

Poster Presentation

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Have you missed a form—from polymorph prediction to risk-assessment

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As the Ritonavir case demonstrated, the correlation between the structures of solid API phases in pharmaceutical formulations and their lattice free energies and therefore solubilities is of crucial importance in drug delivery. In parallel with the obvious experimental approach to polymorph screening and structure determination, we have carried out commercial computational polymorph screens for the pharmaceutical industry for more than a decade now. This experience puts us in a unique position to report on not just a case study, but on what the statistics over 25 such polymorph screens can tell us.

The final products in the form of energy landscapes can be analyzed, as can the prediction process itself. Especially the question how the predictions complemented the experimental data is worth exploring. Statistics can be collated regarding e.g. how often the experimental structure is predicted as rank number 1, or, conversely, the largest energy gap between an experimental structure and rank number 1 can be determined. How often do we conclude that the thermodynamically relevant form has probably already been observed? How often do we conclude that a significantly more stable (and therefore less soluble) form has probably been missed? How often did the predictions guide the discovery of a new form? The CPU resources and the wall-clock time required for a full study can be quantified. We will also try to answer the most important question of all: did the calculations solve the customer's problem?

These results have never been published and the presentation will provide a unique view of commercial crystal structure prediction studies.

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