An Efficient Hierarchical Workflow for Global Minimum Search: From Microsolvated Fluorophores to Bimetallic Mo-Scorpionates

Piotr P. Romańczyk, Wiktor Kasprzyk, Stefan S. Kurek

Biotechnology and Physical Chemistry, Cracow University of Technology, Poland,
email: *piotrom@pk.edu.pl*

Finding global minima and representative conformational ensembles for complex systems with many degrees of freedom remains a tough challenge, often stymied by the cost of molecular dynamics simulations. In this presentation, we outline an efficient, hierarchical computational workflow designed to systematically map conformational landscapes to bypass the expensive molecular dynamics. This computational protocol begins with an initial global minimum search driven by a semiempirical tight-binding method [1], followed by a dispersion- and counterpoise-corrected DFT [2] two-step re-evaluation, involving single-point calculations, and eventually, full geometry optimizations and frequency analyses using the quasi-RRHO approach to properly treat low-lying vibrational modes. The workflow ultimately yields the simulation of ensemble-averaged TDA-DFT spectra. Crucially, our findings demonstrate that multi-level filtering is indispensable for identifying true global configurations, due to a frequent significant reshuffling in the energetic ranking of conformers.

The versatility of this approach is demonstrated across highly diverse systems. For citrazinic acid (CZA), the workflow captures how microsolvation redefines tautomeric stability, successfully reproducing the experimental spectra and the pK_a value. Relying solely on continuum solvation models or arbitrarily chosen local minima of microsolvated structures frequently leads to erroneous thermodynamic conclusions. Furthermore, a rigorous treatment of structural landscapes and optical responses is critical for unraveling the role played by fluorophores, such as CZA, HPPT (4-hydroxy-1*H*-pyrrolo[3,4-*c*]pyridine-1,3,6(2*H*,5*H*)-trione) and its derivatives, in the photoluminescence of citric acid-based carbon dots [3,4]. Moreover, explicit water molecules efficiently lower the proton-transfer barriers governing the formation of HPPT-like molecules and their hydrolysis. Finally, for molecular fluorophores linked by flexible saturated alkylene bridges as well as bimetallic Mo-scorpionate (tris(pyrazol-1-yl)borate) complexes [5], the protocol demonstrates π···π interactions between the fluorophores or bulky scorpionate ligands, which occur even in systems with short bridges. Further applications of the established workflow to even more demanding open-shell species, including mixed-valence systems and the role of ion-pair formation with supporting electrolyte ions, are currently underway. Ultimately, we will also discuss specific scenarios where molecular dynamics remain irreplaceable, highlighting open challenges and opportunities for future collaborative work.

REFERENCES

[1] B. de Souza, GOAT: A Global Optimization Algorithm for Molecules and Atomic Clusters, *Angew. Chem. Int. Ed.* **2025**, *64*, e202500393, DOI: 10.1002/anie.202500393.

[2] S. Grimme, A. Hansen, S. Ehlert and J.-M. Mewes, r^{2}SCAN-3c: A "Swiss army knife" composite electronic-structure method, *J. Chem. Phys.*, 2021, **154**, 064103, DOI: 10.1063/5.0040021.

[3] W. Kasprzyk, T. Świergosz, P. P. Romańczyk, J. Feldmann and J. K. Stolarczyk, The role of molecular fluorophores in the photoluminescence of carbon dots derived from citric acid: current state-of-the-art and future perspectives, *Nanoscale*, 2022, **14**, 14368–14384, DOI: 10.1039/D2NR03176K.

[4] W. Kasprzyk, P. P. Romańczyk, S. S. Kurek and T. Świergosz, A switchable green emitting dye and its phenomenal properties: implications for the photoluminescence features of carbon dots, *Nanoscale*, 2024, **16**, 17079–17089, DOI: 10.1039/D4NR02517B.

[5] P. P. Romańczyk and S. S. Kurek, Molecular electrochemistry of coordination compounds—a correlation between quantum chemical calculations and experiment in: E. Broclawik, T. Borowski, M. Radoń (Eds.), *Transition Metals in Coordination Environments, Challenges and Advances in Computational Chemistry and Physics*, vol. 29, Springer, Cham (2019), pp. 409–438, DOI: 10.1007/978-3-030-11714-6_13.