Charge density study on simple inorganics from synchrotron X-ray powder diffraction to reveal weak interaction of materials.

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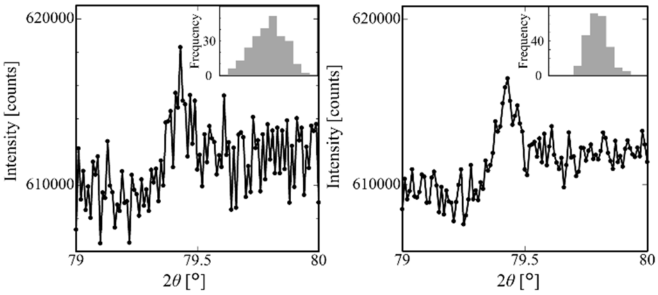
Keywords: charge density, weak interaction, SR powder diffraction

Charge density study of a simple inorganic solid is normally more difficult than that of molecular system. Since, a contribution in diffraction data of bonding electron is lower than that of organic solid. In addition, the function of the inorganic solid is often determined by vary small amounts of aspherical electrons such as metallic bond in metals. To reveal feature of such small amounts of electrons, high quality data are required.

During past decade, the high quality charge densities of materials have been revealed from the powder diffraction at SPring-8 [1] and Petra-III [2]. The diffractometer [2] and the measurement techniques [1] have been developed for accurate charge density studies. Currently, one of the target of the powder charge density study is to reveal weak interactions of inorganic materials.

We have determined a weak metal bonding in aluminium from powder diffraction at SPring-8 [3]. We have successfully visualized an accumulation of electrons at tetrahedral site which is consistent with the result of quantitatively convergent electron diffraction [3]. We have also found atomic orbital like electrons in aluminium. Currently we are analysing this result using a theoretical calculation.

Recently, we have measured accurate multi-temperature powder diffraction data of diamond with seven digit linearity through the data correction of Imaging Plate detector (Figure 1). The charge density study of diamond at 800K have been carried out using the data with $\sin\theta/\lambda > 2.2$ Å^{-1} reciprocal resolution [4].



(*a*) (*b*)

Figure 1. Powder profiles of the 8 8 8 Bragg reflections of diamond for the (*a*) uncorrected and (*b*) corrected data at 800K.

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Discrepancies in refined charge density models of aceclofenac and comparison with the sample standard deviation

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Keywords: charge density, errors.

Aceclofenac belongs to the class of non-steroidal anti-inflammatory drugs that are the most widely used medications to mitigate pain and inflammation. An experimental charge density analysis of the drug aceclofenac has been accomplished using Hansen & Coppens multipolar atom model and MoPro software[1]. Diffraction data sets were measured on two crystals on a Bruker Photon II detector up to resolution 0.35 Angstrom. The merging of the two data sets resulted in slightly improved crystallographic *R*-factors.

The charge density was refined against the data sets #1, #2, and the merged one. The two chlorine and two oxygen atoms were refined using anharmonic thermal motion parameters. Several properties derived from the derived charge densities were computed. The statistical errors of the properties were estimated with the sample standard deviation methodology[2]. The results were compared to the discrepancies between the two models. The residuals resulting from the two data sets show also some degree of correlation. The effect of statistical, systematic and model errors will be discussed.

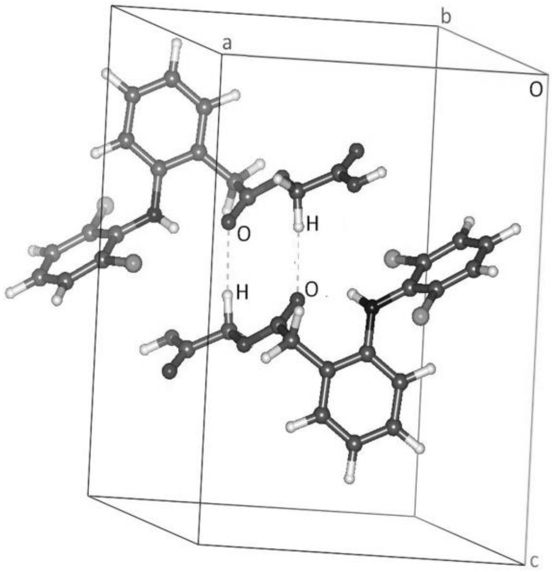

Figure 1:
Crystal packing of aceclofenac

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Evaluation of residual bond density in molecules using simplified virtual scattering centers

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Keywords: bond density, virtual scattering center, residual density.

The Independent Atom Model (IAM) provides a good estimate for the most of routine crystallographic research. A charge density approach, which also describes bonding electrons, requires very high quality data in order to obtain meaningful results. Here we address a 'gray area' of good quality datasets with 0.5-0.8 Å resolution, which show visible deviation from IAM but are not satisfactory for experimental charge density calculations. The suggested methodology follows the well-known virtual atom method (see [1-3] and numerous references therein; historically the first one probably was [1]). Virtual scattering centers (VSC) are placed at fixed calculated positions between C, N, and O atoms with 'occupancies' being different for single, double, aromatic, and triple bonds. Scattering is approximated by a single Gaussian which can be justified by a small value of correction. VSCs are treated as isotropic: multiplication of scattering Gaussian by Debye-Waller factor yields another single Gaussian function to describe both effects (no deconvolution of vibrations and charge density). Usual IAM software was employed. The number of introduced parameters can be as low as one (for overall occupancy of the VSC part of the structure).

Introduction of VSCs makes the effect similar to the scattering of one hydrogen atom per 4-5 C-C bonds, which is substantial enough to justify the effort. Alternatively, each bond can be treated separately (number of additional parameters is roughly equal to the number of bonds). This can lead to further improvement. An attempt was made to handle S-C, S-O, and C-H bonds as well as lone pairs in the same fashion. A number of structures of various organic and element-organic molecules were tested. When it was possible, charge density calculations (MoPro) and/or HARt calculations [4] were performed using the same experimental data. Visible improvement of fitting characteristics was achieved, especially for molecules with aromatic fragments. After removing most of residual bond density from the Fourier difference map, other sources of deviation such as disorder and experimental and data processing limitations can be addressed. Applicability of this algorithm is limited by Coppens's suitability factor S values: compounds with $S < 0.3$ show no or very little improvement. The same procedure was additionally tested at high quality 'benchmark' data sets, for which charge density distributions were experimentally obtained [4,5]. Similar behavior as with 'routine quality' examples was achieved.

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Multi-center interactions in cage compounds by electron-localizability approach

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Keywords: electron localizability, intermetallic compound.

From the application point of view, the intermetallic cage compounds – in particular clathrates - attracted the attention of material's developers during the past decades mainly due to their promising thermoelectric activity. The ELI/ED approach allows differentiation of covalent and ionic contributions to the atomic interactions. With the new tools the formation of the lone pairs around the defects in the covalently bonded framework can be revealed [1], the polar covalent Ba-transition metal interactions were detected in intermetallic clathrates [2], being obviously responsible for unusual thermal transport in these materials [3]. From the point of view of composition, vacancy formation is energetically not favorable in Si clathrates, neither for K nor for Ba guest atoms. Conversely, two vacancies per unit cell may be formed in Ge clathrates fully filled with K, and three vacancies in the case of Ba. The observed electron transfer processes are quantitatively and qualitatively different in Si and Ge. The stoichiometry, thermodynamic stability, and electronic structure of these materials are determined rather by microscopic mechanism. This mechanism can be influential also in other materials with cage structures, e.g., skutterudites or borocarbides [4]. New aspects of the guest-host interactions can be revealed by the pELI-D technique [5] revealing new factors stabilizing the formation of cage structures.

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Local electric fields in supramolecular systems: Measurement and implications in chemistry

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Keywords: charge density, electric field, supramolecular chemistry.

One of the most underexplored features of intermolecular noncovalent interactions is the electric field exerted by molecules on their nearest neighbours. Recent studies have suggested that these electric fields can have significant ramifications in enzyme catalysis as well as in the structure and function of proteins. Hence, a quantitative understanding of the local electric fields in supramolecular systems can be of fundamental importance in chemistry. Recently, vibrational Stark effect (VSE) spectroscopy has been employed to measure local electric fields in supramolecular systems such as enzyme sites as well as solvent systems [1,2]. Although Stark spectroscopy gives us the magnitude of the average field, the dynamic nature of these supramolecular systems as well as the inherent limitations of the method of measurement makes it difficult to obtain a clear directional information of the electric field and its variations around inter and intra-molecular space. In this context, we recently showed that crystalline supramolecular host-guest complexes can be ideal systems to accurately study local electric fields and their directional features –from their accurate experimental charge density distribution. In the example of urea: 18-crown-6 crystalline complex, we found that these local field magnitudes can be as high as 19 GV/m [3]. In addition to these results, I will present the insights from the charge density analyses of a series of crystalline host-guest systems using combined X-ray-neutron diffraction where we have not only investigated the local electric fields, but also their effect on intramolecular bonds – manifested as vibrational frequency shifts – an effect we term as "supramolecular Stark effect" [4].

