

# On the evaluation of molecular dipole moments from multipole refinement of X-ray diffraction data

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## Abstract

Lack of physical constraints in the purely mathematical multipole refinement model can lead to *basis set overlap errors* in the evaluation of static molecular properties from X-ray diffraction data. For the molecular dipole moment, the error is large for several of the crystals tested in this study: DL-histidine, DL-proline, *p*-nitroaniline and *p*-amino-*p*'-nitrobiphenyl. Two restricted models are tested. In the first, atomic charges are constrained at  $\kappa$ -refinement values, while in the second  $\kappa'$ -values based on multipole refinements of theoretical ab-initio structure factors are used to reduce the flexibility of the model. Both models provide a more localized description of the pseudo atoms compared with an unrestricted refinement, but the  $\kappa'$ -restricted model gives a more consistent representation of the molecular dipole moments and superior agreement with the theoretical deformation density for DL-histidine. © 1999 Elsevier Science B.V. All rights reserved.

## 1. Introduction

As the methods for charge density (CD) analysis by X-ray diffraction have developed, the extraction of physical quantities from the results is increasingly relevant. Among the foremost of these are molecular electrostatic moments. In a comprehensive review of the data up to 1992 [1], Spackman has drawn attention to the reproducibility of the results and has summarized the methods for dipole moment determination.

The evidence on X-ray dipole moments points to an enhancement of the electrostatic moments of molecules in crystals, which can be attributed to induced polarization. This is supported by theoretical

calculations. According to results on urea [2], its molecular dipole moment of 5.15 D is increased to 7.04 D in the crystal. It is found that the hydrogen atoms become more positive, and the other atoms more negative, or less positive, upon crystallization, thus accounting for the increase in the dipole moment. A recent calculation on ice clusters [3] indicates that the dipole moment of water in ice IH is 3.09 D, a 67% increase over the isolated-molecule value. Similar results have been obtained for formamide [4,5].

The most straightforward way to derive dipole moments from X-ray diffraction data is by use of the aspherical atom (multipole) refinement [6]. Spackman and Byrom have shown that multipole refinement of the theoretical procrystal (i.e. a superposition of isolated molecules) X-ray data sets leads to a reasonable estimation (within ~10–15%) of the free molecule dipole moments [7], and further that the dipole moments can be retrieved by multipole

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refinement of theoretical structure factors of simple molecular crystals [5]. There are indications that the results may be more severely biased when very diffuse atom-centered functions are part of the basis set used in the refinement, as was the case, for example, for pyridinium dicyanomethylide [8]. Thus, there is a need for a critical evaluation of the procedures used. Such an evaluation is presented here.

## 2. Experimental data

Area detector (CCD) data on DL-histidine (HIS) (space group  $P2_1/c$ ) [9]; DL-proline  $\cdot$  H<sub>2</sub>O (PRO) (s.g.  $Pbca$ ) [10], *p*-nitroaniline (PNA) (s.g.  $P2_1/c$ ) [11] and *p*-amino *p*'-nitrobiphenyl (PANB) (s.g.  $Pca2_1$ ) [12] collected respectively at 110, 100, 20 and 20 K, the last two using synchrotron radiation,

