Extremely fast development of chemistry in last decades was possible mainly because scientists found out how to establish crystalline and molecular structures of the most important compounds (proteins, pharmaceuticals, food additives, fertilizers etc). This would not be possible without X-ray diffraction and all the models of electron density and theory hidden behind the terms: “X-ray data collections” and “structure refinement”. This also means that the quality of X-ray diffraction measurements and models models of electron density used is of a paramount importance for chemistry, physics and material sciences. Therefore, the question arises - can X-ray data be the source not only of the structural parameters, but also the source of information about the exact thermodynamic properties of the crystal? And can this information be useful for some other scientific and commercial applications? We would like to answer such questions by focusing on polymorphic systems.

Polymorphism is the occurrence of a compound in several crystal forms which may differ in the conformation of the molecules or the packing of molecules in the crystal lattice. Polymorphism is a very important phenomenon because different polymorphs of the same substance exhibit different physicochemical properties (melting point, solubility etc.) and different biological activity which is of crucial importance for the pharmaceutical industry. Unfortunately, it is very difficult to predict which polymorph is more stable at a given temperature, because of differences in free energy of different polymorphic forms are very tiny, and it often happens that a form that is more stable at low temperature becomes less stable at room or elevated temperature. This may lead to unexpected and unwanted phase transitions between polymorphic forms. Thus new chemicals, candidates for drugs, are always carefully tested for polymorphism. However, the Holy Grail still remains a theoretical method that would allow for quick prediction of the relative stability of polymorphic forms - estimation of phase transition temperature for a given polymorphic system requires long free energy calculations and is not quite reliable. To shorten calculations vibrational and configurational entropy contributions are neglected, which may lead to incorrect predictions of stability order for polymorphic systems. This may lead to improper stability order for polymorphs.

The main goal of this project is to solve this problem: to propose new theoretical models which, based on data from single-crystal X-ray measurements, will allow to obtain thermodynamic properties for crystal structures, and thus allow for fast determination of stability of polymorphic forms.

In the future our methods will be used routinely for polymorphic systems stability estimation. Moreover, our new models in future can be used routinely to get more accurate structures of organic, inorganic and macromolecular compounds and crystals.