CRYSTAL STRUCTURE PREDICTION AS A TOOL

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With improving hardware and software performance, poor usability has recently become one of the main obstacles to a more widespread use of Crystal Structure Prediction (CSP). The problem has now been overcome in the GRACE program by the implementation of fully automated data flow processes that remove the burden of scores of expert decisions from the user. The approach builds on methods that were already key to success in the 2010 blind test on crystal structure prediction, including dispersion-corrected Density Functional Theory (DFT-D) calculations, the generation of tailor-made force fields from ab-initio reference data, a Monte-Carlo parallel tempering crystal structure generation engine and a DFT-d reranking procedure exploiting statistical correlations.

Analyzing the results of CSP studies performed with the new Force Field Factory and CSP Factory modules throughout 18 months, the current performance of CSP is critically assessed and further method development needs are pinpointed. Studied compounds include 20 small molecules with competing hydrogen-bond motifs, 4 mono-hydrates of non-ionic molecules and the hydrates and chloride salts of several amino acids. The ability to handle flexible pharmaceutical molecules is demonstrated by a validation study on aripiprazole with one and two molecules per asymmetric unit. Salient features of the energy landscapes of other pharmaceutical molecules in the size range of 40 to 70 atoms are discussed.

As a by-product, CSP studies generate tailor-made force fields that may be used with third-party software applications for the calculation of materials properties. The accuracy of these force fields is automatically determined by comparison with calculated DFT-D lattice energies. Accuracy statistics are presented for the compounds listed in the previous paragraph.

Early results are presented on the crystal structure solution of individual nanocrystals from electron diffraction data by means of crystal structure prediction with rapidly generated tailor-made force fields.