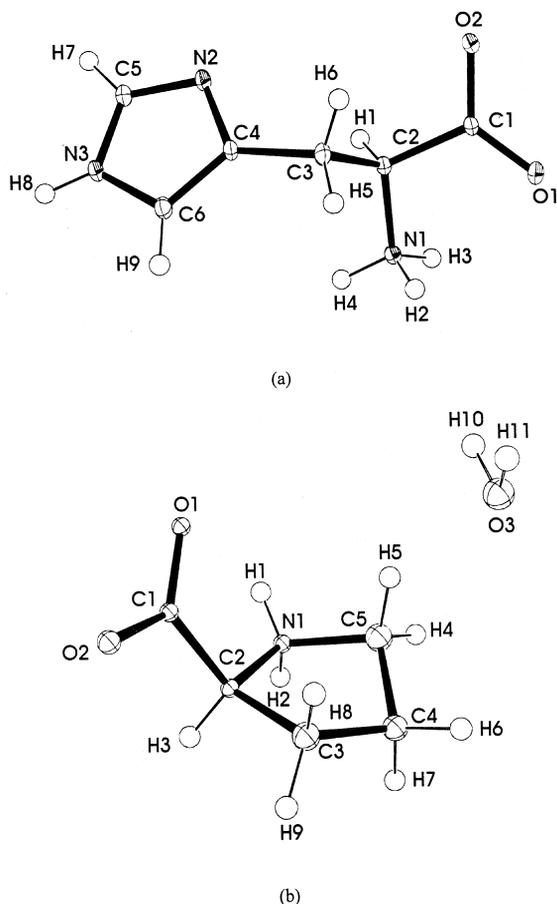


Fig. 1. Molecular structures of (a) histidine, (b) proline  $\cdot$  H<sub>2</sub>O, (c) *p*-nitroaniline and (d) *p*-amino-*p*'-nitrobiphenyl.

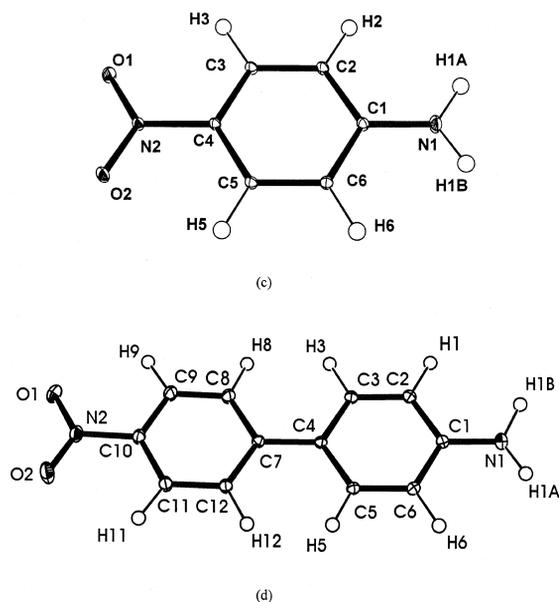


Fig. 1 (continued).

were used in the analysis. The molecular structures are presented in Fig. 1. All four crystal structures contain networks of relatively strong hydrogen bonded molecules, the shortest donor–acceptor distances being N–H(8)  $\cdots$  O(2) in HIS ( $d_{\text{H-O}} = 1.72$  Å), N–H(2)  $\cdots$  O(1) in PRO ( $d_{\text{H-O}} = 1.73$  Å), N–H(1B)  $\cdots$  O(2) in PNA ( $d_{\text{H-O}} = 2.02$  Å) and PANB ( $d_{\text{H-O}} = 1.92$  Å). In the first two cases, these short hydrogen bonds connect molecules related by a lattice translation of the crystal.

## 3. Multipole refinements

### 3.1. General

The Hansen–Coppens multipole formalism [6], as implemented in the XD program package [13], was used for the observed structure factor fitting. The formalism describes the static electron density in the crystal by a superposition of aspherical *pseudatoms*, the charge density of which is modeled by a nucleus-centered multipole expansion

$$\rho_k(\mathbf{r}) = P_c \rho_c(\mathbf{r}) + P_v \kappa^3 \hat{\rho}_v(\kappa \mathbf{r}) + \kappa'^3 \sum_{l=1}^4 R_l(\kappa' r) \sum_{m=1}^l P_{lm\pm} d_{lm\pm}(\mathbf{r}/r) \quad (1)$$

Table 1  
Molecular dipole moments (D)

| Molecule        | Theory <sup>a</sup> isolated molecule | Theory <sup>b</sup> crystal, trimer-dimer | UMM                   | CRMM     | KRMM      |
|-----------------|---------------------------------------|---|-----------------------|----------|-----------|
| DL-histidine    | 14.4                                  | 19.9 18.9                                 | 29.2(24) <sup>c</sup> | 17.5(17) | 17.2(17)  |
| Proline · water | 9.8                                   | 13.5 13.1                                 | 16.2(7)               | 12.2(6)  | 13.4(5)   |
| PNA             | 8.0                                   | 13.3                                      | 16.1 (9)              | 2.4 (7)  | 15.3(9)   |
| PANB            | 9.2                                   | 23.0                                      | 73.5(69)              | 37.3(29) | 43.4 (51) |

<sup>a</sup>SCF calculations on the isolated molecule at the B3LYP/6-311G\*\* level of theory.

