Computing Unknown Compounds: A Balancing Act between Science and Science Fiction

These days, *Inorganic Chemistry*, like many chemistry journals, is receiving a considerable number of manuscript submissions that fall exclusively within the theory and computations category, or *theory* for short. Indeed, theory has slowly but steadily risen in importance almost from the inception of chemistry as a science. It is possible that theory may eventually reach the status of a coequal branch of the field together with the experimental branch. This evolution would seem to be accelerating as the development of new tools for data-based prediction is gathering pace. For the time being, however, chemistry is predominantly an experimental science, and for all we know, it might stay that way. It is worth noting that even Auguste Comte, a 19th century philosopher who is often quoted as having stated that mathematical analysis is antithetical to chemistry, allowed that "facts cannot be observed without the guidance of some theory". We now associate this insight with one of the pillars of the scientific method.

Because of the rising importance of theory, an increasing number of research groups specialize in this area. As a further consequence, many theory research groups hope to reach a readership for their articles beyond the confines of the theory community because their findings may have real-life applications or because they aim at introducing new chemical concepts or clarifying old ones with a new understanding derived from first-principles theory, to state a few common motivations. The increasing number of theory-only manuscripts that are being submitted to chemistry journals in general, and to *Inorganic Chemistry* in particular, therefore primarily reflects this ever-rising importance of theory.

So, you may be asking yourself, what is the point of this Editorial? Primarily, it is that not all theory manuscripts are—nor should they be—created equal. However, every manuscript needs to meet the scope and quality criteria of the journal. First and foremost, a manuscript that is being submitted to *Inorganic Chemistry* should address a question or problem in inorganic chemistry. Instead of attempting to define here what exactly *is* inorganic chemistry, we refer the reader to a previous Editorial[1] that addresses this question according to the viewpoints of the Editorial Board as it was composed in 2019.

Regarding theory submissions, it is worth quoting from that Editorial:

> *"Inorganic Chemistry welcomes studies that use state-of-the-art theoretical/computational methods to contribute to conceptual advances in all areas of inorganic chemistry, especially those that combine experiment and theory. Studies that focus on technical aspects, for example, the choice of density functionals and/or basis sets, or are largely speculative, that is, make predictions that cannot reasonably be subjected to experimental testing, will not be considered."*

In the quote, the words *contribute* and *combine* in combination with *especially* indicate a strong preference for studies that feature state-of-the-art theoretical support of experimental research but also leave an opening for purely theoretical studies. Given the rise in submissions of the latter type, we wish to clarify this aspect further in reference to the word *speculative* in the quotation and the balance of Science versus Science Fiction alluded to in the title of this Editorial.

To avoid misunderstandings: We very much welcome purely theoretical studies! However, it is important to clarify what we expect from a theoretical/computational contribution to *Inorganic Chemistry* as a precondition of a manuscript to be sent out for review. For illustration, we constructed three examples and discuss them in what follows. Individually, and by design, these examples are hypothetical, but they are amalgamated from recent submissions to *Inorganic Chemistry* and therefore broadly representative of the theoretical studies that the Editors of the journal may need to evaluate.

Suppose that one of the Associate Editors receives a manuscript reporting the theoretical prediction of a new transition-metal catalyst based on density functional theory calculations. A majority of the readers and reviewers of *Inorganic Chemistry* associate themselves with the experimental side of chemistry. Many of those readers will not be familiar with the accuracy of the chosen (always approximate) density functional and basis set combination for the relative energies of minima (reactants, products, and intermediates) and first-order saddle points (transition states) on the system's potential energy surface (PES, incl. the enthalpy or Gibbs or Helmholtz energy analogs as needed). Because the handling Editor is responsible for this study to be (a) sound and (b) of value for

both specialized and nonspecialized readers, they will care for the following to be the case: The authors need to make sure they provide solid evidence that the predicted performance of the catalyst is sufficiently accurate. In other words, the authors need to give their readers a sense of the actual or reliably estimated error bars of the calculations. In contrast to a common misconception, this is not a technical side note that can be buried in the Supporting Information. It is necessary information because it defines the significance of the conclusions—both for experimentalists and for theorists. Gathering this information may be accomplished, for example, by studying similar reactions with known catalysts for which reliable experimental data are available for direct comparisons. In the absence of experimental data, a high level of theory may be used on suitable model compounds, and the results can be extrapolated to the target systems calculated at the highest possible (but maybe lower) level. Another way to provide this kind of context would be with the help of already published benchmarks for the chosen theoretical model.

