

Ricardo Mata

Are our theoretical models up to standard? Ask the molecules

Our high hopes on quantum computing and its impact on chemical research may or may not be justified, but one thing is certain. We as chemists do not need to wait for quantum computers to assess the energetics of molecules. We can just ask the molecules directly if we are inventive enough. And with all quantum effects included...

Benchmarking does not necessarily have the best calling. As soon as the word is uttered, images of repetitive experiments pop into mind, the grinding of statistical numbers and tables extending over several pages. As scientists, we are naturally attracted to the unknown. It has a much stronger grip on us than repeating experiments to fill in some tables. Deep down, we don't want numbers, we want adventure. But is benchmarking that boring? Can we be adventurous with benchmarking? Over the past 6 years I have had the wonderful experience of serving as speaker to a DFG-funded Research Training Group titled "Benchmark Experiments for Numerical quantum Chemistry" (RTG2455 BENCH). Its objective? To push the limits of experiments to the point where one can critically evaluate the performance of electronic structure theory and associated computational protocols. And this brought me more than ever in close contact with experimentalists, as we tried to understand what the limitations are on each side. Not only do I receive insights into what my colleagues are doing but on top also get to reflect on my own work, what it means to calculate something and have the nerve to compare it to the 'real world'.

Successful fields of research tend to become standardized, dogmatic. As the success stories pile up we become resilient to new ideas, even when our old practices start to show their limitations. Over the past two to three decades theoretical chemistry certainly has followed this path, victim of its own success, and established quite a few paradigms that are now passed untouched from generation to genera-

tion. The harmonic approximation to simulate molecular vibrations, the choice of hybrid DFT for the optimization of structures, classical transition-state theory, etc... nothing to feel ashamed of. We are just like any other science, and these rough approximations have been in fact quite helpful. Question is, when do they fail? Even widely accepted standards of quantum chemistry are disputed when the systems increase in size [1]. And if even our well-trusted gold standard coupled cluster fails, where do we get our references from? Who or what do we trust?

Experiments as arbiter of theory

We have been working for some years in cooperation with the Suhm group, trying to understand how the energetic balance of molecules is driven by inter-/intramolecular interactions. Through the use of jet molecular expansions they are able to investigate spectroscopically (IR/Raman) ultra-cold molecular clusters, size-selective towards monomers or aggregates. These are ideal conditions for comparison with theory, given how comfortable it is for the theoretician to model isolated molecules near 0 K. From experimental data we learned the shortcomings of MP2 in describing OH bonds [2], or how far one relies in error compensation when simulating vibrational spectra [3]. This ultimately served us as inspiration to involve more theoreticians. Blind challenges were designed, starting with the simple question: how does a single methanol molecule bind to a furan (Figure 1) [4]? Further experiments would even provide a structure and relative energies with error bars below 1 kJ/mol [5], lower than any level of confidence one may have on a computational protocol. And all of this by directly probing the molecules.

Significant forethought and careful design are required to obtain benchmark data [6]. But the same is not to say that one needs to restrict oneself to boring systems. In another close collaboration with an experimental group, we organized a challenge on the protolysis reactions of trisarylferrate anions with alcohols [7]. The bimolecular rate constants in the gas phase were measured and later compared to blind submissions of different theory groups. This adds, of course, a lot more layers of complexity to the problem. One is dealing with chemical transformations, not just the energy difference between cold molecular clusters. Besides the issue with the temperature, the

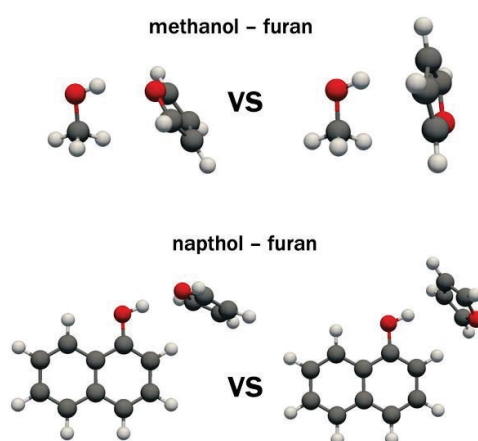


Fig. 1: Examples of closely related molecular balances that can be used to critically test electronic structure theory.

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prediction of rate constants creates a two-pronged challenge. On the one hand, the electronic structure description, as transition-metal complexes are still challenging today. It is possible to control such factors through the choice of reactants. In this particular case, zincates can be a good option [8], being much easier to calculate. The further challenge was the microkinetic modeling. Does one just trust classical transition state theory or go beyond? These are all questions that I found, over time, are best addressed in community challenges. This avoids the monologues that individual peer-reviewed publications tend to promote. Even the writing of these papers is an invitation to discussion, as one needs to find a balanced account of how all the methods performed. Even if we started the challenge with one metric in mind, we have been open to other viewpoints. Can one really boil everything down to root-mean-square deviations, or are relative trends more important? In the end, we shouldn't focus on losers and winners, but on the path for improvement.

Benchmarking is cumulative

Not all of the experimental data we are making use of is necessarily new. Having shown how the study of hydrates through IR-spectroscopy is a sensitive test to theory models [8], further experimental measurements have been collected from other groups. These build up a dataset that can be later used for the training of new models. Older experiments can also be revisited. The Leutwyler group measured the binding energies for dozens of molecular dimers (SEP-R2PI method), many with error bars in the order of 1 kJ/mol [9]. We have been recently reviewing the full series and came to observe some mismatches, particularly when it comes to the conformation of the aggregates. As an example, the naphthol-CO dimer was assigned to the face-isomer (the CO molecule docking on top of the π -system). Microwave experiments from the Obenchain group in combination with our quantum chemical calculations reveal in fact that the edge (hydrogen-bonded) isomer is the global minimum [10]. The energetics check out, one has a structure and a new reference point for benchmarking. This is a result of two different (complementary) experimental techniques and simulations on top. This is something we have observed repeatedly: how one can profit from different methodologies or experimental conditions to gather benchmark data. It is not always the best experiment, it's how one best "cross-interrogates" the molecules. Benchmarks allow us to level with the 'real world' and are a tried-and-true way to push us out of our comfort zone. Let us keep working together and with the molecules.

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