Do metastable polymorphs always grow faster? Challenges of measuring and comparing crystal growth rates of tolfenamic acid polymorphs

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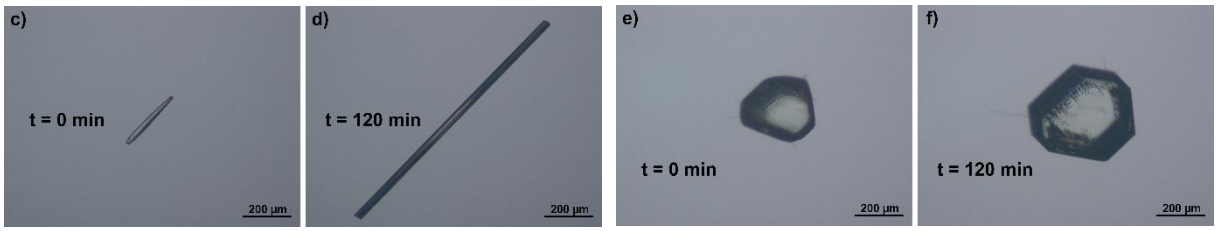
The phenomenon of molecular crystal polymorphism is of central importance for industries that rely on crystallization for manufacturing their products [1]. Modern strategies for the control of polymorphism take advantage of increasingly accurate Crystal Structure Prediction (CSP) methods to identify *a priori* all thermodynamically plausible polymorphs of a given compound.

The computational study and prediction of the kinetics of crystallization impacting polymorphism have received considerably less attention compared to CSP. Nevertheless, the ability to predict crystal growth rates from solution could assist in identifying experimental domains for the selective crystallization of target polymorphs, thus reducing the effort required for experimental screening [2, 3].

Unfortunately, available experimental data for the nucleation and growth kinetics of polymorphs are limited to a handful of systems. If a predictive link between CSP landscapes and crystallization conditions is to be established, the collection, analysis, and dissemination of good quality experimental data on the kinetics of nucleation and growth of large numbers of polymorphic systems becomes necessary.

In this contribution, we report on the crystal growth rates of three polymorphs of the model compound tolfenamic acid (TFA) from isopropanol solutions. After discussing the complications of comparing data measured on single crystals – especially for polymorphs with very different crystal habits – we show how kinetic data can assist in rationalizing the *unexpected* crystallization of the metastable polymorph TFA-IX [4].



References

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