Electron Density Modelling Group

HEAD:

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GROUP MEMBERS:

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RESEARCH PROFILE:

The research group works on developing new methods of electron density modelling for X-ray and electron crystallography, chemistry and structural biology.

Our primary goal is to create methods allowing to obtain more information from routinely collected X-ray diffraction data. On the one hand, these methods are intended to improve the quality of geometric data obtained from such measurements, and on the other hand, they provide access to a new type of information, i.e. to electron density and energy interactions. Our intention is that our methods of electron density modelling and intermolecular energy estimation should fill space between classical mechanics methods (force fields) and quantum mechanics methods: to be more accurate than the first, but definitely faster than the latter. We use the new methods we created (both in experiment and in theory) to understand the role of intermolecular interactions in complexes of proteins and nucleic acids and in crystals of organic compounds. Our main focus is the importance of electrostatic interactions. We are interested in the relationship between intermolecular interactions and crystals architecture, macromolecular structure or molecular recognition in the context of drug design. As part of our research, we obtain our own crystals, determine their structure by X-ray and, as far as possible, obtain experimental electron density by means of high resolution X-ray diffraction measurements on a monocrystal. In everyday practice, we combine the experiment (X-ray and monocrystalline neutrons, small molecule crystallization, DSC / TGA) with theory (classical force fields, optimization of isolated molecular geometry and periodic systems with DFT methods, topology of electron density, interaction energy with DFT- SAPT, etc.).

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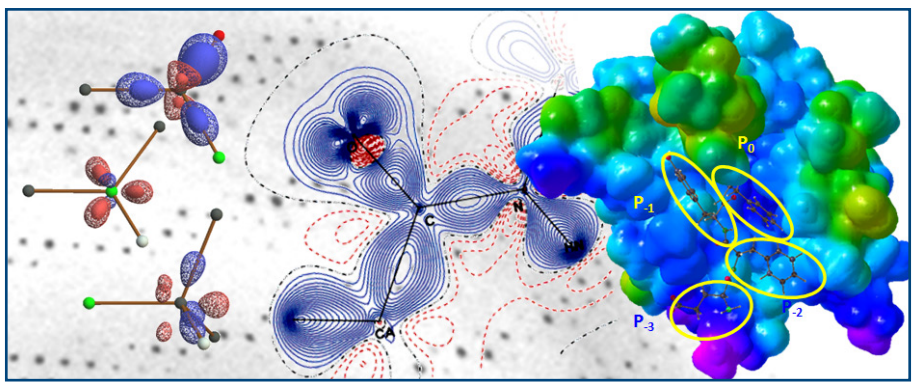
CURRENT RESEARCH ACTIVITIES:

At present, our research is mainly based on the developed in our group pseudoatom databank (University at Buffalo Pseudoatom Databank, UBDB), which enables rapid reconstruction of the electron density of organic molecules and biomacromolecules. We also work on more simplified models of electron density in the context of an even faster estimation of energy interactions and applications that go beyond crystallography. Very recently, we have moved our attention towards application of our tools to electron diffraction and single-particle cryoEM studies.



The biological systems we are currently analyzing are HIV protease complexes with small molecular ligands and IFIT protein complexes from RNA (in collaboration with the Structural Biology Group of dr Górna), starting with publicly available structures. In the case of organic crystals we work on nucleobases and their derivatives.

SELECTED PUBLICATIONS:

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2. B. Gruza, M.L. Chodkiewicz, J. Krzeszczakowska, P.M. Dominiak, Refinement of organic crystal structures with multipolar electron scattering factors, Acta Cryst A. 76 (2020) 92–109.
3. P. Kumar, B. Gruza, S.A. Bojarowski, P.M. Dominiak, Extension of the transferable aspherical pseudoatom data bank for the comparison of molecular electrostatic potentials in structure–activity studies, Acta Cryst A. 75 (2019) 398–408.
4. M.L. Chodkiewicz, S. Migacz, W. Rudnicki, A. Makal, J.A. Kalinowski, N.W. Moriarty, R.W. Grosse-Kunstleve, P.V. Afonine, P.D. Adams, P.M. Dominiak, DiSCaMB: a software library for aspherical atom model X-ray scattering factor calculations with CPUs and GPUs, J. Appl. Cryst. 51 (2018) 193-199.
5. S.A. Bojarowski, P. Kumar, P.M. Dominiak, A Universal and Straightforward Approach to Include Penetration Effects in Electrostatic Interaction Energy Estimation, ChemPhysChem. 17 (2016) 2455-2460.
6. M. Malińska, K.N. Jarzembska, A.M. Goral, A. Kutner, K. Woźniak, P.M. Dominiak, Sunitinib: from charge-density studies to interaction with proteins, Acta Crystallogr. D. 70 (2014) 1257-1270.
7. P. Kumar, S.A. Bojarowski, K.N. Jarzembska, S. Domagała, K. Vanommeslaeghe, A.D.Jr. MacKerell, P.M. Dominiak, A Comparative Study of Transferable Aspherical Pseudoatom Databank and Classical Force Fields for Predicting Electrostatic Interactions in Molecular Dimers, J. Chem. Theory Comput. 10 (2014) 1652-1664.
8. K.N. Jarzembska, M. Kubsik, R. Kamiński, K. Woźniak, P.M. Dominiak, From a Single Molecule to Molecular Crystal Architectures: Structural and Energetic Studies of Selected Uracil Derivatives, Cryst. Growth & Design. 12 (2012) 2508-2524.
9. J.M. Bąk, S. Domagała, C. Hübschle, C. Jelsch, B. Dittrich, P.M. Dominiak, Verification of structural and electrostatic properties obtained by the use of different pseudoatom databases, Acta Crystallogr. A. 67 (2011) 141-153.