

Benchmarking Free-Energy Corrections in Molecular Crystals from Density-Functional Theory

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Molecular crystal-structure prediction (CSP) concerns itself with predicting the isolable polymorph(s) of a given molecular crystal, which are generally assumed to be the most stable. Routine CSP studies using density-functional theory (DFT) calculations do not consider the effects of vibrations (phonons) within the crystal lattice due to the associated computational expense. However, phonons give rise to the zero-point vibrational energy, as well as thermal contributions to the free energy. While ignoring these thermal effects is often a sound approximation, studies using classical force-field methods have shown that free-energy contributions reorder 10-20% of known polymorph pairs [1,2]. Further work is therefore necessary to accurately account for thermal free-energy contributions within a CSP context and ensure reliable stability ordering of the crystal polymorphs.

Our roadmap for this project first consists of using plane-wave DFT to compute highly accurate free-energy differences between polymorph pairs comprising a small subset of the Nyman-Day polymorph library [1]. Once our benchmark data is established, we seek to test various computationally expedient models, ranging from semi-empirical approaches to force fields. The goal is to identify a low-cost methodology that is sufficiently accurate and can be routinely applied to CSP studies of organic molecules.

[1] J. Nyman and G. M. Day, *CrystEngComm*, **17**, 5154-5165 (2015).

[2] J. Nyman and G. M. Day, *Phys. Chem. Chem. Phys.*, **18**, 31132-31143 (2016).