<sup>b</sup>First value: from topological analysis [15] of the theoretical [16] HF crystal density calculated with a 6-21G\*\* basis set. Second value: difference between the dipole moments of the molecular trimer and dimer (B3LYP/6-311G\*\*, [17]), with molecules connected by the short hydrogen bond and related to each other by a simple translation along the lattice parameter of the crystal.

<sup>c</sup>A dipole moment of 16.6 D was obtained for histidine with the UMM model by separating the electron and nuclear charge centers of the hydrogen atoms [9]. However this approach has no clear physical justification.

Here  $\rho_c$  and  $\rho_v$  are spherically-averaged free-atom Hartree–Fock core and valence densities normalized to one electron;  $d_{lm\pm}$  are real spherical harmonic angular functions;  $R_l$  are normalized Slater-type radial functions and  $\kappa$  and  $\kappa'$  are dimensionless expansion–contraction parameters, which can be refined in the fitting procedure along with the populations  $P_v$  and  $P_{lm\pm}$ . HF densities are used for the spherically averaged core ( $\rho_c$ ) and valence ( $\rho_v$ ) shells [14]. The default conventional sets [6,13] of the  $R_l$  functions were used for all pseudoatoms.  $\kappa$ -parameters of the hydrogen atoms were fixed at a value of 1.2. The multipole expansion (1) was truncated at the octupole level ( $l_{\max} = 3$ ) for the non-hydrogen atoms and at the quadrupole level ( $l_{\max} = 2$ ) for the hydrogens. In order to decrease the number of variables in the refinement, chemical and local symmetry<sup>2</sup> constraints were applied. A molecular electroneutrality constraint<sup>3</sup> was applied in all refinements.

### 3.2. Unrestricted multipole refinement (UMM)

In the first stage, high-order refinements ( $\sin \theta/\lambda > 0.7 \text{ \AA}^{-1}$ ) [6] were performed to determine unbiased positional and thermal parameters for the non-

hydrogen atoms. Hydrogen positions were obtained by extending X–H distances to their standard neutron diffraction values (C–H 1.087 Å, N(NH<sub>3</sub>)–H 1.035 Å, N(imidazole)–H 1.053 Å, N(NH<sub>2</sub>)–H 1.010 Å). These distances were kept constant in subsequent refinements. In the next stage a  $\kappa$ -refinement [6] ( $P_{lm\pm} = 0$  in (1)) was performed with all structural parameters, except the isotropic thermal parameters of the hydrogens, being fixed at the previously refined values. In the final refinement all structural and electronic ( $P_v$ ,  $P_{lm\pm}$ ,  $\kappa$  and  $\kappa'$ ) parameters were refined, resulting in the agreement factors  $R(F)$  of 2.4% (HIS), 3.2% (PRO), 1.5% (PNA) and 1.7% (PNAB).

The UMM dipole moments (Table 1, column 4)<sup>4</sup>, show a large to very large enhancement of the dipole moment when compared with theoretical values for the isolated molecules, calculated with the GAUSSIAN94 program package [17] at the B3LYP/6-311G\*\* level (Table 1, column 2). Especially for PANB, the enhancement is unrealistic. Even for DL-histidine, an induced dipole moment of the magnitude found does not follow from either the theoretical calculations of the dipole moments of molecular dimers and trimers, or from HF/6-21G\*\* periodic

<sup>2</sup> For example, atoms in the carboxylate, nitrite, phenyl and imidazol groups were constrained to have mirror symmetry. Charge densities of all hydrogens were considered to have cylindrical symmetry along corresponding hydrogen-heavy atom bond.

<sup>3</sup> For DL-proline the constraint was applied to the asymmetric unit cell, including both a proline and a water molecule.

<sup>4</sup> There is a noticeable charge transfer between the proline and water molecules in the DL-proline crystal, which cannot be reproduced theoretically. To make comparison between theory and experiment possible, the DM of the electroneutral set of the proline and water molecules in the asymmetric unit cell is considered.

structure calculations (Table 1, column 3), performed with the CRYSTAL95 program [16].