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Rational design of multicomponent functional materials using a combined statistical and quantum crystallography approach

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Keywords: multicomponent optical materials, crystal engineering, quantum crystallography

The rational design of tailor-made materials, with fine-tuned predictable properties, is a fundamental objective of modern crystal engineering. Many of the currently reported crystal structure designs are based on trial and error methods, especially when dealing with the complicated case of multicomponent systems. This problem can be tackled by a combination of statistical and quantum crystallography tools, both used for the understanding and predicting intermolecular interactions in the solid state (Figure 1).

In this work we will show how to obtain efficient functional materials by cocrystallisation of two components: a target molecule with suitable electronic properties and a co-former ensuring the proper orientation of the building blocks in a crystal structure with sufficient optical anisotropy. Materials obtained in this way can show a variety of enhanced optical properties such as second harmonic generation, fluorescence, optical activity, chromic properties, large linear birefringence and also pyro- and piezoelectricity.[5],[6] By a careful selection of the building blocks and guided interactions we can not only improve the overall performance of the material but also ensure other conditions are met e.g. transparency in the near UV and vis region, optical and mechanical stability and feasibility of obtaining large sing crystals. Those are particularly important when designing optical materials.

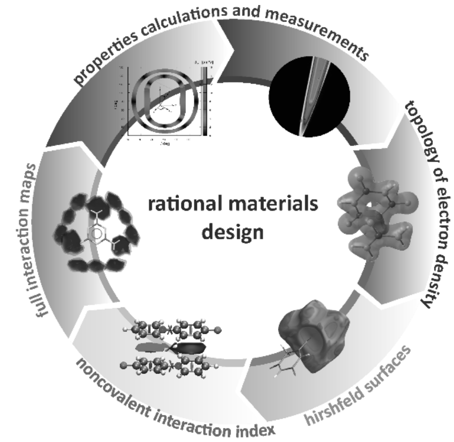

Figure 1: Tools and methods [1-4] necessary for the rational design of functional materials, complemented by properties calculations and experimental measurements.

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Catalytic Functionalization of Aromatic Heterocycles by First Row Transition Metal-Mediated Carbene Transfer Reactions

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Keywords: Nickel-phosphene complex, Homogeneous catalysis, Chemodivergence, C-H functionalization, Cyclopropanation

A robust, air stable first-row transition metal complex [M(L)n(L')] (L, L' = ligands) mediates the transfer of functionalized carbene moiety from the precusor diazo-compound to heterocyclic compounds resulting in either C-H functionalization or cyclopropanation with very good regio- and stereoselectivity in moderate to high yields. The N-protected Indoles are found to be the better substrates for C-H functionalization at C-3 position. C-2 functionalized products are obtained with high yields when the C-3 position is blocked. Substrates with electron withdrawing moiety, e.g., -Boc, -Ac or –Piv on the nitrogen atom are found to produce the corresponding cyclopropanated derivatives. The present synthetic route shows that the much explored and expensive heavier transition metal complexes can be replaced by this less expensive first-row transition metal complex.

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Conformation analysis and tautomeric forms of supramolecular synthons: a charge density viewpoint

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Keywords: supramolecular synthons, charge density, conformational analysis, tautomeric forms.

The development of crystal engineering as a part of supramolecular chemistry was essentially accompanied by generalization of certain terms and approaches from "traditional" chemistry. One of the most well-known examples of such adoption is the concept of a supramolecular synthon, introduced by G. R. Desiraju. The use of supramolecular synthons significantly simplifies the analysis of crystal packing and the construction of pre-defined packing patterns. Due to relatively low energies of the most of intermolecular interactions, the definition of a synthon usually includes only the connectivity, while geometric parameters are not taken into account.

In this work we attempt to use another two concepts from the traditional chemistry, namely "a conformation" and "a tautomeric form" and to apply them to supramolecular synthons. Such an adoption is demonstrated for a set of heterocyclic compounds, including derivatives of 8-hydroxyquinoline (8HQ), pyridine-2-one (P2O) and their co-crystals and salts. Total energy and charge density distribution are compared for different conformations of 0D (dimers) and 1D (chains) synthons and their tautomeric forms. For different conformations of 8HQ dimers it is shown that the connectivity in the synthon is defined by H-bonds, but the observed conformations additionally stabilized by secondary non-specific interactions. Tautomeric forms of supramolecular synthons can be obtained by variation of substituents that do not interact directly with atoms involved in the synthon formation. For example, the presence of an acceptor nitro groups leads to the stabilization of zwitterionic form of 8HQ in crystal, but the intermolecular connectivity remains unchanged in its dimeric (0D) synthon. The dinitro derivative of P2O forms a salt with 8HQ, while for mononitro derivative a co-crystal is observed; in both cases the geometry of the 1D synthon, an infinite H-bonded chain, remains almost the same, as well as the charge density distribution distant from the transferred H-atom.

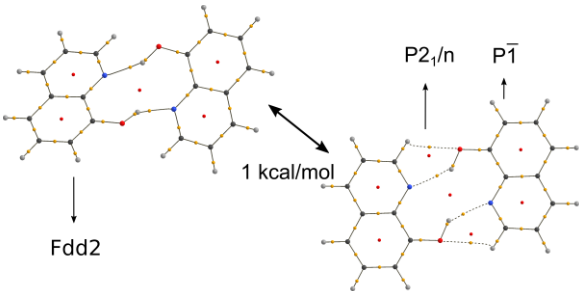

Figure 1: Two conformations of the dimer found in polymorphic forms of 8-hydroxyquinoline

Our results shows that the above concepts can be successfully applied for description of supramolecular synthons and the crystal packing in general.

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The many flavours of halogen bonds

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Keywords: halogen bonds, σ hole interactions, electron density, bond critical points.

The electron density in halogen bonds [1] between heavy halogens, in particular iodine, and small electronegative nucleophiles such as nitrogen and oxygen does not simply increase for shorter contact distances. Examples for three different cases have been observed and will be discussed in detail: a) Very short halogen bonds between electron rich nucleophiles and heavy halogen atoms resemble 3-center-4-electron bonds. The discrete trimolecular aggregate **1** (Fig. 1) represents an example for this case [2]. b) For a narrow intermediate range of halogen bonds, the asymmetric electronic situation for the heavy halogen with a pronounced σ hole leads to rather low electron density in the (3, -1) critical point of the halogen bond. This situation is encountered in the halogen-bonded chain polymer **2** [3]. c) For longer and presumably weaker contacts, the electron density in the halogen bond critical point is only to a minor extent reduced by the presence of the σ hole and hence may be higher than in the aforementioned case. Within this range of longer halogen bonds, the electron density in the bond critical point decreases with increasing distance [4-6]. With respect to the many structurally characterized TFDIB cocrystals, additional arguments for our classification come from C–I bond distances and red shifts in the C–I Raman resonances for **1** and **2**.

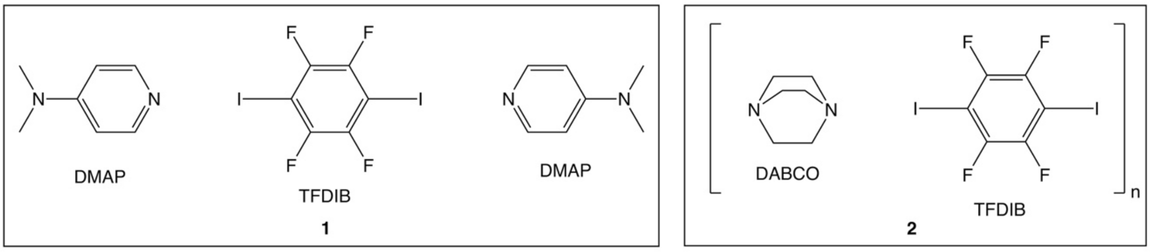

Figure 1: Trimolecular aggregate in **1** and halogen-bonded chain polymer **2**.

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NCI-ELMO: A new method to extract non-covalent interactions in systems of biological interest

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Keywords: Non-covalent interactions, NCI method, ELMO-libraries, biological macromolecules.

Non-covalent interactions play a fundamental role for the three-dimensional structure of macromolecules. They determine secondary, tertiary and quaternary structures of proteins, structure of DNA and are responsible for molecular recognition phenomena. Therefore, a complete and accurate description of non-covalent interaction networks is essential for the understanding of the functions of a biological system.

As is well known, the Non-Covalent Interactions (NCI) method [1,2] is a technique based on the analysis of the electron density and of its reduced gradient for the detection of non-covalent interactions in small and medium-size molecules, for which electron densities can be easily obtained through traditional quantum chemical computations. Unfortunately, since these calculations are unfeasible or impractical for large biomolecules, until now it has been necessary to exploit the promolecular density approximation for the NCI analysis of larger systems. Nevertheless, the promolecular approach describes each electron density as a sum of independent and spherical atomic densities, which is clearly a too drastic simplification.

