Use of density topology information to account for nuclear quantum effects, and as an ingredient for atom refinement algorithms

M. Gimferrer[1]

[1]Institut für Physikalische Chemie, Georg-August Universität Göttingen,
tammannstraße 6, 37077 Göttingen, Germany

E-Mail: marti.gimferrerandres@uni-goettingen.de

Nuclear quantum effects (NQEs) are relevant for a wide range of chemical phenomena, including photochemistry, proton-coupled electron transfer reactions, and even in the description of common intermolecular hydrogen bonds, just to name a few examples. The latter may require a quantum mechanical treatment of atomic nuclei, in particular the protons. Several schemes exist, many of them involving extensive PES calculations, and have in common: 1) the computational costs scale very unfavorably with the system size and the number of quantum nuclei, and 2) density information (electronic or atomic) is lost. Hence, relating such calculations with properties or achieving a deeper understanding of NQEs is hindered. Multicomponent methods offer an alternative. The latter uses wavefunction or density functional theory (DFT) to treat both (selected) nuclei and electrons at the quantum mechanical level and on equal footing. Among these, notable progress has been made within the nuclear-electronic orbital (NEO) formalism.[1] Methods founded on the NEO framework seem promising for the systematic incorporation of NQEs, although their practical application has been somewhat restricted.

Here, we present the recent developments in the NEO framework within the (Mata) group and currently available in Molpro.[2] Special focus will be given to reviewing how these methods apply to account for anharmonicity effects in water-coordinated molecular dimers, and their performance in evaluating the impact of NQEs on intermolecular interactions.[3] Overall, the aim is to make multicomponent simulations efficient and accessible in terms of both computational time and the chemical information one can extract from them, thus extending the day-to-day quantum chemistry toolbox. On a different direction, some preliminary results in incorporating chemical bonding methods developed at Girona[4] into atomic refinement algorithms will be shown. In particular, our attempts to improve the refinement of H-atom positions and anisotropic displacement parameters (ADPs) in small molecules, together with future directions in protein crystallography.

[1] F. Pavosevic, T. Culpitt, S. Hammes-Schiffer, *Chem. Rev.*, **2020**, 120, 4222-4253.
[2] L. Hasecke, M. Breitenbach, M. Gimferrer, R. Oswald, R. A. Mata, *J. Phys. Chem. A*, **2025**, 129, 3560-3566.
[3] M. Gimferrer, L. Hasecke, M. Bödecker, R. Mata, *Chemical Science*, **2025**, 16, 11002-11011.
[4] P. Salvador, E. Ramos-Cordoba, M. Montilla, L. Pujal, M. Gimferrer. *J. Chem. Phys.*, **2024**, 160.