Poster

Symmetry-constrained Monte Carlo for crystal structure prediction

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Crystal structure prediction (CSP) remains a pivotal challenge in the field of material science [1-3], with strong implications that span diverse domains from pharmaceuticals to advanced materials engineering. Despite the strong efforts and the significant progress achieved in the last years, the accurate prediction of the most thermodynamically stable polymorphs remains and intricate endeavour, especially for flexible organic molecules with numerous degrees-of-freedom [4-5]. Many software solutions employ brute force algorithms, to generate putative structures, ranked based on specific criteria such as packing efficiency, cohesive energy and others.

To address this challenge, we presented a novel multi-step method that take into consideration both the thermodynamics and the dynamical stability of crystals [6]. First, we use a symmetry-constrained Monte Carlo (SC-MC) algorithm to produce a set of thermodynamically plausible crystalline structures. This method shares the same philosophy of the Milano Chemistry Molecular Simulation (MiCMoS) platform [7] and, in addition, exploit the presence of the lattice symmetries. In this way, only the symmetry-independent part of the system is refined, with a significant saving in terms of computational time. Subsequently, the selected plausible structures undergo short classical molecular dynamics to assess their mechanical stability. Finally, the remaining stables structures are treated using solid-state Quantum Mechanical software, e.g. CRYSTAL [8], to extract more reliable cohesive energies.

Our approach is validated through comprehensive testing on various organic molecules intended for pharmaceutical and biological applications. A primary emphasis is placed on the investigation of active pharmaceutical ingredients and their potential phase transitions under diverse experimental conditions, as well as the formation of co-crystals. The obtained results demonstrate a sufficient level of accuracy in the crystal prediction when compared against existing experimental structures, although challenges persist in complex cases. A comparison with the outcomes of other CSP software will be taken into consideration. To further improve the accuracy of the proposed method, future works may focus on developing a new *ad hoc* force field tailored for the purpose.

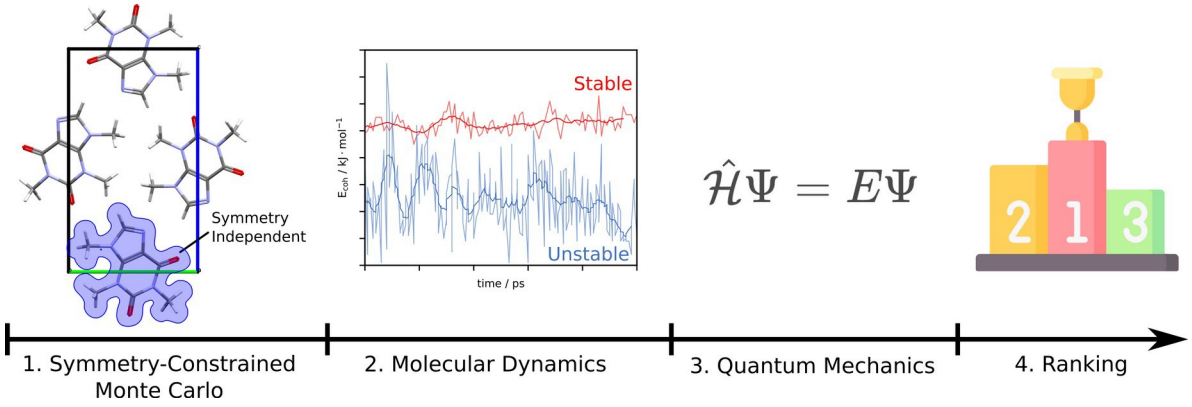

Figure 1. Multi-step crystal structure prediction algorithm.

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