To overcome the limitations of the previous approximation, we have coupled the NCI method with the recently constructed libraries of Extremely Localized Molecular Orbitals (ELMOs) [3-5], giving rise to the new HAR-ELMO technique. ELMOs are orbitals strictly localized on small molecular units [3] and easily transferable from one molecule to another [3,4]. For this reason, databanks of ELMOs have been constructed [5] and now they allow fast and quantum mechanically rigorous reconstructions of electron densities for molecules ranging from small polypeptides to large proteins.

In this presentation, we will show that the novel NCI-ELMO strategy provides as accurate NCI features as those resulting from traditional quantum mechanical calculations. Furthermore, we will analyze a number of common weak interactions in proteins for which quantum mechanical calculations are unfeasible and we will show that the ELMO approach clearly outperforms the promolecular approximation.

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Electron Densities and Stark Fields in Proton Transfer Reactions

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Keywords: Stark Field, hydrogen bonding, proton transfer reactions.

The Stark field experienced by a functional group of a molecule embedded in a solvent cage depends on the local solvent environment [1]. The Stark field is the projection of the molecular electrostatic potential and depends on electron density distribution. Using Stark fields as descriptor, water and methanol clusters were examined. It was observed that the stark tuning rate for the OH group in methanol is higher than in the case water. Interestingly, it was found that a semi-classical model is adequate to describe the hydrogen bonding pattern in water and methanol clusters [2].

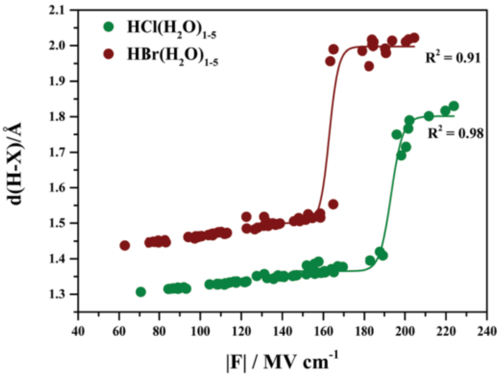

Figure 1: Plot of H–X (X = Cl and Br) distance against electric field along the H–X bond calculated at MP2/aug-cc-pVDZ level for several HX–(H2O)1–5 clusters. The solid lines are non-linear logistic sigmoidal fits to the data points in the region of inflection. The points of inflection for the HCl and HBr clusters were at 193.3 and 162.9 MV cm^{1}, respectively.

Investigations on mineral acid (HX = HF, HCl, HBr and HI) molecules embedded in water clusters revealed that a critical Stark field along the HX bond is required for the acid dissociation. The magnitude of this Stark field decreases with the increase in the acidity, which indicated that HI ionizes at the lowest Stark Field and HF ionizes and highest Stark Field [3]. This results enable molecular level understanding of acid dissociation and concurrent proton transfer processes.

Further, the Stark field experienced by the OH group of phenol embedded in the cluster of ammonia molecules depends on the relative orientation of the ammonia molecules and a critical Stark field of 236 MV cm^{-1} is essential for the transfer of proton from phenol to the surrounding ammonia cluster. The critical Stark field is necessary, however, is not a sufficient condition for the proton abstraction. This, in combination with a suitable solvent orientation along the proton transfer reaction coordinate fulfills both the necessary and sufficient conditions for the facile proton abstraction.

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Elucidating the mechanisms of single molecule magnets using diffraction methods

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Keywords: charge density, single molecule magnets, lanthanides, polarized neutron diffraction.

Single-molecule magnets (SMM) are molecules with the special property that they are able to preserve an induced magnetization after the removal of an external magnetizing field. Such tiny magnets have potential technological applications in e.g. spin-based electronics. The functionality of these materials depend on strong magnetic anisotropy, which is caused by unquenched orbital angular momentum. Both lanthanide-based[1] as well as transition-metal based SMMs exist, but the origin of the magnetic properties in these two types are slightly different. Current state-of-the-art SMM compounds now exhibit magnetic hysteresis at temperatures as high as 80 K, and so after 25 years since their initial discovery, these materials are coming of age. In this presentation, I will show how advanced X-ray and neutron diffraction studies can provide valuable insight into the properties of SMMs.

Firstly, I will show selected results of experimental charge density (CD) studies of transition-metal based SMMs, from which we are developing tools to extract quantitative magnetic properties such as that described using the zero-field splitting parameter. Secondly, I will use CD studies of two dysprosium SMMs to experimentally confirm the predicted oblate shape of the valence density while also indicating the mixed composition of the ground state.[2] Finally, I will show how polarized neutron single crystal data can lead to quantitative knowledge of the local susceptibility tensor, and thus directly the magnetic anisotropy, in a number of SMMs.[3]

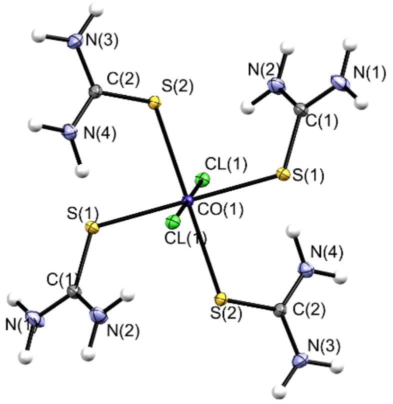

Figure 1: ORTEP drawing of one of the 3d SMM in this work.

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Exporting charge density and chemical bonding know-how elsewhere

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Keywords: phase change materials, HPLC enantioseparations, crystal chemistry bond valence model; localization/delocalization indices, source function for electrostatic potential, bond orders

In a recent paper [1] on *Current Developments and Future of Quantum Crystallography* (QCr), options are discussed on "how QCr can evolve to become a complete and independent domain of natural sciences". While pursuing this goal is clearly a worthy endeavour, it seems also relevant to make an effort to export and sell QCr knowledge in domains where it might be useful but where it is instead yet poorly known. This aspect is explicitly recognised at the end of Ref [1]: "it is important to dynamically fill the emerging new definition of QCr with applications and examples in order to be acknowledged as useful and meaningful", which will eventually "allows for beneficial interactions with neighbouring research areas where important innovations are expected".

Three recent cases, where such an attempt has been humbly pursued, will be discussed. The first concerns chalcogenide phase-change materials, widely used for data storage and photonics, as they can be transformed between amorphous and crystalline states having significantly different optical properties and a pronounced difference in resistivity. This properties contrast of the two states has been reasoned in terms of a distinct mode of bonding in the crystalline state, named metavalent bonding (MVB). Since the changes observed upon crystallization concern either purely structural evidences, or a set of dynamical and out-of-equilibrium properties, the question arises of whether MVB reflects in specific bonding features also in terms of the usual bond characterizations based on electron distributions and bond descriptors derived thereof. By using electron sharing indices and charge transfer descriptors to set up a 2D map of bonding in solids, it was shown that specific combinations of their values may lead to steep variations in a third dimension related to material's properties [2]. Such a susceptibility is a technologically relevant feature of bonding, yet often overlooked in usual bond descriptions.

A second case concerns application of QCr methods in assisting the enantioseparation outcome in the HPLC environment, where the role of σ-holes (due to chalcogen, halogen bonds) in influencing enantioseparations has been recently disclosed. By extending the Source Function formalism to the electrostatic potential (EP), the group atomic contributions to the EP maxima related to the σ-holes can be identified and then used as a precious help to properly design the structural properties of the HPLC test probes [3].

To conclude, a series of studies [4] is addressed, aimed at revealing and exploiting, for various purposes, the empirical links between QCr bond indicators and Bond Valence (BV) parameters of the Pauling's BV method, largely applied in conventional crystal chemistry.

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Spin-resolved atomic orbital model refinement for combined charge and spin density analysis: application to the $YTiO_3$ perovskite

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Keywords: charge, density, joint refinement, orbital model.

We realized previously the joint refinement of charge and spin densities of the $YTiO_3$ perovskite (figure 1) using the MoPro/Mollynx software based on the famous Hansen & Coppens model[1]. Recently, a new model was developed in our laboratory in order to refine spin-resolved electron density based on atomic orbitals. This new algorithm allows the simultaneous refinement of x-ray diffraction and polarized neutron diffraction data. This atomic orbital model was applied to the $YTiO_3$ perovskite. The radial extension, orientation and population of outer atomic orbitals for each atom are modelled. A comparison of the orbital and multipole models will be is presented

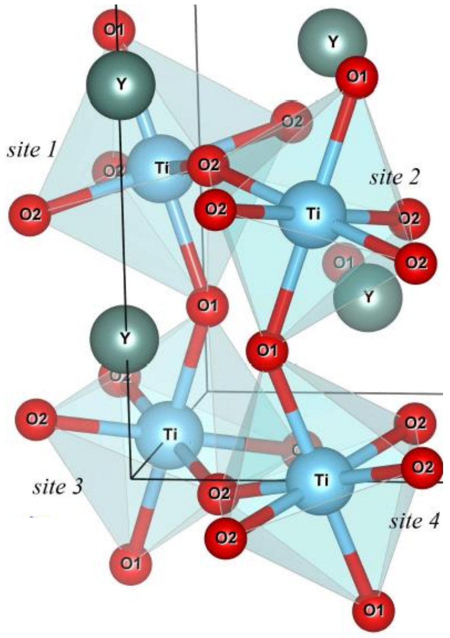

Figure 1: Structure of $YTiO_3$

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Chemical bonding in boron polymorphs and boron-rich compounds

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Keywords: charge density, boron, electrostatic potential

Recently we have developed software for the computation of the electrostatic potential of dynamic densities inside crystals [1]. The method of computation is based on an inverse Fourier transform of the dynamic structure factors. Our software can generate these structure factors for the multipole model and the independent atom model (IAM) as well as for densities obtained by the maximum entropy method (MEM).

