Advancing quantum crystallography for better insight into structure and properties of crystals

Objective of the project and research to be carried out. This project aims at preparation of new methods of extraction of more accurate and precise structural information (geometrical, electronic and thermal parameters) from single crystal X-ray diffraction (XRD) experiments than this is possible now by using presently available methods of refinement of X-ray data. We want to develop and modify presently used methods of crystal structure refinement, in particular, refinement of single crystal X-ray data using so called Hirshfeld atom approach. Modifications are based on introduction of new aspherical atomic scattering factors which seem to be more effective than those presently used, extension of applicability of so-called Hirshfeld Atom Refinement (HAR) to cover a wider range of crystals including large biological macromolecules (in particular proteins and their complexes). We also propose creation of a databank of aspherical Hirshfeld type like atomic electron density fragments which will enable reconstruction of electron density fragments in proteins and other large molecules (also in small molecules). In general, such databank entries will allow for more reliable refinement of structure and estimation of properties of studied systems.

Proposed research requires development of a new software platform for testing novel approaches for crystal structure refinement (namely application of new partitions of electron density leading to new atomic scattering factors). This would involve basic and flexible refinement program as well as tools for integration of the new developments with mature commonly used crystallographic refinement codes. Availability of this kind of tools is essential for rapid testing of new ideas and methodologies. We also propose verification of the true precision and accuracy of the proposed new methods by statistical analysis of results of multiple measurements and refinements performed for a series of model organic, inorganic and macromolecular crystals of increasing complexity. The series consists of single crystals of a few simple model organic compounds such as, for example, oxalic acid, glycine, carboxylic acid salts and complexes, more complex metalorganic compounds with different metal ions and hydrogen atoms, and others, small and larger proteins such as lysozyme, crambin etc. As HAR seems to work correctly even for small resolution, we also want to test its applicability in high pressure structural studies of model crystals.

Reasons for choosing the research topic. Development of science, and through applicative research, also development of economy and well-being of modern societies is based on scientific information. Most of the accomplishments on the interdisciplinary bio/chem/phys border - also in pharmacy, medicine, materials science, crystal engineering, chemistry, solid state physics – use structural information. Structural information is a knowledge of three dimensional arrangement of atoms in the solid state including knowledge of geometrical parameters such as bond lengths and valence and torsion angles, details of crystal symmetry and thermal motion of atoms. It has been established for more than 1.4 million of organic, inorganic and macromolecular (usually very important biological and biochemical) structures. All this structural information is gathered in structural data banks such as Cambridge Structural Databank (CSD – for organic compounds), Inorganic Crystal Structure Databank (ICSD – for inorganic crystals) and Protein Data Bank (PDB) for structures of macromolecules. Almost all this information was obtained by refinement of different crystal structure models against measured X-ray diffraction data. Ca. 99.7% of all refinements were accomplished by using the most primitive Independent Atom Model which assumes that spherical atoms in the ground state do not interact among themselves and do not exchange electron density. IAM was introduced by more than a century ago. As IAM is based on a very crude and unreal assumptions and approximations (for example not interacting atoms although they form molecules!), structural information obtained by applying IAM is characterized by low accuracy and precision. Only ca. 0.3% of all refinements of all structures were accomplished by using more advanced methods which utilize aspherical scattering factors in the refinement procedures. However, most of such studies requires good scattering of X-rays by single crystals and more complex measurements than the routine ones, which - in general - is not always possible. Within last years, a new crystallographic methods, called Quantum Crystallography, (QC) have appeared on the border between crystallography and quantum chemistry. These methods allow for obtaining more accurate and precise structural and electronic results than using the most routine and common approaches. The most promising QC method is called Hirshfeld Atom Refinement (HAR). HAR utilizes aspherical Hirshfeld atomic scattering factors and supplies far better results of refinement than other methods. Within our project we want to improve HAR through creation and verification of more sophisticated versions of HAR as those presently used thus creating a tool which will be supplying better quality structural information. Additionally we hope that application of a new databank of aspherical Hirshfeld type atomic electron densities in refinement and reconstruction of electron densities of protein structures will also supply high quality structural information which could be used in studies of mechanisms of different illnesses as well as in drug design and other applications in all fields of science.