

Experimental charge densities of organic nanocrystals from 3D electron diffraction

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Three-dimensional electron diffraction (3D ED) has emerged as a groundbreaking technique in structural science, enabling crystallographic analysis of nanocrystals beyond the reach of traditional X-ray diffraction (XRD) [1]. In contrast to XRD, 3D ED uniquely addresses the challenges posed by micro- and nanocrystals by exploiting the strong electron–matter interaction to precisely localize atoms in the crystals, particularly hydrogen, and to capture subtle features of charge density. In this study, we report the first comprehensive experimental analysis of the charge density of organic crystals—specifically L-alanine and urea—using high-resolution 3D ED data collected with a cryogenic transmission electron microscope.

By incorporating dynamical scattering effects into a full multipole model refinement strategy based on the Hansen-Coppens formalism[2], this method goes beyond the atomic model refinement using the Transferable Aspherical Atom Model (TAAM) approach[3,4] and enables quantitative modeling of experimental electronic charge density distributions. The multipole model derived from 3D ED data was validated by comparison with theoretical models refined from 3D ED data simulated using periodic density functional theory (DFT) as well as with high-resolution XRD data. Good agreement was found for key parameters, including deformation electron density, total electrostatic potential, and topological features of electron density according to Bader's Quantum Theory of Atoms in Molecules (QTAIM).

These findings underscore the transformative potential of 3D ED as a robust tool for quantum crystallography. Its ability to overcome the limitations of conventional XRD—particularly in precisely refining hydrogen positions and probing nanocrystalline materials—represents significant progress in the field, opening new avenues for the detailed exploration of chemical bonds and intermolecular interactions in organic systems.

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This research was funded through the OPUS LAP program by the National Science Centre, Poland (grant No. 2020/39/I/ST4/02904 awarded to PMD) and by the Czech Science Foundation (grant No 21-44862L awarded to LP). Acknowledgment is also extended to the Polish high-performance computing infrastructure PLGrid (HPC Centers: ACK Cyfronet AGH, WCSS) for providing computer facilities and support within computational grant no. PLG/2024/017098.