Chemical bonding involving the element boron is still an unsolved problem [2]. Several polytypes of boron are firmly established, while other polytypes are under discussion. It is not known, which polymorph is the stable polymorph at ambient conditions. Boron is difficult to purify and it tends to form compounds with well-ordered crystal structures in which as little as 1 out 30 atoms is not a boron atom, for example $B_{50}N_2$. We will discuss chemical bonding in α-boron, γ-boron and boron carbide in relation to the electrostatic potential of the dynamic electron densities of these polymorphs and compound [3].

The polymorph β-boron has the most complex crystal structure of all known and presumed polymorphic forms of boron [4]. It has the centrosymmetric rhombohedral space group R-3m and has approximately 320 boron atoms in the hexagonal unit cell of volume V = 2465 Å^3 [5]. The crystal structure involves a well-ordered set of atoms B(1)–B(15) arranged in B_{12} icosahedral clusters and a larger, condensed cluster B_{28}-B-B_{28}. Slack *et al.* [5] have proposed that there exist five so-called partially occupied sites (POS), at which a boron atom is accommodated in 5–50% of the unit cells. We will discuss our attempts at deriving an accurate electron density for β-boron, and we will report a new boron-rich compound instead.

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Shifting from electron density to electrostatic potential perspective

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Keywords: electron density, electrostatic potential, X-ray diffraction, electron scattering, quantum crystallography, TAAM.

Electron density and electrostatic potential are the key properties of molecules and their assemblies. Many other chemically or biologically relevant properties originate from them. In drug discovery field, for example, molecular electrostatic potential is used to screen for drug-like molecules. Point charges are used to generate potential grids. We propose to use electrostatic potentials computed from Hansen-Coppens multipole model parametrized thanks to recently extended the University at Buffalo Databank of pseudoatoms [1]. When energy of electrostatic interactions between molecules is of interests, another density model called aug-PROmol can be used [2] to speed up calculations. The model provides simpler representation of electron density and electrostatic potential allowing faster calculations but still gives energies of very good accuracy.

Electron density and electrostatic potential are also important concepts for X-ray or electron beam scattering based experiments. Various models of electron density emerged in X-ray crystallography to interpret diffraction data. Among others there are pseudoatom databases which aim to replace IAM (Independent Atom Model) by TAAM (Transferable Aspherical Atom Model) in crystal structure refinement. To ease the usage of this methodology we interfaced our new software library DiSCaMB [3] with Olex2 [4] program. Results of TAAM refinements on large data set clearly shows [5] all advantages and disadvantages of TAAM comparing to IAM and HAR [6].

The time comes for electron crystallography which is currently developing very rapidly. It is approaching the stage at which it could benefit from usage of more accurate scattering models, similarly as X-ray crystallography does. This can easily happen with the help of tools and knowledge accumulated over the past thanks to our quantum crystallography community. With simulated data for carbamazepine crystal, we compared IAM and TAAM refinements on electron diffraction data with X-ray to understand the possible benefits of using TAAM in electron crystallography [7].

Support of this work by the National Centre of Science (Poland) through grant OPUS No.UMO-2017/27/B/ST4/02721 is gratefully acknowledged.

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Charge density view on bicalutamide molecular interactions in monoclinic polymorph and androgen receptor binding pocket

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Keywords: anticancer drug, electrostatic interaction, complementarity.

The non-steroidal anti-cancer drug bicalutamide is on the World Health Organization's List of Essential Medicines. It has low solubility in water and demonstrates antiandrogen activity as a selective antagonist. The high-resolution single crystal X-ray measurement of the monoclinic polymorph of bicalutamide and the aspherical atom databank approach served as a basis for a reconstruction of the charge density distribution of the drug and its androgen receptor (AR) and albumin complexes. The contributions of various types of intermolecular interactions to the total crystal energy or ligand:AR energy were estimated. The cyan and amide groups secured the ligand placement in the albumin (Lys137) and androgen receptor binding pocket (Leu704, Asn705, Arg752), also determined the packing of the small molecule crystals. The total electrostatic interaction energy on average was -230 kJ mol^{-1}, comparable to the electrostatic lattice energy of the monoclinic bicalutamide polymorph. This is the result of similar distributions of electropositive and electronegative regions on the experimental and theoretical molecular electrostatic potential maps despite differences in molecular conformations. In general, bicalutamide interacted with the studied receptors with similar electrostatic interaction energies and adjusted its conformation and electrostatic potential to fit the binding pocket in such a way as to enhance the interactions, e.g. hydrogen bonds and π…π stacking.

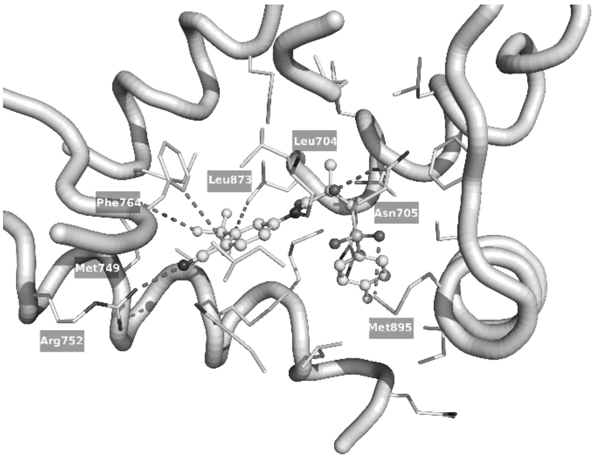

Figure 1: Bicalutamide (shown as balls and sticks) in the binding pocket of the AR (PDBID: 1z95). Selected side chains of protein residues are represented as grey sticks, while the rest of the protein backbone is shown as a ribbon. The strongest interacting residues are labeled and the closest contact to the ligand atoms are shown as dashed lines

From densities and density matrices to open quantum systems

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Keywords: electron density, density matrices, quantum chemical topology.

Although partitions of the physical space into chemical fragments are now common in the theory of chemical bonding, e.g. the quantum atoms defined in the Quantum Theory of Atoms in Molecules (QTAIM) [1], not so many works have tried to deal with a chemical fragment as truly open quantum systems. Using techniques borrowed from the theory of open quantum systems, we show how the partial trace over the environment degrees of freedom can be defined in real space [2]. The subsystem reduced density operators so defined are shown to be intimately linked to the Electron Distribution Functions (EDF) formalism devised years ago [3].

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Unusual Al=Al bonding in $[LiAl_2H_4]^-$ complex anions

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Keywords: QTAIM analysis, CCSD method, geometry optimization.

Lundell et al. [1] identified $[LiAl_2H_4]^-$ clusters in an aluminum rod coated by a very thin layer of $LiAlH_4$ powder and ablated by a pulsed Nd:YAG laser beam. In this way obtained clusters in the resulting plasma were investigated via combined photoelectron spectroscopy and PBE0/6–311++G** calculations of possible structures in singlet ground spin states to confirm the formation of a conventional Al=Al double bond in the most stable isomer of C_2 symmetry (Fig. 1). Chemical bonding analysis via Adaptive Natural Density Partitioning (AdNDP) [2] method gives the bond order of 1.76 for Al=Al double bond in this cluster. The short Al-Al distance of 2.46 Å in this structure is in agreement with this conclusion.

We have optimized the geometries of $[Al_2H_4]^q$ structures, q = 0, -1 or -2, and of the most stable isomer of $[LiAl_2H_4]^-$ in their lowest spin states by CCSD method and standard 6-311++G** basis sets. Their electron structure has been investigated in terms of Quantum Theory of Atoms-in-Molecule. The non-nuclear attractor has been observed between both Al atoms in the above structures, which might be explained by unusual shapes of their frontier molecular orbitals. $[LiAl_2H_4]^-$ clusters are held together primarily by Al-H and Li-H bonds. No Li-Al bond paths are detected. The double Al=Al bond in the most stable isomer of $[LiAl_2H_4]^-$ is weaker than Al-H bonds but stronger than the Li-H ones.

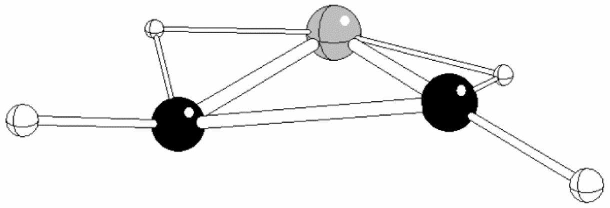

Figure 1: Structure of the most stable isomer of $[LiAl_2H_4]^-$ (Al – black, Li – grey, H – white) [1]

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Vorticity and circulation of the induced current density: Simplifying a vector field

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Keywords: current density, aromaticity, magnetic properties, quantum topology.

