron densities of polypeptides and proteins.

In this presentation, the results of the first HAR-ELMO refinements will be shown. In particular, after illustrating preliminary tests performed on small systems, the first applications of the new technique to polypeptides and proteins will be presented and discussed.

[1] D. Jayatilaka, B. Dittrich, *Acta Cryst. A* **2008**, *64*, 383.
[2] S. Capelli, H.-B. Bürgi, B. Dittrich, S. Grabowsky, D. Jayatilaka, *IUCrJ* **2014**, *1*, 361.
[3] M. Woińska, S. Grabowsky, P. M. Dominiak, K. Woźniak, D. Jayatilaka, *Sci. Adv.* **2016**, *2*, e1600192.
[4] B. Meyer, A. Genoni, *J. Phys. Chem. A* **2018**, *122*, 8965.