

The project goal. Diamond and graphite are both crystal structures of the same element (carbon), but with differently arranged atoms in a crystal. This arrangement alone can significantly influence their properties, so that the first is one of the hardest materials known, while the second is soft and easily breakable. The same can be true for organic molecules, which can also arrange themselves differently in a crystal forming different crystal forms known as polymorphs. When polymorphism concerns drug molecules, it can have a decisive influence on the applicability of such drug, because it can affect its water solubility, stability, hardness, manufacturability and so on. The process of experimental search for polymorphs is lengthy and expensive and one can almost never be sure that each possible experimental conditions were tested. Current computational methods offer a possibility to theoretically predict the formation of polymorphs, but they say nothing on how to realize experimentally such predictions. Our research aim at finding a link between the predicted crystal structures of drug molecules and the best methods for their crystallization.

Description of research. First we plan to look at molecules which are potentially monomorphic, that is they crystallize in only one known polymorphic form. To do that we will use computational crystal structure prediction methods to find molecules for which only one stable crystal structure is predicted. We will also look at molecules, which are experimentally known to form one crystal structure, but computational predictions say that more polymorphs should be accessible. For both sets of molecules we will conduct crystallization experiments at various conditions to potentially find new polymorphs or mark molecules as monomorphic. We also plan to investigate new ways of crystallizing polymorphic forms which are difficult to obtain in a laboratory. Finally we will build a database linking crystal structures of different polymorphs with crystallization conditions.

Reasons for attempting this particular research topic. Crystallization is a very complex process, with many different factors influencing its outcome. In order to be able to understand it, and as a result to predict its outcome and redirect according to our needs, we first have to gain an insight into the factors deciding on its direction. Our research is a road to understand this process and its relationship with the resulting crystal structures.

Substantial results expected. We expect to answer the question whether monomorphic molecules exist and if yes, what is their secret. We also hope to understand why some of the predicted polymorphic forms are so difficult to crystallize and how can we use computational predictions to guide crystallization. The crystallization conditions database will hopefully serve in the future to rationally design crystallization experiments and to gain a deeper understanding of the crystallization process.