The magnetically induced current density (***J***(***r***)) field helps us to understand several macroscopic magnetic properties (e.g. NMR chemical shifts, magnetic susceptibilities) of molecules.[1,2] Moreover, it has been related with the aromaticity of main-group compounds.[3,4] The main property that it is studied of this vectorial field, is the direction of the rotations of the main currents (tropicity). However, the quantitative analysis of it is cumbersome. We show that it is possible to compress the information of the tropicity of ***J***(***r***) in the scalar field, $\mathbf{B} \cdot \nabla \times \boldsymbol{J}(\boldsymbol{r})$ that we call triple product of ***J***(***r***) (tp ***J***(***r***)).[5] The topology of this scalar field has similarities with the laplacian of the electron density and contrary to the laplacian, it can easily distinguish between main-group aromatic and antiaromatic molecules. From the vorticity of ***J***(***r***) ($\nabla \times \boldsymbol{J}(\boldsymbol{r})$) we also define a current index named the circulation, C, that contrary with other magnetic aromaticity indices, it can be defined for individual rings in polycyclic molecules. It reproduces the Clar's rule for polycyclic aromatic hydrocarbons.

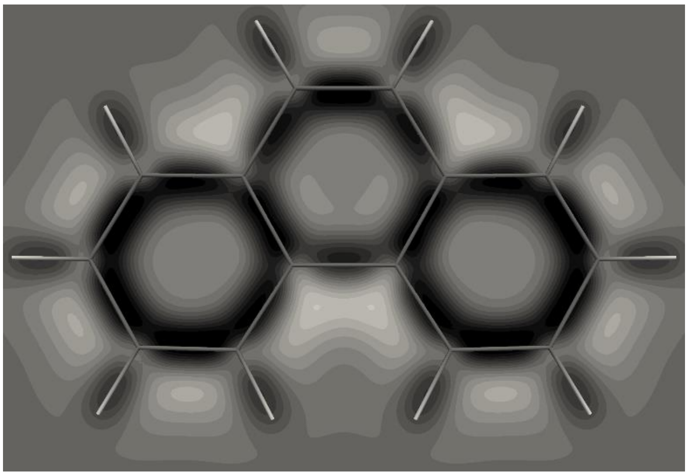

Figure 1: tp***J***(***r***) of Phenanthrene. Diatropic region (black) of the central ring is smaller than for lateral rings.

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Prof. Dr. Christian Griesinger

Max Planck Institute for Biophysical Chemistry

to be announced

Loading Dependent, Molecular Level Structural Model of Polymer Micelles using Solid-state NMR, PXRD and Calculations

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Keywords: Intermolecular Interactions, Solid-state NMR, Short-range Order, Calculations.

Structural insights into self-assembled and drug-loaded polymeric micelles are difficult to obtain due to their complex nature and lack of long-range order. Our view on such systems is therefore dominated by the look from the outside as well-defined core-shell nanoparticles. For applications in drug delivery, we would like these particles to be highly loaded yet this often deteriorates physico-chemical properties, e.g. the dissolution rate [1, 2].

By using solid-state NMR complemented by information from PXRD and calculations (sometimes referred to as "NMR Crystallography" [3]), it is possible to observe loading dependent structural changes and key intermolecular interactions. This model on the molecular level can help to explain observed properties and rationalize polymer modifications, which could lead to improved polymeric drug delivery vehicles.

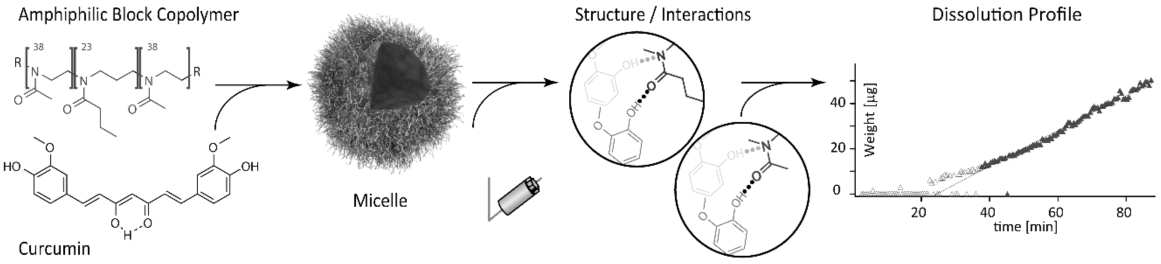

Figure 1: Schematic summary: The amphiphilic block copolymer forms polymeric micelles in the presence of hydrophobic guests. Investigation of the resulting assemblies by solid-state NMR and complementary tools yields key intermolecular interactions. Based on this data, pharmaceutically relevant properties can be explained.

The research described above benefits strongly from the interplay between various analytical tools and thus different views on the systems bridging different length scales and degrees of order. This interplay or overlap of different techniques is still small and there is a lot more to try with and learn from each other.

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Electron Density and Dielectric Properties of Highly Porous MOFs: Binding and Mobility of Guest Molecules in $Cu_3(BTC)_2$ and $Zn_3(BTC)_2$

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Keywords: charge density, polarizability, dielectric constant

Two isostructural highly porous metal–organic frameworks, the well-known $\{Cu_3(BTC)_2\}_n$ (BTC = 1,3,5-benzenetricarboxylate), often appointed with the name HKUST-1, and $\{Zn_3(BTC)_2\}_n$, have been investigated as models for the buildup of dielectric properties, differentiating the role of chemi- and physisorbed guest molecules and that of specific intraframework and framework-guest linkages. For this purpose, electron charge density analysis, impedance spectroscopy, density functional theory simulations, and atomic partitioning of the polarizabilities have been exploited.[1] These analyses at different degrees of pores filling enabled one to observe structural and electronic changes induced by guest molecules, especially when chemisorbed. The electrostatic potential inside the pores allows one to describe the absorption mechanism and to estimate the polarization of guests induced by the framework. The dielectric constant shows very diverse frequency dependence and magnitude of real and imaginary components as a consequence of (I) capture of guest molecules in the pores during synthesis, (II) MOF activation, and (III) water absorption from the atmosphere after activation. Comparison with calculated static-dielectric constant and atomic polarizabilities of the material has allowed for evaluating building blocks' contribution to the overall property, paving the way for reverse crystal engineering of these species.

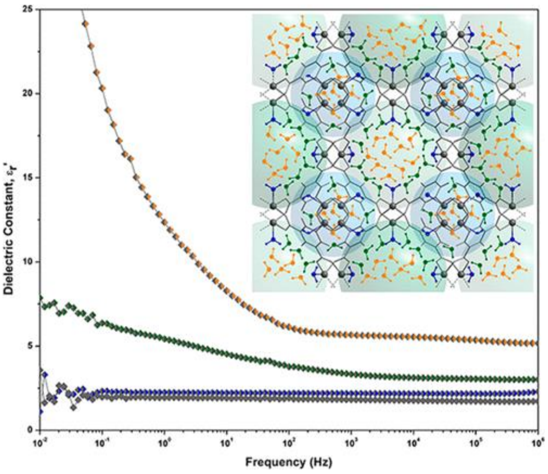

Figure: the dielectric constant in different preparations of HKUST-1, corresponding to a different location of water molecules in the sample.

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Experimental charge density of grossular under pressure - a feasibility study

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Keywords: charge density, high pressure, minerals.

We would like to present results of an attempt to determine experimental charge density distribution for a single crystal under high pressure. As our model compound we have chosen a mineral called grossular ($Ca_3Al_2Si_3O_{12}$). Main experiment was conducted on the CRISTAL beamline at the SOLEIL (France) synchrotron source. Combination of three important parameters such as short wavelength of the X-ray beam (λ=0.41 Å), wide opening angle of the diamond anvil cell used (effective opening angle 98°) and high symmetry of the investigated structure (space group Ia-3d) allowed us to collect almost 100% complete data up to resolution 0.38Å. Using this experimental data a refinement of the Hansen-Coppens pseudoatom multipole model was performed.

Simultaneously, as a kind of a benchmark, the same particular crystal of grossular was measured on an in-house diffractometer (λ=0.56Å) at ambient pressure. Complete data was collected up to resolution of 0.38Å. Refinement of the multipole model was also conducted.

We compare our results with literature data. Especially, with experimental charge densities obtained for the mineral called pyrop ($Mg_3Al_2Si_3O_{12}$), which in fact is isostructural with grossular. This particular results are interesting because were published most recently and describe measurement at quite low temperature of 30K (Destro et al., 2017) [1].

Comparison of properties of charge density at bond/interaction critical points as well as maps of the total electron density, Laplacian and deformation density revealed significant resemblance between obtained by us experimental charge density under pressure and the mentioned above benchmarks.

We think that use of a new type of diamond anvil cells characterized by wider opening angle and access to relatively short X-ray beam can, in the case of high symmetry compounds, open a path to determination of changes of electron density distribution in function of pressure.

