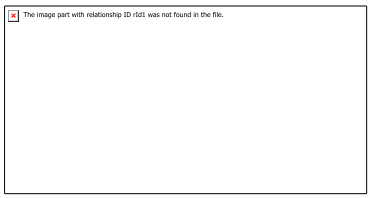

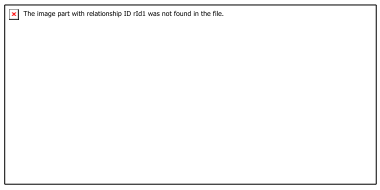

NCCR MARVEL Distinguished Lecture

Can we predict how pharmaceuticals will crystallize?

Prof. Sally Price
University College London, UK

Thursday 6 September 2018, 16:15, Room MXF1

Abstract: Crystal Structure Prediction (CSP) methods were developed on the assumption that an organic molecule would crystallize in its most stable crystal structure. Even implementing this approach is a challenge to computational chemistry methods,[1] as shown by the Cambridge Crystallographic Data Centre's blind tests.[2] Polymorphism adds additional challenges, as this is usually a kinetic phenomenon with metastable polymorphs being unable to transform to the more stable structure in the solid state. CSP is being developed as an aid to polymorph screening [3] through calculating the crystal energy landscape, the set of crystal structures that are thermodynamically plausible as polymorphs. However, the crystal energy landscape usually includes more crystal structures than known polymorphs, raising the question as to why more polymorphs are not found.[4] This can be due to the approximations in the calculations, particularly the use of lattice energies rather than free energies but also the lack of consideration of kinetics. Sometimes the prediction of a putative polymorph can allow the design of a specific experiment to find it, for example by using an isomorphous crystal of another molecule as a template.[5] More commonly, the crystal energy landscape can rationalize observations of complex crystallization behavior, such as the occurrence of disorder [6].Whilst the crystallization behavior of some molecules is easily predicted, many pharmaceuticals and chiral compounds really challenge our understanding of crystallization and ability to model thermodynamics[7].

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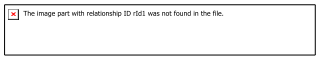

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5. Srirambhatla, V. K.; Guo, R.; Price, S. L.; Florence, A. J., Isomorphous template induced crystallisation: a robust method for the targeted crystallisation of computationally predicted metastable polymorphs. *Chemical Communications* **2016,** *52*, 7384-7386.

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7. Buchholz, H. K.; Hylton, R. K.; Brandenburg, J. G.; Seidel-Morgenstern, A.; Lorenz, H.; Stein, M.; Price, S. L., Thermochemistry of Racemic and Enantiopure Organic Crystals for Predicting Enantiomer Separation. *Crystal Growth & Design* **2017,** *17* (9), 4676-4686.