More accurate models of the electrostatic potential of biological macromolecules and organic crystals necessary for proper interpretation of data from cryo-electron microscopy and from electron diffraction – feasibility study

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Although cryo-electron microscopy and electron diffraction methods have made enormous progress in the last years and an increasing number of atomic and near atomic resolution structures are becoming available, interpretation of collected data is continued to relay on a very approximate scattering model. The model is based on spherical independent atoms, ignoring the charge redistribution due to chemical bonding. This approximation leads to unnecessary loss of information which is avoidable. Time has come to change it.

We propose to base interpretation of data from cryo-electron microscopy and from electron diffraction methods on more realistic electron scattering models.

We will develop new models from detailed electron densities of molecules and crystals. The models will considerably deviate from the conventional spherical independent atom model. Thanks to our new models more information will be extracted from electron scattering experiments on biological macromolecules and organic crystals, and improved quality of geometric data and quantitative estimates of molecular electrostatic potentials will become available.

Accurate structural descriptions of macromolecules are of crucial importance to understand the processes of life at the level of single molecules and atoms. They found applications in structure-function correlation studies, rational drug design, elucidation of the catalytic mechanism of enzymes and others. In the case of small molecules, determination of their atomic structure in crystalline state allows to understand their physicochemical properties and design new materials. Structural information for (pseudo)polymorphs of active pharmaceutical ingredients, for example, is essential in drug discovery and development process. Similarly, in pigments industry, determination of crystal structure of organic pigments is necessary to understand the influence of crystal packing on color, thermal stability, light fastness and many other properties.

We expect that after using the models proposed by us in the analysis of electron scattering / diffraction data, cryoEM and ED techniques will achieve highest precision and accuracy of structural models Thus introduction of our models will significantly affect structural biology, pharmacology and nanotechnology.