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New technologies for experimental charge density

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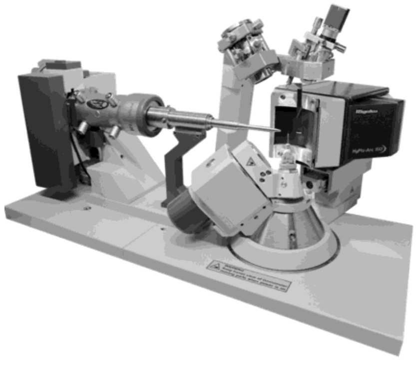
Keywords: arc, anode, charge, CrysAlisPro, density, HyPix, HPC, silver, Rigaku, rotating.

A high-resolution (sinθ/λ > 1) dataset for charge density refinement is the ultimate trial for the whole diffractometer instrument. A complete dataset with all data observed is a test of source performance and detector sensitivity. High redundancy data is, on the other hand, a challenge for system stability, reproducibility, and smart strategy software.

This presentation will focus on Rigaku Oxford Diffraction's ultimate solution for such measurements, the XtaLAB Synergy-S/R systems with ultra-low noise Rigaku HPC technology featuring high 32-bit dynamic range and 70Hz frame rate in the curved HyPix-Arc 150° detector. This enables the user to easily collect charge density resolution data from a single theta position with molybdenum radiation, minimalizing distortions, scaling problems, and the always-unavoidable parallax effect. Rigaku instruments can be also configured with a silver source both as a sealed tube or rotating anode option. The fast and precise Universal Kappa Goniometer and true shutterless mode guarantees minimal experiment time. A variety of low temperature LN2 or He2 cryo-devices are supported for high quality low temperature data.

All Rigaku systems are provided with the comprehensive CrysAlis^{Pro} software, featuring a user-friendly interface which supports Rigaku hardware, and data from third party instruments and synchrotron beam datasets. The fast, powerful strategy module allows efficient collection of complete, redundant data for all wavelengths e.g. molybdenum and silver Kα radiation.

Examples of collected datasets on the Synergy system will be shown.



A Synergy-DW with HyPix-Arc 150°

The MetalJet X-ray source with indium anode. High brightness at 24 keV.

Emil Espes[1]

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The power and brightness of electron-impact micro-focus X-ray tubes have long been limited by thermal damage in the anode. This limit is overcome by the liquid-metal-jet anode (MetalJet). This is possible due to the regenerative nature of this anode and the fact that the anode is already molten, which allows for significantly higher e-beam power density than on conventional solid anodes.

Over the last years, the MetalJet technology has developed from prototypes into fully operational and stable X-ray tubes, such as the MetalJet D2+ seen in Fig. 1, running in many labs over the world. Key applications include X-ray diffraction and scattering but also advanced X-ray imaging such as phase-contrast imaging.

This presentation will review the current status of the technology specifically in terms of stability, lifetime, flux and brightness. It will specifically discuss performance using indium rich anode alloys, offering a bright home-lab X-ray source with K-alpha emission at 24 keV.

Figure 1 The MetalJet D2+ X-ray tube

Direct conversion in CdTe: accurate data from hard X-rays without detour

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Keywords: -

Hybrid Photon Counting (HPC) detectors provide accurate data and highest signal-to-noise thanks to the absence of dark current as well as readout and reset noise. An energy discriminating threshold improves data quality in the presence of fluorescence background. The absence of detector background and digital counting in every pixel enable ten orders of dynamic range. Direct conversion in Si- or CdTe-sensors perfectly complements the advantageous properties of single-photon counting. Scintillation based detectors rely on the conversion from X-ray to light prior to the actual detection process. HPC detectors directly convert from X-ray to the detected electrical signal. The small and sharp point-spread function enabled by direct conversion minimizes overlap of signal and background. Quantum efficiency is maximized since no intermediate signal can be lost before detection. HPC detectors with CdTe-sensors provide more than 90% quantum efficiency for Mo-, Ag-, and In-radiation. The unique features of HPC ensure highest data quality critical for challenging charge-density studies.

This presentation will give an overview of the experimental characterization of detector properties such as quantum efficiency, point-spread function, and count rate capability. Furthermore, results from laboratory diffraction experiments will be presented.

Shine Bright Like a Diamond: Microfocus X-ray Sealed Tube Sources with Diamond Hybrid Anode Technology

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[c] Bruker AXS Inc., Madison (WI), USA

Keywords: -

Diamond exhibits several unique properties, such as high thermal conductivity, low thermal expansion, extreme hardness, chemical inertness and a fairly high transmission coefficient for X-ray radiation. The thermal conductivity of diamond is about 5 times higher than that of copper and the highest known conductivity of all bulk materials. Therefore, diamond is increasingly replacing traditional materials for the thermal management in challenging applications where a high local heat load needs to be dissipated, such as in heat sinks for high-power microelectronic devices. In X-ray sources, diamond can be used as a transparent heat sink directly coupled to the anode material. This improves the heat dissipation considerably and allows for an increase in tube brilliance by applying a higher power load on the anode.

The IµS DIAMOND is a new type of microfocus sealed tubes using a unique anode technology, the diamond hybrid anode. It takes advantage of the exceptional high thermal conductivity of diamond by using a bulk industrial diamond as a heat sink, which is coated with a thin layer of the target material, such as Cu, Mo or Ag, making the heat dissipation in a diamond hybrid anode more efficient. Consequently, the IµS DIAMOND can accept a higher power density in the focal spot on the anode. The intensity loss over time for the IµS DIAMOND is only a few percent over 10,000 h of full power operation, which is significantly lower than the intensity degradation observed for microfocus rotating anodes. Therefore, the intensity of the IµS DIAMOND is higher than the average intensity output of a modern microfocus rotating anode.

The IµS DIAMOND establishes a new class of X-ray sources, combining an intensity output that exceeds the average intensity of a microfocus rotating anode with all the comfort and lifetime of a standard microfocus sealed tube with a bulk anode. It is available for Cu-Kα radiation for applications such as protein and small molecule crystallography, and now also for Mo-Kα and Ag-Kα radiation, which are the wavelengths of interest for applications in charge density studies and high-pressure crystallography. In this contribution, we will be discussing the main features of the IµS DIAMOND and presenting selected results to demonstrate the impact of this new class of microfocus sealed tube X-ray sources on the data quality for applications in X-ray crystallography.

Is Heisenberg wrong? Insights into 'noise free' detectors

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Keywords: CPAD, detectors, mixed-mode.

Modern single-crystal X-ray diffraction nowadays relies entirely on two dimensional pixel array detectors (PADs). Their underlying CMOS technology allows shutterless data collection which has widely eliminated experimental overhead time. Today, two different techniques are competing in the home laboratory market.

HPADs, now available for a number of years, count individual X-ray events, based on electron-electron hole pairs and apply an internal threshold to suppress the background noise including the noise originating from the sensor. These detectors produce clear images, which at a first glance are perfectly noise free. However, the need for a threshold introduces a new source of noise for HPADs: charge sharing between pixels resulting in signal loss and the limited count-rate capability of HPADs is another source of errors. Signal loss occurs if two individual X-ray photons arrive at the same pixel within a too short time interval which typically occurs with well diffracting charge density samples especially for the important low resolution reflections. In the majority of HPAD detectors ultra-pure silicon (Si) is used as the primary absorber material for the X-ray photons, which has rather poor absorption properties for hard radiation corresponding to limited sensitivity for Mo- and Ag X-rays that are applied in charge density research.

Mixed-mode detectors offer the advanced technical alterative to HPADs. This rather new technology is now implemented at large research facilities, such as free electron laser sites. For the home market Bruker has developed the PHOTON III series of detectors. Large monolithic sensors without gaps are standard in these detectors. An ultra-low noise floor as well as high read-out speed and frequency of modern CMOS sensors allows the identification of individual X-ray events, very similar to the HPAD detectors. However, mixed-mode detectors first integrate individual X-ray events and then count in a second step. This approach does not require any threshold and truly counts all X-ray events. Consequently, mixed-mode detectors do not suffer from charge sharing. Furthermore, mixed mode detectors can cope with higher count rates. X-ray photons are efficiently absorbed within thin high-Z absorber layers minimizing parallax and leading to a small signal point spread.

Technical details and users benefits of the large area mixed-mode detectors, especially for experimental charge density data collections will be presented.

Interacting Quantum Atoms (IQA) and the Relative Energy Gradient (REG) method: how to extract chemical insight from wave functions

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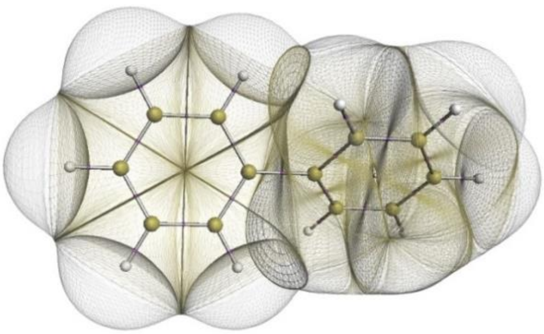
Keywords: Quantum Chemical Topology (QCT), Quantum Theory of Atoms in Molecules (QTAIM), Relative Energy Gradient (REG), rotation barrier, S_N2, peptide hydrolysis, gauche effect, base pairs

Figure 1: Topological atoms in biphenyl



Much chemical insight ultimately comes down to finding out which fragment of a total system behaves like the total system, in terms of an energy profile.