Examination of the results of the UMM refinements indicates that some of the multipole density functions have quite low  $\kappa'$  values, and are thus quite diffuse. This leads to a lack of locality of the pseudoatoms, which overlap significantly with neighboring centers. This overlap affects the electrostatic moments, which are obtained by summation over the pseudoatom densities. The effect is discussed in some more detail below. Two less flexible, restricted multipole models (RMM), which provide more localized functions are tested in the following analysis.

### 3.3. Restricted multipole models

#### 3.3.1. The charge-restricted multipole model (CRMM)

There is no unique physically meaningful definition of the atomic charges<sup>5</sup>. In general, atomic charges are meaningful only for the specific property being described. The spherical  $\kappa$ -refinement model consisting of the first two terms on the right-hand side of Eq. (1), provides a quite localized description of the pseudo-atom densities. To retain this feature, in the CRMM model the valence monopole populations are kept fixed at the  $\kappa$ -refinement values. The model fits the experimental structure factors essentially as well as the UMM model (the  $R(F)$ -factors and residual densities changed within a few hundreds of a percent and at most  $\pm 0.05 \text{ e}/\text{\AA}^3$ , respectively), indicating the ambiguity in the unrestricted evaluation of the model parameters.

#### 3.3.2. The $\kappa'$ restricted multipole model (KRMM)

In the KRMM model the  $\kappa'$  parameters are fixed. They determine the radial extent of the aspherical deformation functions, which are among the least stable of the multipole refinement parameters. Especially for terminal oxygen atoms, values as low as 0.5 are sometimes obtained, which implies exceptionally diffuse deformation functions. Our theoretic

cal calculations on crystals of DL-histidine, DL-proline, PNA and PANB, and subsequent refinement of the theoretical structure factors, indicate much smaller, but consistent deviations from unity. They give average  $\kappa'$  values of 0.93(2) for C, 0.89(6) for N and 1.14(5) for the O pseudoatoms, the numbers in parentheses representing the standard deviations of each distribution. This qualitatively agrees with model C of Refs. [5] and [7], which showed oxygen atom deformation functions to be unchanged or contracted (i.e.  $\kappa' > 1$ ), and those for C to be expanded, while N atoms were found to be expanded in the theoretical crystal, and approximately unaffected in the procrystal. The  $\kappa'$  parameters from the calculations on real crystals do not correlate with electronegativity, but are likely more related to the nature of the bonding around each of the atoms, as they describe only the deformation functions. The advantage of using  $\kappa'$  values from the theoretical structure factors is that in this case correlation of the multipole parameters with the positional and thermal parameters in the refinement is eliminated. While at this stage the average  $\kappa'$  values given here should not be considered as an optimal set, they were used as constants in the current refinements. Results are listed in the last column of Table 1.

## 4. Discussion

The dipole moments according to the CRMM and KRMM models (Table 1, columns 5 and 6) are similar for all compounds but PNA, for which the CRMM model gives a value that is even lower than that of the isolated molecule. On the other hand, the KRMM model consistently produces results in reasonable agreement with theoretical values. Deformation density maps from the different refinements of DL-histidine (Fig. 2), illustrate the increased localization achieved in the KRMM refinement, especially in the case of the O(2) atom, which is the acceptor of the shortest hydrogen bond in the structures examined. The KRMM map is satisfyingly close to the theoretical crystal deformation density reproduced in Fig. 2d.

The failure of the unrestricted (UMM) procedure requires further comment. In the current case of crystals with relatively strong hydrogen bonds, the

<sup>5</sup> The theory of atoms in molecules [18] can be considered to provide the most fundamental definition of the atomic charge. However, this method can not be used a priori to interpret a set of diffraction data.

