s1.m3.p4 **Charge Density Studies of Biological Macromolecules : beyond the Spherical Atom Model.** Benoît Guillot, Christian Jelsch, Angélique Lagoutte, Chethampadi Gopi Mohan, Virginie Pichon-Pesme, Eric Chabriere and Claude Lecomte, *LCM3B, CNRS, Faculté des Sciences, Université Henri Poincaré, Nancy 1, BP 239, 54506 Vandoeuvre-les-Nancy, France.*
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Keywords: Proteins; Charge Density; Refinement

At subatomic resolution, electron density reveals fine details related to charge transfer and deformation of the valence electron density due to chemical bonding and intermolecular interactions. A spherical atom model of electron density (IAM model) does not allow to take into account these features in the refinement. However, in small molecules charge density studies, the Hansen & Coppens [1] multipolar model is commonly used. It allows the asphericity of the atomic electron density to be parameterized and quantified against experimental data. With increasing number of biological macromolecules structures solved at subatomic resolution, it becomes necessary to extend charge density studies methods from small molecules to larger systems. Here we present the software MoPro [2] which is dedicated to structural and charge density refinement of such structures. MoPro implements spherical and multipolar atomic models, and combines methods usually applied both in biological macromolecules and in small compounds crystallography fields. We will also present some applications of these methods to several macromolecular systems, including 0.66Å resolution Human Aldose Reductase [3,4] and 0.62Å resolution RD1 Antifreeze protein [5].

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s1.m3.p5 **Hierarchical Description of Protein Structure Fragments obtained from Analyses of Promolecular Electron Density Distributions.** Laurence Leherte, *Facultés Universitaires Notre-Dame de la Paix, Namur, Belgium. E-mail: laurence.leherte@fundp.ac.be*

Keywords: Protein Fragments; Promolecular Electron Density; Hierarchical Structure

A theoretical method applied to describe protein structures in terms of hierarchically related substructures is presented [1]. The approach is based on the location of local maxima (peaks) in promolecular electron density (ED) distributions established at continuously varying smoothing degrees t. The local maxima are determined using a hierarchical clustering algorithm [2] wherein peaks obtained at a given level are used as starting points for discovering peaks at the next higher smoothing level through gradient trajectories of the ED distribution. The use of such an approach allows to assign molecular fragments to peaks, at any smoothing level. Promolecular ED distributions are analytically represented using either the Promolecular Atom Shell Approximation (PASA) [3] or Cromer-Mann-based coefficients as available in the program XTAL [4]. For an atom *a*, the ED is given by:

$$\rho_{a,t}(\mathbf{r}-\mathbf{R}_a)= Z_a \sum_{i=1}^{4or5} w_{a,i}\left(\frac{\beta_{a,i}}{\pi}\right)^{3/2}(1+4\beta_{a,i}t)^{-3/2}\, e^{\frac{-\beta_{a,i}|\mathbf{r}-\mathbf{R}_a|^2}{1+4\beta_{a,i}t}}$$

and the corresponding scattering factor is:

$$f(s) = Z_a \sum_{i=1}^{4or5} w_{a,i} e^{-\frac{4\pi^2(1+\beta_{a,i}t)s^2}{\beta_{a,i}}} \qquad \text{where } s = \sin\theta/\lambda$$

In such expressions, t is equivalent to $u/2$, where u is the overall isotropic mean square atomic displacement.

Analyses of decomposition patterns show that the amino-acid residues have similar decomposition structure regardless of their position in the protein sequence, the protein conformation, and the influence of the crystal packing. At the particular value of t = 1.5 bohr^2, fragments are similar to the groups of atoms used by Guo *et al.* [5] in their globbic description of a protein structure. An interest of such decomposition results lies in the possible link with ED map interpretation programs based on the use of protein fragments databases.

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