A simple example is that of the water dimer, where this system is regarded as held together by a hydrogen bond. The hydrogen bond consists of two atoms (H···O), which energetically behave similarly to the total system $(H_2O)_2$. However, from a quantum mechanical point of view, each atom in the total system interacts with *any other* atom. Thus, the view that the *hydrogen bond by itself governs the energetic stability* of the water dimer needs rigorous justification.

We propose a solution for this general and important problem by presenting the Relative Energy Gradient (REG) method[1]. This automatable and unbiased method operates on the IQA[2] energy contributions calculated according to the real-space partitioning of Quantum Chemical Topology[3, 4].

The REG method, as implemented in the in-house program ANANKE, is able to explain the gauche effect[5], the torsional barrier in biphenyl[6], the arrow-pushing scheme of an enzymatic reaction (peptide hydrolysis in the HIV-1 Protease active site)[7], halogen-alkane nucleophilic substitution (S_N2) reactions[8] and the factors controlling the nature of complementary hydrogen-bonded networks as found in nucleic acid base pairs[9].

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Impact of experimental electronic structure on better chemical bonds understanding.

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Keywords: charge, density, chemical bond, coordination compound

It seems that results of charge density studies using the accurate data could improve our understanding basic character of the chemical bond. The Kepert model as well as the VSEPR theory can be both confirmed and improved.

On the example of tetrakis(μ$_2$-acetato)-diaqua-di-copper(II) and tetrakis(μ$_2$-acetato)-di-aqua-di-chromium(II) complexes [1] „clasical coordination bond“ is defined. Equatorial - axial interactions are explained *via* Cu $d_{x^2-y^2}$ orbital interaction with donor atom lone electron pair.

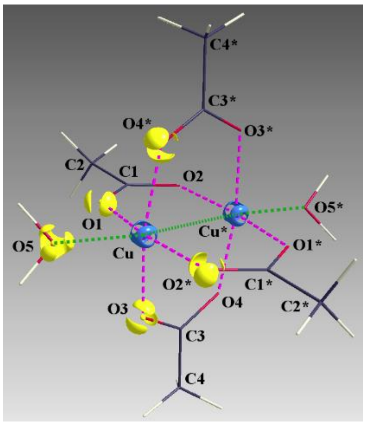

Figure 1: 3D plot of the Laplacian of electron density around Cu at isosurface value of 1650 e/Å^5 and around O1, O2*, O3, O4* and O5 at isosurface value of 90 e/Å^5.

In the Ti(IV) complex with peroxo ligand the question of Ti-O2 interraction is disccussed. This interaction could be *via* lone electron pair of two oxygen atoms or *via* the multipole bond.

Interesting interaction was found in *bis*(clonixato)-*bis*(1H-imidazole)-copper(ii) complex, where Cu-H7 distance is 2.571 Å and the angle Cu-H7-C7 is 160.03°. Hydrogen bond with Cu fully populated d_{z^2} orbital is expected.

In radical precursor (3-(2'-tetrahydropyranyloxy)-4-methylthiazole-2(3H)-thione) a noncovalent interaction was found between two negatively charged atoms N1 and O1. Laplacian of this bond has a positive value and the shape of VSCC is not a typical σ-bond, but the intermediate between the covalent bond and noncovalent interaction.

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Exploiting Quantum Chemistry to Refine Crystallographic Structures of Proteins and Polypeptides

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Keywords: Hirshfeld Atom Refinement, Extremely Localized Molecular Orbitals, proteins.

Hirshfeld Atom Refinement (HAR) is a new and promising refinement technique of crystallography that strongly relies on quantum chemistry concepts and calculations [1-2]. In fact, recent studies have interestingly shown that, by exploiting only X-ray diffraction data (even at resolutions as low as 0.8 Å), this method allows determinations of hydrogen atoms positions as accurately and precisely as from neutron diffraction measurements [3].

Given the excellent results obtained for organic molecules [3], HAR could be successfully used to refine crystallographic structure of proteins. Nevertheless, since the technique requires a tailor-made quantum chemical calculation at each iteration of the refinement, its extension to large systems is prevented by the large computational cost.

To overcome this drawback, HAR has been coupled with the recently constructed ELMO libraries [4] that exploit the intrinsic transferability of the Extremely Localized Molecular Orbitals (ELMOs) [5,6] to quickly and reliably reconstruct wavefunctions and electron densities of macromolecules ranging from small polypeptides to proteins. This gave rise to the new HAR-ELMO technique, which significantly reduced the computational cost associated with the original Hirshfeld Atom Refinement and, therefore, extended the applicability of HAR to very large molecules [7].

In this presentation, after briefly reviewing the main features of the ELMOs transferability and of the ELMO databanks, the first results obtained through the novel HAR-ELMO strategy will be shown. In particular, the validation of the method on small systems will be discussed, highlighting advantages and disadvantages compared to the traditional Independent Atom Model (IAM) and to the original version of the HAR method at Hartree-Fock level. Finally, the first HAR-ELMO refinements of polypeptides (e.g., Leu-enkephalin, fibril-forming segment of the human prion protein) and proteins (e.g., crambin) will be presented, also illustrating possible ways to further improve the proposed technique.

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Going beyond the ELMO approximation: the QM/ELMO approach

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Keywords: Multi-scale methods, Extremely Localized Molecular Orbitals, Biological systems.

Quantum mechanics (QM) methods have a predominant role in the theoretical study of chemical systems, but their computational cost prevents their use in the investigation of very large molecules (e.g., proteins). To overcome this drawback, several approximate strategies have been proposed over the years, ranging from hybrid quantum mechanics/molecular mechanics (QM/MM) techniques to fragmentation methods. [1]

Among the latter, an important category of techniques is based on the chemical transferability principle, namely on the observation that molecules generally consist of elementary units (e.g., functional groups) keeping their main features unchanged in different systems. Following this principle, electron density fragments and localized molecular orbitals can be thus predetermined on appropriate model molecules and afterwards transferred to the large systems of interest, obtaining approximate electron densities and wave functions at a significantly reduced computational cost.

To this purpose, new libraries of extremely localized molecular orbitals (ELMOs) have been recently quantum mechanically proposed to study molecules ranging from small polypeptides to large proteins. [2-4] Nevertheless, although the ELMO approximation enables to obtain satisfactory quantum mechanical descriptions, this approach lacks accuracy and flexibility, especially when dealing with particular bonding patterns (e.g., in protein-ligand interactions), for which polarization and charge transfer are crucial.

To address this problem, we extended the local self-consistent field method [5] and developed a new multi-scale ELMO-based QM/QM' technique. The crucial region of the system, (e.g., the active site or the metal center of a protein) is treated self-consistently at HF or DFT level of theory, while the remaining QM' part and the frontier regions are described using transferred ELMOs. The use of the ELMOs increases the quality of the calculations compared to the more standard QM/MM techniques and, at the same time, it allows to save computational time compared to fully QM calculations.

Here, other than a brief introduction on the theoretical background of the new technique, we will present preliminary test calculations that have been performed to evaluate the general applicability, the advantages and the disadvantages of the novel approach. Finally, we will also discuss the possible applications of the QM/ELMO method in the field of quantum crystallography, especially in the refinement of protein crystallographic structures (HAR-QM/ELMO strategy).

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Electron Transfer Reductions of N-heterocyclic and Cyclic Alkyl Amino Carbene Stabilized Silicon Halides and their Intermediates

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Abstract: Polycrystalline silicon has found huge applications as an electronics material in the silicon industry for its efficient semiconducting properties and improvement of display of the electronic devices. The reduction of tetra valance silicon halides or silica/silicates leads to formation polycrystalline silicon at very high temperature. Recently the use of neutral ligand like singlet carbene made the reduction of silicon compound easy at much lower temperature in the laboratory to produce neutral ligand supported silicon compounds. The solution chemistry is hard to follow all the times and conclusions on their chemistry were made based on the isolated silicon compounds under given reaction conditions. The details of experimental observations were utilized as a back ground and different level of theoretical calculations on electron transfer reductions of N-heterocyclic carbene and cyclic alkyl amino carbene stabilized silicon halides and their intermediates were carried out to show the possible mechanistic path ways. This will help us to control reaction products. Additionally, we can predict the intermediates and studied their stabilities and distribution of electron densities. This will further help us to design new synthetic routes for the isolations of unusual carbene-silicon species in more rati9onal reaction conditions. Our theoretical calculations helped us to explain many experimental observations. All these theoretical calculations gave great impact on side by side comparisons between the difference in carbene-silicon chemistry of NHC and CAAC carbenes under nearly identical conditions.