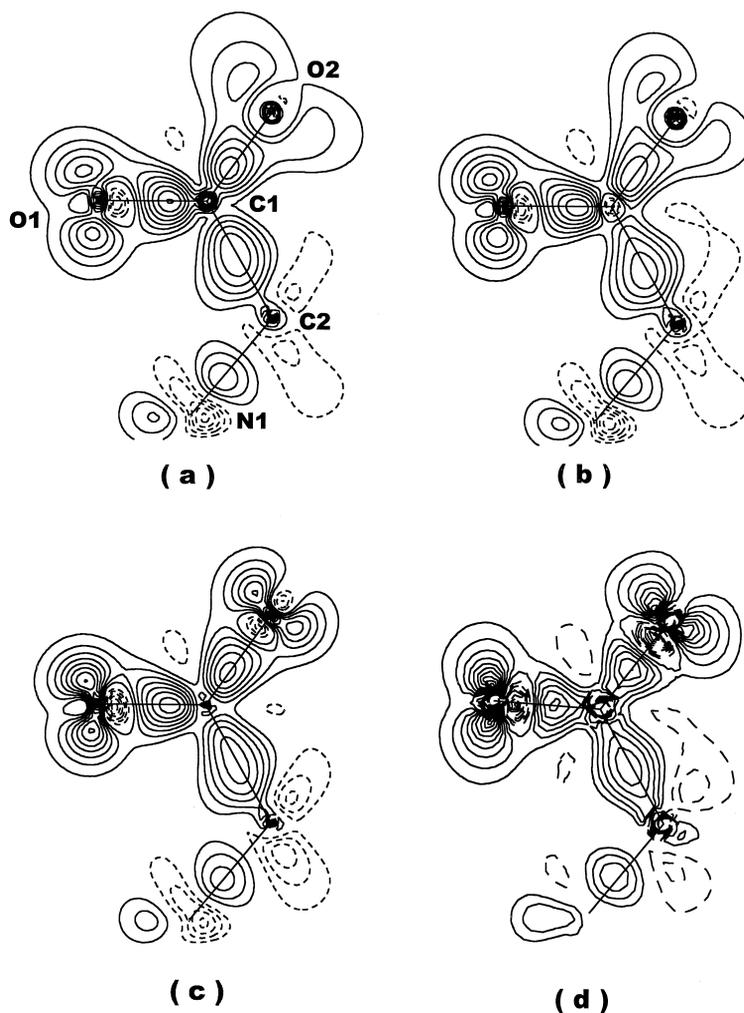


Fig. 2. Deformation density in the COO plane of DL-histidine. Contours at  $0.1 \text{ e}\text{\AA}^{-3}$ , zero contour omitted, negative contour broken. a) according to the UMM model, b) according to the CRMM model, c) according to the KRMM model, d) theoretical deformation density in the crystal.

deformation functions on the H-bond acceptor oxygen atom, if unrestricted, can partially describe the hydrogen atom deformation density, thus leading to an ambiguity in the partitioning of crystal space, which is crucial for the evaluation of molecular properties.

In the multipole model the lone pair densities on the oxygen atoms are essentially described by a combination of dipole,  $D1+$ , (with the positive lobe directed away from the  $\sigma$ -bond) and quadrupole,  $Q22+$ , (with a positive lobe perpendicular to the  $\sigma$ -bond) functions. When these are enhanced, oxy-

gen-centered density is removed from the O–C or O–N bonds. This density is compensated for by increased population of the  $sp^2$ -type deformation functions on the C and N atoms, respectively. In the UMM refinement the C and N atoms of the carboxyl and nitro groups become strongly negative, in contradiction to accepted chemical concepts. The charge migration can occur because the mathematical approach of fitting the multipole model does not take into account quantum-mechanical requirements, such as the Pauli exclusion principle and energy minimization criteria.

A relatively small charge migration between the donor and acceptor groups in the intermolecular H-bonds can have a large effect on the molecular dipole moment when the donor and acceptor groups are well separated intramolecularly, as is the case for many of the H-bonds in the four test structures.

In conclusion, the lack of the intrinsic physical constraints in the multipole refinement of the charge density from the X-ray diffraction combined with the overlap of the basis sets employed affects the evaluation of molecular properties like electrostatic moments, inter- and intramolecular charge transfer and intermolecular electrostatic interactions. The experimental basis set overlap error is greatly reduced by restricting the multipole charge density model. We obtain the most consistent set of dipole moments by using a set of  $\kappa'$  values based on multipole refinement of static crystal-theoretical structure factors. Discrepancies with theory remain, in particular for PANB, for which the experimental value obtained with the restricted models is considerably larger than that from theory. It is possible that this difference is related to the circumstance that PANB is the only acentric structure in this analysis.

Further analysis will include integration of the experimental model density within the topologically defined molecular boundary [18] to give additional information on the observed differences between experiment and theory, which may be due to shortcomings in the HF calculation, or to remaining inadequacies of the model. Such an analysis is currently being undertaken.

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