[MS39-02] GuideX: a Systematic Approach to Managing and Archiving Crystallization Data

Trixie Wagner, [a]Bernhard Rode, [a]Claudia Meyer, [a]Ekkehard Görlach, [a]Ina Dix, [a]Jayesh Patel,[a] Philippe Piechon,

[a]*Novartis Institutes for BioMedical Research, 4002 Basel, Switzerland*.
E-mail: trixie.wagner@novartis.com

In the pharmaceutical industry the three-dimensional structure of a molecule plays a critical role in drug development and the investigation of structure-activity-relationships (SAR). The classical and still most reliable way to obtain those 3D models is single crystal x-ray structure analysis. The bottleneck of this technique, however, is the necessity to grow single crystals suitable for the analysis. This is especially challenging when only a few milligrams of the compound of interest are available and automation or large scale screens are not possible. Despite many efforts to understand the theory behind crystal growth the method of choice in practice is often enough trial and error mixed with experience and gut feeling. Hence, it is difficult to share any of this knowledge within the broader crystallographic community. [1], [2] The attention the recently published "crystal sponge method" has received, however, emphasizes once again the need for novel, non-conventional approaches.[3] Our own idea to reduce the bottleneck is based on the hypothesis that the crystallization propensity is dominated by the intrinsic properties of the individual compound. It aims at a statistical and systematic analysis of our in-house crystallization records to derive predictive classification tools and maps of crystallization propensity in descriptor space. To be able to extract significant information from our data, however, it was first necessary to develop a highly systematic and ordered procedure for the crystallization process which allows tracking of all activities, parameters and results. This procedure will be presented. The associated data of more than 300 crystallization requests per year (from the experimental parameters to the results of each trial) is stored electronically in a specifically designed Oracle database. The data can be entered on the fly simultaneously to the experimental work at the hood, the visual inspection at the microscope and the crystal quality check on the diffractometer via GuideX, an in-house touch screen application which is directly linked to the above mentioned database. Since we use defined sets of qualifiers to describe all observations from solubility behavior to crystallization results we are also able to derive fingerprints for each compound which might lead to a new kind of classification. First results and findings will be presented and will be the foundation for further systematic investigations. We consider our GuideX "crystallization data management system" the first step on the way to deriving structure based rules which then can guide the crystallization protocol for unknown organic compounds and thereby significantly reduce the time and material spent on this process.

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