Challenges for what we call accurate experimental charge density. Is there an accurate experimental charge density or is the theory also just a hoax?

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Keywords: charge, density, quantum, quantum crystallography

There are several (at least three) panel titles where this theoretical work fits in, i.e. “Data and model quality”, “Charge, spin and momentum densities from computational methods” as well as “Why measure, just compute!”.

“Data and model quality” panel, for a theoretical work, why? One can easily prove and benchmark experimental models (e.g. IAM, multipoles or MEM) against theoretical data to see how these models match with the theoretical reference. The other point “data quality” is much too tough to be assessed by a theorist, but we believe in what the experimentalists and the companies can achieve in the future with respect to data resolution or robustness (i.e. pushing down the side effects and errors), *vide infra*.

“Charge, spin and momentum densities from computational methods” is a wise panel choice because this is a charge density study from computational methods, but that would be a boring choice.

“Why measure, just compute!” is the panel I would like to choose. It is something like David Locke (empiricism) meets Rene Descartes (rationalism), which is the philosophy level I can grasp a little. Still, David and Rene cannot really live one without the other and the same holds for experiment and theory, respectively. The experiment gives the theory the work to improve the interpretation of the experiment and this comes always with improving itself. And in a some of the next ICDM, I might have to join the panel “Why compute, just measure!” so good luck to the experimentalists and companies, *vide supra*.

So finally let me sketch what will be considered **herein**: We will compare the charge density representations against theoretical data (structure factors) for an organic compound [1] and copper/chromium acetates [2]. Where for the organic compound [1,3], multipolar and MEM methods shall be matched against DFT (including experimental data). In the case of the metal acetates [4], the comparison of theoretical methods will be highlighted first, to assess the energetics, spin state preference and electron density topology with respect to single reference and multireference methods. Subsequently, a comparison of charge density derived from experimental data [2] and/or upon experimental models will be compared with theoretical ones [4] to investigate what can theory and experiment learn from each other; and what is the theoretical hoax in the chosen experimental establishment and/or *vice versa*.

Acknowledgements: APVV-15-0079, VEGA 1/0718/19 and 1/0598/16, SIVVP (ITMS code 26230120002).

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[4] Malček, M.; e*t al. to be submitted.*

Transient charge density in polar crystals from femtosecond x-ray diffraction

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Keywords: femtosecond powder diffraction, transient charge density, macroscopic polarization.

The interplay of electronic and lattice degrees of freedom is important for structural dynamics and functional properties of crystalline materials. In polar and/or ionic crystals, Coulomb interactions mediated via local electric fields play a central role in coupling electronic and nuclear motions [1]. Femtosecond x-ray diffraction allows for following such correlated dynamics at the atomic level by providing momentary atom positions and charge density distributions [2,3]. In this talk, prototypical results on charge and lattice dynamics in polar and ionic materials are presented. The systems studied include polycrystalline acetylsalicylic acid ($C_9H_8O_4$, aspirin) and the protoype ferroelectric ammonium sulfate [$(NH_4)_2SO_4$]. In aspirin, time resolved terahertz experiments have shown that the nonlinear response of the 1-THz methyl rotation is connected with a field-induced dynamic breakup of electron-phonon correlations [4]. Complementary x-ray diffraction studies provide transient charge density maps, showing that coherent sub-picometer displacements of the methyl groups induce electron relocations over 100 pm, a hallmark of correlated charge dynamics [5]. The transient charge distributions provide detailed information on the local forces acting on the methyl rotators. In ferroelectric ammonium sulfate, we identify a new soft mode and map phonon-induced modulations of electron density in space and time [6]. The large-amplitude charge relocations are distinctly different from the paraelectric phase and connected with strong changes of the ferroelectric polarization. Based on a novel theoretical formalism, we establish a direct link between transient microscopic charge densities and macroscopic electric polarizations [7].

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Latest developments in dynamic quantum crystallography

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The use of quantum mechanics in crystallography has a long history, however in most applications the quantum mechanical modeling has focused on the description of the electron density. Much less attention has been devoted to the nuclear motion, although the atoms in the crystal are of course vibrating, even at the lowest temperatures. This is unfortunate. Not only does the atomic and molecular motion define important physico-chemical properties such as the mechanical and thermodynamic stability of the crystal, but the concerted motion of atoms give rise to thermal diffuse scattering which affects the Bragg intensities. In other words, from the point of view of X-ray scattering the electron density and the nuclear density are communicating vessels, and the two densities together define the total charge density.

Ultimately, the quantum-mechanical models of electron density distribution and nuclear motion should amalgamate into a common model, which can be compared and refined against the experimental evidence, and which can be used to understand solid state properties at the atomic level. We will present our approach to refine lattice-dynamical models against diffraction data [1,2], and in order to approach this common model, we present models where we have put focus on providing a thorough model for both the electron and nuclear density. Whereas for L-alanine we have performed a joined refinement of a multipole model and normal modes [3], we have also recently tested an other approach, where the aspherical charge density modeling precede the refinement of a normal mode model . We discuss the pros and cons of these approaches, and demonstrate their usefulness for deriving bulk properties of crystalline materials.

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Coloring the electron density

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Keywords: density, population, space partitioning.

The electron density is one of the most prominent objects in the quantum description of molecules and solids. Besides the high quality determination of the electron density, be it experimental or as the result of a quantum mechanical calculations, it is also the interpretation and its utilization in the description of chemical bonds that is a part of intensive ongoing research. When the integrals of the density are involved, the view on the electron distribution can be strongly influenced and controlled by the choice of the space partitioning over which the integration is performed [1]. Some relations between discrete and continuous distributions will be discussed.

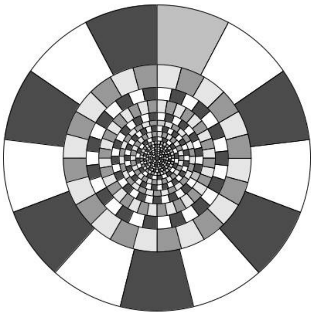

Figure 1: Space partitioning for the Ne atom. Microcells enclosing 10^{-8} same-spin electron pairs.

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Measuring accurate single crystal diffraction data using a Pilatus3 CdTe detector

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Keywords: pixel array detector, data quality, experimental charge density.

Pilatus3 detectors were released in 2012 and are widely established in macromolecular crystallography with over 4,000 PDB entries. The specifications of the Pilatus3 CdTe were quickly recognized as promising in charge density investigations, mainly due to the detection efficiency in the high-energy X-ray regime. Moreover, the dynamic range and low noise should overcome the perpetual problem of detecting strong and weak data simultaneously. However, to the best of our knowledge there is no publication available presenting high resolution data collected with a Pilatus3 CdTe detector.

Our experience with this detector family revealed two aspects that lead to systematically underestimated intensities at the two extremes of the detected intensity scale. Herein, Rubrene and $FeSb_2$ are representatives for the two cases. Additionally, a LaB_6 powder sample was consulted to validate the findings of the single crystal studies where counting statistics and reproducibility are more delicate.

The first aspect is indicated by systematically too low intensities for weak reflections, revealed by a variation of exposure time and beam attenuation. The origin was found in the data processing, specifically in the outlier rejection and data averaging.

The second case affects the most intense reflections and is connected to the maximum flux of the diffracted beam but not the total number of counts. As the widely discussed charge sharing should not affect strong reflections in any systematic manner, we utilized a maximum flux estimation procedure to identify unproblematic flux ranges. Disregarding this issue leads to unreasonably large extinction parameters.

Our results conclude that only the combination of careful data collection and processing can result in high quality data.

lamaGOET: GUI interface for HAR, HAR-ELMO and wavefunction fitting in Tonto and other softwares

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Keywords: HAR, charge density, XCW, XWR, Tonto.

The use of aspherical models in crystal-structure and electron-density refinement has become more and more popular over the past years. One of such methods is Hirshfeld Atom Refinement (HAR)[1,2] which is performed within Tonto, a program and library for quantum crystallography and quantum chemistry. To run Tonto and to have access to its full features, one needs to setup an input file called stdin. Example input files can be found in the "tests" folder provided with the software installation, but usually building your own input file is not such a trivial task, especially when using more advanced functionalities.

The lamaGOET graphical interface allows the user to perform a HAR using different softwares for the wavefunction calculation, such as Gaussian or the original Tonto. Another new and unpublished feature included inside lamaGOET is the use of the ELMOdb program where the wavefunction can be transferred from the ELMO data base constructed by Genoni *et al*.[3]. LamaGOET is the only interface that allows the use of the ELMO data bank to perform HAR, also called HAR-ELMO[4].

The lamaGOET script not only provides a graphical interface which facilitates the creation of input files for Tonto jobs related to HAR and HAR-ELMO,but also allows the use of more advanced features inside Tonto such as X-ray Constrained Wavefunction (XCW) fitting[5] and X-ray Wavefunction refinement (XWR = HAR + XCW)[6]. The XCW procedure allows access to the "experimental" wavefunction. The lamaGOET also include options to use Tonto to calculate and plot desired experimental properties from the derived wavefunctions.

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