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Computational Studies

Important for the Definition of Terminology in Computational Chemistry

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The essay by R. Hoffmann, P. von R. Schleyer, and H. F. Schaefer III[1] addresses an important point of theoretical studies that has bothered me for a long time and that I consider to be very important to increase the awareness of the chemical community regarding (now ubiquitous) quantum chemical results. This point is the question of what it means when a quantum chemist predicts a molecule to be "stable". I often realized that non-experts, when confronted with results from quantum chemical calculations, are not aware of the fact that computational chemists often use "stable" synonymously with "local minimum on the potential energy hypersurface," which is by far not sufficient to meet the stability criteria of synthetic chemists.

The authors discuss this issue with great competence. In principle, all the points that are addressed are known. However, the increasing number of scientific publications in which little care has been taken with respect to the choice of descriptors like "stable" and to the conclusions that can be drawn on the basis of some modeling approach demands a clarifying essay such as that written by R. Hoffmann, P. von R. Schleyer, and H. F. Schaefer III.[1]

It must be emphasized that this is not an easy task because of the multifaceted sources of error. On the one hand, these errors comprise approximations in the theoretical technique, such as the choice of the one-electron basis set, the choice of the approximate density functional, or the quality of the total wave-function approximation, but also the setup of the atomistic model structures. On the other hand, the question of stability also requires us to look for "destabilizing" side reactions, which is seldom considered because of the huge computational effort that this would require and the fact that such degrading side reactions are not necessarily sharply definable.

The list of points to be taken into account when "stability" of a compound is addressed is longer than one might think at first sight, but the authors have condensed it to the most important ones. I may, however, add two more examples to illustrate the difficulties encountered when assessing the "stability" of a molecule.

The authors suggest that molecular dynamics (MD)—in addition to locating transition states—can be a means to probe kinetic stability of a molecule. Though I understand the purpose of their suggestion, I would like to stress that many technical difficulties arise, as most processes are not spontaneous on an MD time scale (e.g., because this time scale is too short or because only a single molecule is studied—instead of 1 mole). Hence, if a MD trajectory were run, only explosives would be classified as unstable, because only these tend to show spontaneous events in an MD simulation. For many other molecules, even those molecules that would usually be called unstable, a constrained or restrained MD might be needed to better understand their reactivity in simulations. This example demonstrates that it is also necessary to specify a certain practice in computational work in order to assess the significance of a computational study.

My second example relates to the statement in the Essay that the exact total energy of He can easily be computed to more significant figures than can be determined in the laboratory. But this precision, of course, can only be achieved for a particularly chosen many-electron Hamiltonian (usually the one that corresponds to Schrödinger's nonrelativistic quantum mechanics).

But the choice of the Hamiltonian can matter a lot, especially if very accurate total energies are desired. Depending on the accuracy needed to answer a given scientific question, relativistic effects come into play. Even in the case of He they matter: Kinematic relativistic effects and retardation of the electron–electron interaction can play a role. Then quantum electrodynamical effects and retardation effects of the electron–nucleus interaction will contribute. Also, the motion of the nucleus must be considered. These effects are small in the case of He, but they may still affect the total electronic energy starting at about the fourth digit behind the decimal point (in Hartree atomic units). Unfortunately, the various relativistic corrections can be of similar magnitude, and a Pandora's box is opened if one tries to accurately include all these effects in the Hamiltonian.

The authors suggest in their concise essay new labels to distinguish the different notions of stability, namely "viable" and "fleeting", which will certainly be picked up by many computational chemists and which will help experimentalists to judge the quality of theoretically predicted results. Therefore, I fully supported publication of this Essay in *Angewandte Chemie* in order to increase the awareness for the stability issue in theoretical modeling and warmly recommend reading this nice piece of text.

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