As another example, let us assume that a researcher wishes to report a new interesting molecule—be it made up from nonmetal atoms or (purely) metal atoms—that may also be predicted to be aromatic in some sense. Among the questions that would ideally be addressed in the study are the following: Is there a chance for the molecule to be viable (thus, experimentally accessible), and under what conditions? It is necessary but not sufficient to verify by calculations that the molecular structure is a minimum on the PES. For good advice on this topic in terms of how predictions become reasonable or—more importantly—relevant to chemical research, which also applies to the other examples mentioned herein, we recommend an article by Hoffmann et al. that elaborates on this question.[2] Next, what would be the experimentally relevant ramifications of the proposed aromaticity, given that aromaticity is not easily reduced to a single descriptor.[3] What properties, spectroscopic or otherwise, can be predicted for the new molecule that would allow its unambiguous identification by experimental means? Finally, once more, how reliable are those predicted properties? Regarding the latter point, it may be necessary to consider alternative systems in the calculations as well, to make sure that the predicted properties represent as much as possible a "fingerprint" of the new molecule.

As a last example, think of a manuscript reporting a study predicting new crystal structures under high pressure and claiming that one of the predicted new phases has a particularly high thermal conductivity. If the authors consider the topic of the study to be of interest to the *Inorganic Chemistry* readership, they might want to ponder the following questions: Can the authors cite other cases when such predictions have been confirmed experimentally? How likely or unlikely is it that the predicted structures actually exist and that they are accessible via some experimental route? What goes into the calculation of the thermal conductivity and what are the expected error bars for such a calculation? (Similar considerations apply to other predicted properties of interest.) If high pressure is required for the stability of the material, what are the chances that there is an application later on?

Generally, when the synthesis of a new compound is proposed, it would make sense for the authors to check with some of their experimental colleagues to get an idea whether there is a viable synthetic route. To reiterate, when considering the readership of *Inorganic Chemistry*, there is a good chance that the manuscript will be declined without review if it is not clear to a nontheoretician that the calculations are accurate and reliable. In other words, a hypothetical proposed compound is usually of low value for the community if there is little chance of realizing and characterizing it by experimental techniques. An exception may apply to compounds that cannot be accessed, for instance, because they contain unstable isotopes, although in this case a particularly strong motivation would likely be needed for the study. We also acknowledge that there remain some aspirational goals of chemistry that are unlikely or at least very difficult to realize in the laboratory, but nevertheless exciting and important, because we can potentially learn something new about bonding or other intrinsic chemical or physical properties. This means that when it comes to the all-important question of whether a theoretical manuscript's content is suitable for *Inorganic Chemistry*, there is some room for interpretation and discussion—although not in terms of accuracy and meaningfulness for our field.

Not every theory study predicting hitherto unknown species or materials may need to consider all the points listed in the above examples to be suitable for *Inorganic Chemistry*, whereas in other cases, additional work may be needed to convince our readers that the predictions are accurate and reliable. This is to say that different types of studies and different types of systems require different levels of scrutiny. What is important, however, is that theoretical predictions of unknown systems stay close to the experimental aspects of the subfield of the study and provide as much guidance to the experimental community as reasonably possible. Perhaps a useful exercise would be if the authors of a study predicting new compounds and their properties imagined being an experimentalist who may have the equipment and know-how to confirm the predictions but needs to be convinced that it is worth their time and effort and expenses. What would it take to convince such a person? This may well make the difference between Science Fiction and Science.

Jochen Autschbach, Associate Editor orcid.org/0000-0001-9392-877X

Stefanie Dehnen, Editor-in-Chief orcid.org/0000-0002-1325-9228

REFERENCES

(1) Tolman, W. B.; Balch, A. L.; Bart, S.; Cossairt, B.; Dehnen, S.; Halasyamani, P. S.; Kageyama, H.; Meyer, F.; Morrow, J.; Mukherjee, P. S.; Neese, F.; Power, P. P.; Sessoli, R.; Yam, V. W. W.; Zhou, H.-C. What IS Inorganic Chemistry? *Inorg. Chem.* **2019**, *58*, 9515−9516.

(2) Hoffmann, R.; Schleyer, P. v. R.; Schaefer, H. F., III. Predicting Molecules−More Realism, Please! *Angew. Chem., Int. Ed.* **2008**, *47*, 7164−7167.

(3) Hoffmann, R. The many guises of aromaticity. *Am. Sci.* **2015**, *103*, 18−22.